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Update on the Management of

HEAD & NECK PARAGANGLIOMAS

ABSTRACT BOOK

GRUPPO OTOLOGICO

FONDAZIONE MARIO SANNA ONLUS

Our current understanding of paraganglioma with a focus on the head and neck region

Karel Pacak

Section of Medical Neuroendocrinology, Eunice Kennedy Shriver NICHD, NIH, Bethesda, MD 20817, USA

Paragangliomas (PGLs) are classified as neuroendocrine tumors because they are derived from neural crest cells and produce (synthesize) catecholamines that are either released from a tumor or metabolized in tumor cytoplasm to metanephrines and 3-methoxytyramine. Based on the newest WHO classification: a/ pheochromocytomas are now classified as intra-adrenal PGLs; b/ the term of nodular adrenal hyperplasia was dropped and replaced by “micro-pheochromocytoma”; c/ now all PGLs are considered potentially metastatic since they may metastasize years after complete surgical resection; and d/ the term metastatic is defined by disease presence in bones or lymph nodes only. Furthermore, the diagnosis of these tumors is based on the measurement of catecholamine metabolites not catecholamines themselves.

Currently, there are only some specific clinical signs and symptoms that are considered statistically significant between those who have or do not have paraganglioma (palpitations/sweating/tremor/weight-loss/constipation/nausea). Hypertension alone (without specific signs and symptoms of catecholamine excess) is not considered indicative of these tumors. In high-risk patients (e.g., those presenting with adrenal incidentaloma, genetic predisposition for PGL, etc.), the measurement of plasma metanephrines and 3-methoxytyramine offer better diagnostic performance than urine measurements. For patients who have a low likelihood of having these tumors (e.g., those presenting with only symptoms and signs of catecholamine excess) either plasma or urine metanephrines can be measured. The localization of these tumors is based on anatomic and functional imaging with newer findings demonstrating that functional imaging may be cluster-specific (e.g., dependent on the type of genetic mutation); specifically, that the the use of Ga- or Cu-DOTATATE PET/CT is most effective for metastatic, head and neck as well as succinate dehydrogenase pathogenic variant-related PGLs. At present, the use of Lu-DOTATATE, as well as I-MIBG (high-specific-activity) are instrumental radiotherapeutic agents; that have a disease control rate of approximately 90%. Based on the latest data, surveillance improves outcomes of patients with either genetic predisposition or previous diagnosis and can “cure” paraganglioma.

Head and neck PGLs (HNPGLs) rarely present with clinical symptoms and signs of catecholamine excess because only about 3.7-5% of them produce norepinephrine. Nevertheless, up to 30% of HNPGLs produce and release 3-methoxytyramine into circulation. About 40-56% of these tumors are hereditary, most commonly due to succinate dehydrogenase subunits A-D pathogenic variants (with SDHD being the most common). However, there is an exception for jugulotympanic PGLs that are hereditary in only 24% of patients and are more commonly found in women. Based on current evaluation guidelines related to these tumors: a/ MRI with angiography should be performed for HNPGL staging, since it is the most sensitive radiological technique; b/ regarding functional imaging studies: Ga-DOTATATE or F-FDOPA PET/CT should be utilized for the detection of HNPGLs; c/ a “watch and wait” approach is recommended to characterize tumor behavior of HNPGLs because they are often very slowly growing tumors (exceptions are tumors with an urgent indication for surgery); d/ restraint should be exercised for the surgical resection of vagal PGLs, due to a high risk for vocal cord paralysis; e/ primary lesions with distant metastasis should be operated on only in some patients, usually with palliative intent; f/ preoperative angiography is recommended for tumors larger than 4 cm; and g/ local therapeutic radiation is recommended for radiologically progressive/symptomatic HNPGLs, especially in older patients with multiple comorbidities.

Furthermore, local therapeutic radiation is also recommended for post-surgical residual or recurrent progressive HNPGL. Most recent data relating to succinate dehydrogenase mutated HNPGLs (especially those related to SDHB pathogenic variants) reveal that these tumors are not necessarily more metastatic compared to those that arise sporadically (without an identified pathogenic variant). The highest rate of metastatic disease is found in carotid body PGLs, and the lowest is found in jugulotympanic tumors.

In summary, recent advances in biochemical diagnosis using plasma 3-methoxytyramine, novel functional imaging modalities (now also using Cu-DOTATATE PET/CT) and promising novel targeted radiotherapies using alpha-emitters and hypoxia-inducible factor inhibitors, represent promising venues in diagnosis and management of these tumors including HNPGLs.

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Epidemiology of HNPGLs: the paraganglioma valley story, revisited

Giuseppe Opocher[1], Francesca Schiavi[2], Serena Dematté[3], Maria Enrica Cecchini[3], Massimiliano Ferrara[2], Stefania Zovato[2]

[1]*University of Padova*

[2]*Veneto Institute of Oncology, Padova*

[3]*Santa Chiara Trento Hospital*

Based on the anecdotal evidence of high incidence of type 1 paraganglioma syndrome in Trentino we had identified and characterized a very large founder effect for the SDHD c.341G>C p.Y114C mutation and characterized a huge number of patients with paraganglioma syndrome type 1. (J Clin Endocrinol Metab 2012 Apr;97(4):E637-41). The reason for that is a 600 years old founder effect occurred in a country which was for many years, a geographic ed linguistic isolate. Actually the allele prevalence estimation is 1,5 % of the general population of the area, predicting a large number of carriers and of at risk individuals. Following this discovery we have continued to collect samples and clinical data of people resident in a geographic area of the valley “alta valsugana”. We have so far analyzed 734 individuals of which 409 resulted carriers of the SDHD c.341G>C p.Y114C founder mutation. In 244 of them the mutation was inherited from the father and therefore were considered at risk for developing a head and neck paraganglioma. We received a complete clinical data of 167individuals. The largely prevalent phenotype was the multiple carotid body tumor. We detected 178 carotid body tumors and in 107 individuals the carotid body tumor was bilateral. Vagal paraganglioma was present in 25 while the jugulotympanic paraganglioma was present in 35 individuals. Thoracic paraganglioma was detected in 6, while pheochromocytoma only in 1 case. Few had malignant paraganglioma. Penetrance was confirmed high. In conclusion, tanks to the continuous collection of samples and carriers identification the paraganglioma valley story is still an open story and a very large number of individuals with ahead and neck paraganglioma had been characterizes, mainly with benign bilateral carotid body tumor.

Genetics in the diagnosis and Management of Head and Neck Paragangliomas

Francesca Schiavi

UOSD Familial Cancer Clinic, Veneto Institute of Oncology IRCCS, Padova, Italy

Pheochromocytomas (PCCs) and Paragangliomas (PGLs), all together called PPGLs, are rare neuroendocrine tumors that arise from specialized cells called paraganglia. PCCs develop in the adrenal medulla, whereas PGLs arise from sympathetic and parasympathetic paraganglia.

Genetics plays a significant role in the development of PPGLs. Several hereditary syndromes have been associated with an increased risk of developing these tumors and nowadays at least 20 susceptibility genes have been identified. Up to 40% of PPGLs are associated with inherited mutations in these driver genes. These tumors carry the highest known heritability rate of any human neoplasm. The most common driver genes involved in the development of PGLs derived parasympathetic paraganglia in head and neck area are succinate dehydrogenase (SDH) genes. Pathogenic variants in the genes encoding the four subunits of the mitochondrial enzyme SDH (SDHA, SDHB, SDHC, SDHD) and its assembling factor SDHAF2, have been identified in a significant proportion of head and neck PGLs.

Clinical manifestations, risk of malignancy and penetrance are influenced by the mutated gene, as is the pattern of inheritance: autosomal dominant for all SDHx genes, modified by maternal imprinting for SDHD and SDHAF2 genes. Genetic testing is available to identify hereditary pathogenic sequence variants associated with head and neck PGLs. This information can be valuable for diagnosing affected individuals, assessing the risk for tumor development in at-risk family members, and guiding appropriate surveillance and management strategies.

Due to the high heritability, genetic testing has been recommended in all patients with PPGLs, and genetic counseling is mandatory for individuals with a personal or family history suggestive of hereditary PGL syndromes. Patients with genetic PPGLs should be treated in specialized centers dedicated to the diagnosis, treatment, and surveillance of this rare neoplasm.

Impact of genetics on the Management of Paraganglioma patients and their families

Alfonso Massimiliano Ferrara

Familial Cancer Unit, Istituto Oncologico Veneto IOV IRCCS, Padova, Italy

Regardless of site of origin, about 40% of paraganglioma (PGL) patients carry a germline mutation in one of the susceptibility genes reported so far, including, in descending order of frequency: *SDHB, SDHD, SDHC, SDHA, SDHAF2, FH, MDH2, VHL, RET, HIF2A,* and *GOT2 EGLN1, NF1, TMEM127, MAX, SLC25A11,* and *DNMT3A*. Current evidence supports genetic testing as a key component of the management of PGL patients and their families, in order to guide follow-up surveillance and treatment selection. In fact, genotype-driven management allows to identify: *a)* subjects predisposed to multifocal/recurrent disease (*i.e.*, *SDHx, EPAS1*, and *FH* mutation carriers), metastatic PGL (*i.e.*, *SDHB, MAX*, and *FH* mutation carriers) and other tumor types (*i.e*., SNC hemangioblastomas, retinal angiomas, endolymphatic sac tumors, renal cell carcinomas in *VHL* carriers, peripheral nerve sheath tumors, gliomas, pilocytic astrocytomas, duodenal neuroendocrine tumors in *NF1* carriers, medullary thyroid carcinomas in *RET* carriers, etc); *b)* subjects carrying mutations associated with lower disease risk, as in the case of maternally-inherited *SDHD* mutations, where PGL seems to occur rarely (≤5%); *c*) patients who may benefit from specific treatments, such as temozolomide, effective against metastatic *SDHB*-related PGL. These examples demonstrate that genetics is paramount to tailor the diagnosis, treatment, and follow-up strategies of PGL patients. Strict adherence to the international recommendations on the genotyping of susceptibility genes is mandatory in all PGL patients, including cases with disease presenting in the head and neck region.

Single-cell Transcriptomic and Whole-exome Sequencing Atlas of Jugulo-tympanic Paragangliomas

WANG Shengming, ZHANG Boya, Dongzhen YU, CHEN Zhengnong

Otolaryngology Institute of Shanghai Jiao Tong University, Department of Otolaryngology Head and Neck Surgery, Shanghai Key Laboratory of Sleep Disordered Breathing, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai

Objectives: Jugulo-tympanic paragangliomas (JTPGL) are tumors that develop from sympathetic or parasympathetic ganglia in the lateral cranial base and are the second most common head and neck paragangliomas. Though there has been research on the cellular components and mechanisms of paragangliomas, the sophisticated transcriptomic atlas is still lacking for further investigation in JTPGL. Here we applied single-cell RNA sequencing (scRNA-seq) along with whole-exome sequencing (WES) to depict the atlas with detailed features to reveal the heterogeneity in the JTPGL.

Methods: scRNA-seq and WES were performed on four JTPGL samples. With the help of bioinformatics tools, annotation and clustering, copy number variation, pseudotime analysis, cell-cell communication, and regulatory network inference were carried out to depict the atlas. Public data of carotid body paraganglioma and vestibular schwannoma were collected, and comparisons were made to reveal the heterogeneity and characteristics of JTPGL.

Results:

- After quality control, transcriptomic of 17393 cells were collected and showed that JTPGL mainly consisted of endothelial cells, epithelial cells, glial cells, mast cells, monocytes/macrocytes, T cells, neuroendocrine cells, and fibroblasts, with fibroblast being the main component (41.48%).
- Several gene mutations were observed in all JTPGL samples, while only 2 showed the conventional SDHx mutations.
- Both WES and scRNA-seq postulated the occurrence of copy number variation in JTPGL, with fibroblast that had a high possibility to have this type of somatic genetic alteration.
- Fibroblasts had high heterogeneity within JTPGL and could be further clustered as myofibroblasts and inflammatory fibroblasts. Compared with other lateral skull base tumors, myofibroblasts were the distinct subtype in JTPGL, while inflammatory fibroblasts shared some expression features with fibroblasts in vestibular schwannoma.
- Myofibroblasts had unique features in pseudotime analysis and regulatory network inference. Some transcription factors that had high activity in myofibroblasts, like TWIST1 and NFATC4, had been reported to be related to tumor immunomodulation.
- Cell-cell communication analysis showed that fibroblasts had the most robust interaction with other cell types. Pathways like KIT-KITLG between mast cells and fibroblasts and PDGF between endothelial cells and fibroblasts were first postulated by scRNA-seq and verified by immunofluorescence in JTPGL.

Conclusions: These results offered the foundation for the protumor mechanism of fibroblasts in the JTPTL microenvironment. They deepened the knowledge of the role of fibroblasts in tumorigenesis and provided an essential resource for the future intervention of JTPGL.

Destabilization of the mitochondrial proton pumps and mitochondrial remodeling distinguishes head and neck paraganglioma from parasympathetic nerve

Diana Liberata Esposito[1,2], Sara Pagotto[1], Rossano Lattanzio[1,2], Silvia Perconti[1], Simone De Fabritiis[1], Isabella D'Amario[1,3], Giuseppe Fancello[4], Gianluca Piras[4], Michele Vacca[5], Simone Vespa[1], Elena Sofia Scialis[6], Francesca Schiavi[7], Elisa Taschin[7], Mario Failli[8], Francesco Napolitano[9], Adriano Zangrandi[10], Alberto Schena[10], Carlo Terenzio Paties[10], Mattia Russel Pantalone[11], Cecilia Söderberg Nauclér[11], Fabio Verginelli[1,12], Mario Sanna[4], Lavinia Vittoria Lotti[5], Renato Mariani-Costantini[1]

[1]*Center for Advanced Studies and Technology (CAST), "G. d'Annunzio" University, Chieti, Italy (rmc@unich.it, desposit@unich.it)*
[2]*Department of Innovative Technologies in Medicine & Dentistry, "G. D'Annunzio" University, Chieti, Italy*
[3]*Department of Medicine and Aging Science, "G. D'Annunzio" University, Chieti, Italy*
[4]*Otology and Skull Base Unit, Gruppo Otologico, Piacenza, Italy*
[5]*Interdisciplinary Department of Medicine, Università degli Studi di Bari "Aldo Moro", Bari, Italy*
[6]*Laboratory of Ultrastructural Biopathology, Department of Experimental Medicine, "La Sapienza" University of Rome, Rome, Italy*
[7]*Familial Cancer Clinic and Oncoendocrinology, Veneto Institute of Oncology, IRCCS, Padua, Italy*
[8]*Department of Chemical, Materials and Industrial Production Engineering, University of Naples Federico II, 80125 Naples, Italy*
[9]*Computer, Electrical and Mathematical Sciences and Engineering Division (CEMSE), Computational Bioscience Research Center (CBRC), King Abdullah University of Science and Technology (KAUST), Thuwal, Saudi Arabia.*
[10]*Department of Oncology-Hematology, Service of Anatomic Pathology, Guglielmo da Saliceto Hospital, Via Taverna 49, 29100 Piacenza, Italy*
[11]*Cell and Molecular Immunology, Experimental Cardiovascular Unit, Departments of Medicine and Neurology, Center for Molecular Medicine, Karolinska Institute SE-171 76, Stockholm, Sweden*
[12]*Department of Pharmacy, "G. D'Annunzio" University, Chieti, Italy*

Using transcriptional profiling we highlighted the top genes and pathways differentiating head and neck paraganglioma (HNPGL) from Jacobson's nerve (JN), site of temporal bone PGL, next, targeting proteins, we investigated the morpho-functional and biochemical correlates in *SDHx/TMEM127*-characterized HNPGLs, derived xenografts (PDXs) and cells. KEGG enrichment analysis based on the 859 genes upregulated in the HNPGLs evidenced, in descending order, oxidative phosphorylation, estrogen receptor signaling, mt dysfunction, granzyme A signaling, telomerase signaling, neutrophil extracellular trap signaling, sirtuin signaling, Gαs signaling, and CREB signaling in neurons as top ten pathways. Most of these pathways converged on the mitochondrial (mt) proton pumps [complexes I (CI), III, and IV], and ATP synthase (CV).

The topmost ten genes were *DLK1*, *CHGB*, *COL22A1, SLC35D3*, *RGS4*, *NDUFA4L2*, *INSM1*, *RGS5, ADM*, and *HAND2-AS1,* implicated in hypoxia adaptation, neuroendocrine differentiation, vasculo-angiogenesis, and adipogenesis. Although not among the top ten, *EPAS1/HIF2A* and *COX4I2* were significantly overexpressed. The ten most discriminative pathways for the 1052 downregulated genes comprised members of the NAD+/NADP+-dependent *ADH*/*ALDH* gene superfamilies, suggesting NAD(H)/NADP(H) redox imbalance due to mt dysfunction. Targeted studies confirmed HIF2A as main HIFA isoform in HNPGLs and PDXs. RGS4 and RGS5 protein upregulation suggested cooperation between the HIF pathway and the post-translational cysteamine (2-aminoethanethiol) dioxygenase (ADO) mt O2-sensing system. Chief HNPGL cells always presented striking increases in mt mass, mt respiratory surface, and mt-associated ER, combined with the expression of proteins driving mt fusion, cristae biogenesis, and permeability transition pore closure. The mitochondria presented swelling and cristolysis in all HNPGL and PDX cells.

These mt aberrations were cleared in derived cultures, suggesting dependence on the *in vivo* microenvironment. NDUFA4L2 and COX4I2, that cooperate in downregulating CI, were intrinsic HNPGL OXPHOS markers. WB analysis of the labile CI-V subunits highlighted post-transcriptional CI/CIII-CV loss in a substantial HNPGL subset, regardless of *SDHx* status, while CII loss, never complete, occurred only in *SDHx*-mutated tumors. Comprehensive scanning of the mt genome (44 HNPGLs) ruled out a significant role of somatic mt DNA mutations**.** Thus, comprehensive remodeling of the mt electron transfer chain, mostly unrelated to mutational mechanisms, and massive reshaping of the mt network, adaptive to persistent stress, are key features that distinguish HNPGLs from JNs. This might drive tissue-specific tumorigenesis in head and neck paraganglia.

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Clinical management of head and neck paraganglioma patients and their families: the view of an endocrinologist

Massimo Mannelli, Letizia Canu

Endocrinology Unit - Dept. of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence Italy

Head-Neck paragangliomas (HNPGL) are parasympathetic tumors located in the paraganglia of the head and neck region. At variance with sympathetic paragangliomas and pheochromocytomas (PPGL), they are generally not functioning and their hormonal activity, if any, is limited to dopamine release. Therefore, they are silent on the endocrinological ground and their clinical picture is characterized by the occurrence of a neck mass or the neurological failure due to the compression of cranial nerves. Sometimes, they are incidentally diagnosed at neck sonography or CT or MRI.

HNPGL can be sporadic or genetically determined. A positive family history or the occurrence of multiple HNPGL (synchronous or metachronous) are strong predictors of a genetic form which, in our experience, is present also in 18.8% of patients apparently classified as sporadic. Genetic analysis is the cornerstone of the clinical management of the patients and must be performed in each patient affected by HNPGL. Familial forms of HNPGL mostly depend on a germinal mutation in one of the genes encoding the subunits (A, B, C, D, A2F) of the mitochondrial succinate-dehydrogenase (SDH), causing the occurrence of familial paragangliomatosis 1 to 5. By far, the most common syndromes are PGL1, caused by germ-line mutation in the *SDHD* gene, and PGL4 caused by mutation in the *SDHB* gene. PGL1 is characterized by the occurrence of multiple HNPGL, often associated with PPGL. It presents a high penetrance (about 70% at 65 yrs) and a lower biological aggressiveness (about 5 % metastatic).

Conversely, PGL4 is mostly characterized by the presence of abdominal PPGL, sometimes associated to HNPGL, by a lower penetrance and a high occurrence of metastatic disease (about 40%). More rarely HNPGL are associated to germ-line mutations of *SDHC*, *SDHA*, *SDHA2F* genes and very rarely to mutations in *VHL* (von Hippel Lindau) and *FH* (fumarate hydratase) genes. *SDHD* and *SDHA2F* genes are maternally imprinted (silenced) and therefore the clinical picture develops only in case of paternal inheritance.

Patients affected by a genetic form, as well as the family members found to be carriers of the mutation, must undergo a lifelong follow-up for the early diagnosis of other HNPGL and, most important, for the occurrence of PPGL. The screening as well as the clinical management of these endocrine tumors is generally assigned to the endocrinologists and the diagnosis is based on plasma or urinary differential metanephrine assay. The association of PPGL and HNPGL in the same syndromes has compelled the endocrinologists to be involved in the management of patients traditionally not included in their field of competence as those affected by HNPGL. The management of patients with HNPGL is still largely debated presenting many options such as surgery, radiosurgery, embolization, radiometabolic or medical therapy, wait and see. The decision is almost always difficult depending on many factors as whether the HNPGL is sporadic or familial, single or multiple, metastatic or not, small or large in size, where it is located and the patient's age. The management has to be tailored on the single patient and decided by a multidisciplinary team.

Distributive pattern of SDHD mutation amongst Czech patients with HNPGLs

Anasuya Guha[1], Ales Vicha[2], Tomas Zelinka[3], Martin Kana[4], Zdenek Musil[5], Karel Pacak[6], Jan Betka[4], Martin Chovanec[1], Jan Plzak[4], Jan Boucek[4]

[1]Department of Otorhinolaryngology, Charles University, 3rd Faculty of Medicine and University Hospital Kralovske Vinohrady, Prague, Czech Republic.
[2]Department of Pediatric Hematology and Oncology, Charles University, 2nd Faculty of Medicine and University Hospital Motol, Prague, Czech Republic.
[3]Department of Internal Medicine, Charles University, 1st Faculty of Medicine and General University Hospital, Prague, Czech Republic.
[4]Department of Otorhinolaryngology and Head and Neck Surgery, Charles University, 1st Faculty of Medicine and University Hospital Motol, Prague, Czech Republic.
[5]Department of Biology and Medical Genetics, Charles University, 1st Faculty of Medicine and General University Hospital, Prague, Czech Republic.
[6]Section of Medical Neuroendocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, USA.

Introduction:

Head and neck paragangliomas (HNPGLs) are rare neuroendocrine tumors, of mostly benign nature. Amongst gene mutations that lead to hereditary paragangliomas, Succinate Dehydrogenase Subunit D (*SDHD*) is the most mutated gene in HNPGLs. Germline mutations also occur in around 30% of HNPGLs that are regarded sporadic due to the absence of a family history ("occult familial" cases). Our aim was to evaluate the frequency and pattern of *SDHD* germline mutation in Czech patients with HNPGLs.

Materials and Methods:

A total of 105 patients with HNPGLs were referred to the Otorhinolaryngology departments of 2 tertiary centers between 2006 – 2021. All underwent complex diagnostic work-up and were recommended to undergo genetic examination.

Results:

Eighty patients of 13-76 years completed all including genetic analysis. Carotid body tumor was the most frequently diagnosed tumor. Multiple PGLs were seen in 15 patients; around 60% were males. The *SDHD* mutation was found only in 12% of Czech patients, where 78% were occult familial cases. The mutation showed a higher affiliation for patients ≤ 40 years old with multiple tumors.

Conclusions:

A similar *SDHD* mutation variant was shared amongst unrelated patients but a founder effect could not be established. HNPGLs in Czech patients has a lower affinity for *SDHD* thus confirming that the pattern of *SDHD* mutation distribution differed from most studies worldwide.

Key words: HNPGL; CBPGL; paraganglioma syndrome; genetic mutation; *SDHD* gene

Impact of Succinate dehydrogenase (SDH) gene mutation in Head and Neck Paraganglioma (HNPGL)

Hikari Shimoda[1], Jun Yokoi[1], Natsumi Uehara[1], Takeshi Fujita[1], Megumi Kitayama[2], Kiyoto Shiga[3], Tatsuo Matsunaga[4], Hiroyuki Ozawa[5], Akinobu Kakigi[1], Ken-ichi Nibu[1]

[1]Department of Otolaryngology, Kobe University School of Medicine, Hyogo, Japan
[2]Clinical Study Support Center, Data Center Department, Wakayama Medical University Hospital, Wakayama, Japan
[3]Department of Head & Neck Surgery, Iwate Medical University School of Medicine, Morioka, Iwate, Japan
[4]Division of Hearing and Balance Research, National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Center, Tokyo, Japan
[5]Department of Otolaryngology, Head and Neck Surgery, Keio University School of Medicine, Tokyo, Japan

Background:

Head and neck paragangliomas (HNPGL) are arising from neuroendocrine ganglia originating from the parasympathetic ganglia. Carotid body tumor (CBT) is the most common followed by vagal paraganglioma and Glomus tumor in head and neck. Familial paraganglioma syndrome is known to occur in head and neck, and recent advances in molecular genomics have revealed that mutations in the succinate dehydrogenase (SDH) gene, an enzyme complex present in the mitochondrial membrane, are involved in nearly 40% of HNPGLs. The purpose of this study was to clarify the clinical features and therapeutic outcomes of HNPGLs in Japan based on the genetic analysis of SDHs.

Patients and Methods:

Forty-four consecutive patients with head and neck paraganglioma who visited Department of Otolaryngology-Head and Neck Surgery, Kobe University Hospital from November 1998 to January 2023 were included in the study. Data on gender, age, duration of disease, family history, Shamblin classification (for CBT), treatment (surgery, radiation, watchful follow-up without treatment), comorbidity of other PGLs, multiple lesions, functional tumor, metastasis, and status of SDH gene were obtained from medical records. In surgically treated patients, immunohistochemical staining (ICH) for SDHB was also performed.

Results:

In 44 patients, there were 21 males and 23 females. The mean age was 50.7 years old ranging from 11 to 78. Thirty-nine patients had CBT, two patients had glomus tumor (tympanic type), two patients had vagal paraganglioma, and one patient had sympathetic paraganglioma. Eight out of 39 patients with CBT had bilateral disease, and one of the two patients with glomus tumor had CBT. According to the Shamblin classification, there were 3 sides in group I, 21 sides in group II, and 24 sides in group III. Thirteen patients underwent surgical extirpation, and one of them had postoperative irradiation. Fifteen patients underwent irradiation alone, and 14 patients were followed up without treatment. Germline pathogenic variants of the gene encoding SDH were detected in 19 of 39 patients (48.7%). SDHB variants were detected in 10 patients and SDHD variants in 9 patients. Two of the 10 patients with SDHB gene mutation showed metastasis (1 cervical lymph node metastasis, and 1 distant metastasis). Four of the 9 patients with SDHD mutations had bilateral CBT. In addition, one of these 4 patients had pheochromocytoma. Familial paraganglioma was observed in one patient with SDHB mutation (CBT) and three patients with SDHD mutation (1 glomus tumor, 1 paraganglioma of the mediastinum, and 1 unknown details).

Conclusions: The present results suggest the usefulness of genetic testing for SDH in the management and genetic counseling of the patients with HNPGLs. Genetic testing for germline mutations of SDH should be recommended for all patients with HNPGs.

Head and Neck Paragangliomas: Overview of Institutional Experience

Yonghong Huan, MD, Jason Brant, MD, Bonita Bennett, BSN, Maria Bonanni, NP, Tanaya Oliphant, Swar Vimawala, MD, Ayelet Rubenstein, Alex Graboyes, Debbie Cohen, MD*

University of Pennsylvania, 3400 Spruce St, Philadelphia, PA 19104

Paragangliomas of head and neck and skull base (HNPPGLs) are rare, mostly slow growing and hypervascular tumors arising from neural crest-derived cell clusters located along jugular foramen, middle ear, carotid bifurcation and vagal nerve. There is a high rate of genetic mutation in HNPPGLs, with up to 40% with germline mutations and 30% somatic mutations. We conducted a comprehensive retrospective review of our institutional experience with clinical evaluation and management of HNPPGLs. Among our cohort of 174 patients with HNPPGLs diagnosed from 1981 to 2023, 116 (67%) were women. The mean age at the first tumor diagnosis was 50 years with a range of 11 to 82 years. There were 242 tumors identified among the entire cohort; carotid body tumors were the most common type (101), followed by jugular (59) and tympanic (27). The majority of patients had one tumor; however, many patients had multiple tumors (ranging from 2 to 8), especially among those with genetic mutations.

These patients could present with multiple synchronous tumors at the time of detection or develop multiple tumors over the years, sometimes over a decade apart. Our routine genetic evaluation screens for germline mutation. Among the 98 patients (56% of the cohort) with genetic screening, only 2 had additional somatic testing. There were 60 patients (61% of the tested or 34.5% of the cohort) with identified genetic mutations, and SHDx mutations accounted for the vast majority, including SDHB (25), SDHD (21), SDHC (7), and SDHA (2). A few other known PPGL related mutations were identified among the cohort, including VHL (1), MEN1 (1) and TMEM127 (1). HNPPGLs tend to be less biochemically active compared to nonHNPPGL. There were 118 patients (67.8% of the cohort) with at least one biochemical evaluation of metanephrines or catecholamines. If biochemistries were elevated, patients were blocked with alpha antagonists prior to undergoing any procedures including embolization, surgery, MIBG and radiation therapies. CT and MRI, which provides detailed anatomical information critical for the treatment planning of surgery and radiation, were the most commonly used imaging modalities for the evaluation of HNPPGLs. Functional scans with somatostatin analogs were used to evaluate multifocal and metastatic disease.

For our entire cohort of 174 patients, 120 patients had surgery with many patients undergoing preoperative embolization a day prior to surgery, 22 patients had radiation therapy, and 5 patients had MIBG as treatment. Surgery remained the most definitive and commonly used treatment of HNPPGLs for local disease control, though radiation with stereotactic radiosurgery (SRS) or conventional external beam radiation (EBRT) was used in surgically challenging or inoperable cases. In the more recent years at our institution, there has been an increased number of patients referred for routine genetic testing and biochemical evaluations for suspected HNPPGLs. The number of genes on the testing panel has also been steadily increasing in the recent years.

Given the rarity and complexity of HNPPGLs, and the associated high rates of hereditary predisposition and increased risk of recurrence and malignancy with certain genetic mutations, the current practice at our institution has evolved to now refer all patients with suspected HNPPGLs for genetic screening and biochemical evaluation. We also have weekly multidisciplinary meetings to discuss the care of each patient. Our single center experience highlights the need for referral for genetic testing and biochemical evaluation and for a team based approach to improve the clinical outcomes of patients with HNPPGLs.

Clinical and molecular characteristics of HNPGL individuals with bilateral and multifocal disease

Hilary C. McCrary MD MPH, Anne Naumer, MS, Wendy Kohlmann, MS, Neil S. Patel, MD, Samantha Greenberg, MS,MPH, Evan L. Tooker, Luke Buchmann, MD

Departments of Otolaryngology-Head and Neck Surgery, University of Utah Health, Salt Lake City, Utah.

Objectives:

Hereditary paragangliomas of the head and neck (HNPGL) have been described as more likely to be bilateral and multifocal, present at an earlier age, have positive family history, and have a higher rate of occurrence in multiple anatomical sites within the head and neck region. This study presents the clinical and genomic characteristics a cohort of patients with bilateral and/or multifocal HNPGL at a single institution over more than 10 years.

Methods:

A retrospective and prospective analysis was conducted on a cohort of patients diagnosed with bilateral or multifocal HNPGLs or PPGL from 2009-present. All individuals had a HNPGL diagnosis at initial presentation and were evaluated in the head and neck oncology or neurotology clinics. Clinical data including demographics, age at diagnosis, tumor location, family history, and genetic testing results were collected and stored in an institution specific database.

Results:

57/211 (27%) of HNPGL patients had one or more tumors (152 total tumors) including pheochromocytoma (n=2), gastrointestinal stromal tumor (n=1) and extra-adrenal PGLs (n=8). 49 (86%) completed germline genetic testing utilizing an expanded panel. A SDHX pathogenic (PV) or likely pathogenic (LPV) mutation were identified in 30 (61%) individuals (16.6% (n=5) SDHB, 10% (n=3) SDHC, and 73.3% (n=22) SDHD). 56% of germline carriers were male and 44% female, in the non-carrier cohort 18/19 (99%) were female. Of the 19 who have negative testing of the *SDHx* gene, 79% had a test that included other PGL genes (VHL, FH, MAX, RET, NF1, TMEM127) which were also negative. Individuals identified to carry a germline PV were younger at their first diagnosis of a HNPGL (mean age 34.5, $\pm$14.0)) than the sporadic group (mean age 58.3, $\pm$14.3) p-value<.0001. One (5%) patient in the PV negative group had a family history of PGL, but 25 (85%) in the PV positive group had $\geq$1 affected relatives (p-value<0.0001). Four patients with PVs (3 SDHD, 1 SDHB) reported a negative family history. Only one patient presented with malignant disease, a 29-year-old woman with a carotid body tumor and disease in more than one lymph node. Tumor site was also predictive of PV status. PVs were identified in 9 (100%) of individuals who had a HNPGL and other tumors outside of the head/neck, 14/19 (73%) of those with mixed types of HNPGL (ex. Carotid body and skull base), but only 7/20 (35%) of those with bilateral carotid body tumors (Fisher's exact p-value<.00008).

Conclusions: Our conclusions are consistent with previous studies highlighting the clinical and genetic characteristics of hereditary and sporadic bilateral and multifocal paragangliomas involving HNPGL. The presence of a germline mutation in SDHX genes was strongly associated with younger age of onset, variable topography of multiple paraganglioma tumors, and familial clustering. Additionally, this small study suggests that the incidence of germline SHDX PV in older patients presenting with multifocal HNPGL only and negative family history is lower than previously thought.

Hereditary Paraganglioma/Pheochromocytoma Syndrome Care Management using a Holistic Family Approach.: Benefits of a Centralized Multidisciplinary and Dedicated Team for Supporting Research and Families Living with Hereditary PGL syndrome

Luke Buchmann, MD; Anne Naumer, MS; Wendy Kohlmann, MS; Neil S. Patel, MD; Samantha Greenberg, MS, MPH; Jennie Vagher, MS; Evan L. Tooker; Hilary C. McCrary MD MPH

Department of Otolaryngology-Head and Neck Surgery, University of Utah Health, Salt Lake City, Utah.

Objectives:

The intent of identifying individuals with hereditary paraganglioma/pheochromocytoma syndrome is to implement screening for early tumor detection in order to reduce morbidity associated with treatment of advanced tumors. However, there are many challenges to screening these patients including evolving recommendations, requirements for specialized technology, diverse tumor types requiring different specialists, and the need to screening from childhood into adulthood. In 2018, Huntsman Cancer Institute established a multidisciplinary clinic to coordinate screening and plan treatment for adults and children with hereditary PGL/PCC. The clinical team includes a head and neck oncologic surgeon, genetic counseling, nurse, social worker, and research coordinators. Patients are encouraged to attend clinic yearly, and multigenerational families often attend together (ex. parents and children) to minimize appointments. Additional team members, including an oncologist, endocrinologist, urological oncologic surgeon, a pediatric oncologist, and a neuroradiologist are available for consultation, also participate in a bi-monthly case conference during which upcoming patients, test results, treatment plans and research goals are discussed.

Methods:

Since 2011, 345 individuals, representing 130 families, have been identified as carriers of a germline SDHx, TMEM127, or MAX pathogenic variants. Patient data are entered into a HCI custom database which interfaces with electronic medical records and tumor registry data. Additional data including demographics, detailed tumor information, screening procedures, and family data are manually entered and updated as the team learns of new information. Patients attending the multidisciplinary clinic are presented at a bi-monthly treatment planning meeting, and their clinical, screening, and treatment data are updated at those time. Chart review was performed for those not attending the clinic to determine what PGL related care they were receiving.

Results:

Currently 332/344 (96%) of our enrolled patients are living, and 181 are female (55%). Since establishing the multidisciplinary clinic in 2018, 192/344 (56%) individuals from 80 families had at least one visit. Prior to establishing a specialty clinic, 35/187 (18%) had documentation of a follow-up visit related to hereditary PGL/PCC in their records. The median age of attendees was 40 (range 8-88) and non-attendees 45 (range 6-92). There was no difference in gender between those attending and not attending. 71% of attendees and 34% of non-attendees were unaffected. The most frequent reasons for non-attendance were insurance issues, moving away, and active PGL or cancer diagnosis.

Conclusions: Accommodating parents and children in one visit with a consistent group of providers improves annual visit compliance. Possible reasons may include a reduction in the burden of separate visits for adults and children, decreasing the anxiety that can accompany establishing rapport with new caregivers and navigating new locations. Additional benefits to individuals living with PGL predisposition include psychosocial support for themselves and maturing children, help with navigating a complicated and extensive screening protocol, and access to research enrollment. Our experience suggests that unaffected carriers are especially likely to opt for follow-up in a multidisciplinary clinic. As future research involving genotype-phenotype correlations becomes available, we anticipate that we will be able to tailor management to individual needs.

What clinicians should know about the genetics of paragangliomas?

EF Hensen, EPM van der Kleij-Corssmit, JP Bayley, JC Jansen

Department of Otolaryngology and Head and Neck Surgery, Leiden University Medical Center, Albinusdreef 2, PO-box 9600, Leiden 2300 RC, The Netherlands.

Aim:

To discuss current insights in the genetics of paraganglioma and the impact of genetics on clinical decision making, counseling and clinical screening.

Methods:

Overview of the literature and research conducted at the Leiden University Medical Center on the topic of paraganglioma genetics, genotype- phenotype correlations and inheritance patterns, with a focus on the succinate dehydrogenase (SDH) associated genes.

Results:

Currently, approximately 20 different genes are associated with the occurrence of paraganglioma-pheochromocytoma. Germ line mutations in these genes explain approximately 40% of the cases. Approximately 15-20% of paragangliomas are caused by mutations in succinate dehydrogenase (SDH) associated genes (*SDHA, SDHB, SDHC, SDHD* and *SDHAF2*). Disease risk however varies greatly between these SDH genes (estimated from 1,5% in SDHA-linked to almost 100% in SDHD-linked disease). In addition, different genes seem to cause different clinical expressions (phenotypes), reflected in differences in tumor predilection site, metastatic potential, and other associated tumors. Recent research shows that not only the type of gene but also the type of mutation may drive these phenotypic differences. Last, different genes show different patterns of disease inheritance, from autosomal dominant to autosomal dominant with a parent-of origin effect, causing the disease to skip generations and obscuring its familial occurrence.

Conclusions: The insights in paraganglioma genetics is increasing rapidly. Paraganglioma phenotype seems not only determined by the causative gene, but also by mutation type. In addition, specific (SDHx) genes confer specific disease inheritance patterns. This information is of great importance in the counseling of patients and families and can be used to tailor clinical follow-up, screening and management of individual paraganglioma patients.

Pathology of head and neck paragangliomas

Adriano Zangrandi, Alberto Schena, Alessandro Ubiali, Serena Trubini, Carlo Terenzio Paties

Unità Operativa di Anatomia Patologica, Ospedale "Guglielmo da Saliceto", AUSL Piacenza, Via Taverna 49, 29121, Piacenza, Italy.
Email addresses: a.zangrandi@ausl.pc.it; carlopaties@yahoo.it

We present a single institution series of 362 head and neck tumours from 324 patients (age range 12-87 years, median = 49 years) referred by "Gruppo Otologico" to the Anatomic Pathology Unit of the Piacenza Hospital between 1995 and 2023 with suspected paraganglioma (PG) diagnosis. The series includes 104 males and 220 females. As to site, 275/324 patients (84.8%) presented with jugulotympanic tumours, 7 (2.1%) with carotid body tumours, 10 (3.1%) with vagal tumours, 32 (9.8%) with multiple head and neck tumours, 5 (1.5%) with metastases to cervical lymph nodes. Females prevailed and tended to be older than males, both overall (mean age 51.9 versus 45.9 years) and at each site. We revised the slides available for each case, assigning a score based on section quality and representativity, ranging from "0" (poor) to "3" (optimally preserved). Histological review evaluated fibrosis, embolization, necrosis and haemorrhage, evidence of bone or carotid artery infiltration, sustentacular cell number and proliferative activity. Despite frequently suboptimal morphology, histologic diagnosis was always obtained, confirming the clinical diagnosis of PG. Our basic immunohistochemistry panel included synaptophysin, chromogranin A, S-100, SOX-10, and Ki67; 175 patients referred between 2002 to 2023 were also tested for SDHA and SDHB protein expression. Other markers were rarely employed for differential diagnosis.

Histological and immunohistochemical features were correlated with clinical presentation, biological behaviour, SDHB/SDHA expression, and whenever possible germline SDHx mutation status. Out of 133 cases analysed for SDHx status, only 92 were matchable with SDHB and SDHA immunohistochemistry. Loss of SDHB protein was observed in 83/175 tested cases, including 27/32 with genetically-proven SDHx mutation and 18/60 for which SDHx mutations were ruled out by genetic testing. Loss of SDHA protein was observed in 17/175 tested cases, including 5/8 with detected SDHA/SDHAF2 mutations, and 2/60 for which SDHx mutations were ruled out by genetic testing. Females were always more numerous than males: SDHB-negative tumours, 50 females vs 33 males; SDHB-positive tumours, 56 females vs 19 males; SDHA-negative tumours, 13 females vs 4 males. Multiple head and neck PGs were more frequent in females (19 vs 13 males). Twelve out of 14 (12/14) multiple PGs tested had SDHB-negative immunostaining. The 5 metastatic cases occurred in 2 patients with multiple head and neck PGs and in 3 patients with jugulotympanic PG. These tumours always showed one or more feature(s) consistent with malignant behaviour, such as major atypia, increased proliferative activity and marked intra-tumour variability in sustentacular cells density. Two out of 5 (2/5) metastasizing tumours showed loss of SDHB expression and SDHx gene mutation (one at SDHB, one at SDHD).

Our data indicate that jugulotympanic PGs can be aggressive, and that the biological and clinical behaviour correlates to SDHx gene status and SDHB immunostaining. These parameters should therefore be considered for surgical and follow-up protocols. Enforcement of comprehensive immunohistochemistry protocols, particularly regarding SDHB and SDHA immunostaining, is strongly recommended in the routine pathologic report of PG. Genetic evaluation of the SDHx genes may be appropriate to confirm immunohistochemical results and investigate cases with sub-optimal histology.

Nuclear Medicine and Imaging in Head and Neck Paragangliomas: Diagnosis and Management

David Taieb

Department of Nuclear Medicine, Aix-Marseille University, La Timone University Hospital, Marseille, France.

Head and neck paragangliomas (HNPGLs) are rare neural crest-derived tumors that are a subset of pheochromocytoma/paraganglioma (PPGL) neoplasms. These tumors are specifically associated with the parasympathetic nervous system, but they can coexist with sympathetic PPGLs, especially in patients harboring SDH mutations (mostly SDHD). The very good results obtained with gallium-68 (68Ga)-labelled somatostatin receptor analogs (SSAs) have simplified the imaging approach to HNPGLs (regardless of the genotype) and can also be used for selecting patients for peptide receptor radionuclide therapy (PRRT). New international guidelines dedicated to SDHD and SDHB patients have been published and will be discussed.

The additional value of 68Ga DOTATOC PET/CT compared to MR imaging of the head and neck region in patients with head and neck paraganglioma

J.M. de Bresser1, B.J. Petri1, A.J.A.T. Braat2, M.J.C. van Treijen3, B.P.M. van Nesselrooij4, G.J.de Borst1, J.A. Rijken5

[1]Department of Vascular Surgery, University Medical Centre Utrecht, Heidelberglaan 100, 3584 CX, Utrecht, The Netherlands
[2]Department of Nuclear Radiology, University Medical Centre Utrecht
[3]Department of Endocrinology, University Medical Centre Utrecht
[4]Department of Clinical Genetics, University Medical Centre Utrecht
[5]Department of Head and Neck Surgical Oncology, University Medical Centre Utrecht

Objectives:

The Dutch guideline for patients with head and neck paragangliomas recommends performing an MRI and/ or CT scan of the head and neck area in all paraganglioma patients or carriers of associated alterations in the PGL genes. It furthermore suggests that additional nuclear imaging may be considered in these patients. Currently the 68Ga-DOTATOC PET/CT is one of the most sensitive and specific modality for detecting paragangliomas. In this study we evaluate the similarities and/ or differences when comparing the standard imaging results with the results of a 68Ga-DOTATOC PET/CT when focusing on the head and neck region.

Methods:

In this single-center prospective cohort study, data was obtained from consecutive patients visiting the outpatient clinic of the University Medical Center Utrecht, a tertiary referral center for HNPGLs, between 2016 and 2023 with at least one head and neck paraganglioma or a genetic mutation suspected of causing HNPGLs. All patients underwent a computed tomography (CT) and/or magnetic resonance imaging (MRI) of the head and neck region conform the standard path of care in the Netherlands. After written informed consent these patients underwent an additional 68Ga-DOTATOC PET/CT and imaging results of the head and neck region were compared for each patient.

Results:

Thirty-four patients underwent both MR imaging of the head and neck and an additional 8Ga-DOTATOC PET/CT. Thirty-four patients carried a mutation (97 %) in genes coding for *SDHA* (n = 3, 8.8%), *SDHB* (n = 11, 32.4%), *SDHC* (n = 1, 2.9%) and *SDHD* (n = 18, 52.9%).
In thirteen patients (n = 13 / 34, 38.2 %), there was a difference in the report of both modalities focusing on the head and neck region. Ten patients (n = 10 / 13, 76.9 %) showed unexpected,
additional SSTR2 uptake on the 68Ga-DOTATOC PET/CT. In three patients (n = 3 / 13, 23.1 %), the 68Ga-DOTATOC PET/CT discriminated between paraganglioma suspected lesions on MR imaging without SSTR2 expression. In three patients (n = 3 / 13, 23.1 %), the result of the additional 68Ga-DOTATOC PET/CT led to a change in the management of these patients. Twenty-one patients (n = 21 / 34, 38.2%) showed no difference between the outcomes of the MRI and 68Ga-DOTATOC PET/CT.

Conclusions:

Performing an additional 68Ga-DOTATOC PET/CT in paraganglioma patients yielded different findings in twenty-five percent than initially seen on standard MR imaging of the head and neck area; both false negative and false positive findings were observed. Because of this considerable difference in imaging findings and the proven high sensitivity and specificity of a 68Ga-DOTATOC PET/CT in detecting paragangliomas, performing this extra scan seems to be of added value in the management of these patients.

Rates of Tumor Diagnosis Detected on Baseline Screening of Asymptomatic Germline Mutation Carriers of Paraganglioma Predisposition Genes

Hilary C. McCrary MD MPH, Anne Naumer, MS, Wendy Kohlmann, MS, Neil S. Patel, MD, Samantha Greenberg, MS, Evan L. Tooker, Luke Buchmann, MD

Departments of Otolaryngology-Head and Neck Surgery, University of Utah Health, Salt Lake City, Utah.

Aims/Objectives:

An estimated 30-40% of paragangliomas are associated with germline *succinate dehydrogenase mutations (SDH)* and early detection of these mutations is critical for appropriate management and surveillance. Guidelines recommend surveillance begin between ages 5-15 for asymptomatic mutation carriers. This study aims to describe the experience of one institution's tumor detection rate at the time of baseline screening following identification a familial SDHX pathogenic variant (PV) or likely pathogenic variant (LPV).

Methods:

A retrospective observational analysis was conducted. Individuals with germline mutations associated with head and neck paragangliomas (HNPGL) found through family variant testing were included. Baseline screening using either magnetic resonance imaging (MRI) or positron emission tomography (PET/CT) scans with radiotracers targeting paragangliomas were reviewed.

Results:

At least one screening exam (WB MRI or PET/CT) was completed for 131 asymptomatic carriers of germline mutations in SDHA, SDHB, SDHC, SDHD, and TMEM127 genes who are currently over the age of 10 from 2009-2022. Most baseline screens were completed within 6 months of the identification of the germline mutation (range 1-31 months). Baseline screens identified 22 tumors in 17 individuals (13%) with germline mutations (10 SDHB, 1 SDHC, and 6 SDHD). Male carriers accounted for 10/17 (59%) and females 7/10 (41%) and the age range of diagnosis was 10-45 years of age with a diagnosis in five children under the age of 15 years. HNPGLs were the most common type identified comprising 12/22 (54%) including bilateral tumors in thirteen- and fifteen-year-old females and a single tumor in a thirteen-year-old female. In addition, eight extra-adrenal tumors, one pheochromocytoma, and one renal cell carcinoma were identified. Two tumors, an organ of Zuckerkandl paraganglioma and a renal cell carcinoma were metastatic at the time of diagnosis. Surgical intervention was required for 17/22 (77%) and observation, with yearly imaging and plasma metanephrines, was recommended for the remainder.

Conclusions:

Tumor detection on baseline screening following the identification of a germline mutation associated with an increased risk of paraganglioma using MRI or PET/CT scans is significant. This study highlights the importance of evaluating asymptomatic individuals for familial SDHx and other genes conferring a high risk of PPGLs. The early identification of germline carriers may contribute to earlier detection of tumors and inform future treatment.

Radiological Anatomy of Petrous Bone and Jugular Foramen

Prof. Roberto Maroldi

Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, ASST-Spedali Civili, Brescia, Italy.

Since the petrous bone and the jugular foramen include a complex crossroads of neurovascular structures, an appropriate imaging strategy requires both high spatial resolution MR and CT scans, possibly with sub-millimetric volumetric acquisitions. As an example, the 3D *volume* acquired can be, subsequently, reconstructed along oblique planes (simil-Stenvers, simil-Poschl) that improve the analysis of specific structures of the petrous bone. The 3D volume can also be re-processed using Maximum-Intensity or Minimum-Intensity projections which improve, respectively, the assessment of high-signal (vessels filled by contrast agent) or low-signal structures (usually cranial nerves surrounded by CSF or enhancing venous channels). The variables for acquiring the CT study are rather limited, while a comprehensive MR investigation includes several distinct sequences (*multiparametric approach*). The CT protocol includes, at first, an acquisition without contrast agent, then an arterial and a venous phase, and last, a thin slice bone algorithm reconstruction. The reconstructions with bone algorithm are essential to assess both large and tiny canals running within the temporal bone and to scrutinize the bony boundaries of the jugular foramen. In the *multiparametric approach* with MR, distinct sequences are designed to show not only arterial (ICA), venous (IJV, inferior petrosal sinus), and fluid-filled structures (such as the membranous labyrinth and the IAC), but also to identify the intracranial path of lower cranial nerves (MR cisternography) and, more recently, to directly identify the extracranial course of cranial nerves (neurography sequences).

Surgical anatomy of the infratemporal fossa approach type A and its extensions

Wenlong Tang MD

Changzhi Medical College Affiliated Heping Hospital, Shenzhen ENT Institute
Changzhi Medical College, China

Infratemporal Fossa Approach Type A is designed to allow access to the jugular foramen regions, the infralabyrinthine and apical compartments of the petrous bone, the vertical segment of the ICA, and the upper jugulocarotid space. The approach is designed primarily for extensive extradural lesions involving these areas, such as Class C1-C4 paragangliomas of the jugular foramen. The key point in this approach is the anterior transposition of the facial nerve and which provides optimal control of the infralabyrinthine and jugular foramen regions, as well as the vertical portion of the ICA. Besides the facial nerve they include the tympanic bone, the digastric muscle, and the styloid process. These structures are removed to allow unhindered lateral access. Based on the ITFA, various extensions are dictated by the extent of the pathology. This presentation will thoroughly review the surgical anatomy of the infratemporal fossa approach type A and its extensions step by step.

Surgical Anatomy of the Lower Skull Base

Essam Saleh

Consultant of Otology & Skull Base Surgery, King Abdullah Medical City, Makkah, Saudi Arabia and Professor of Otolaryngology, Alexandria University, Egypt

Aim:

The aim of the present work is to present the surgical anatomy of the lower skull base and jugular foramen area as seen from the lateral approaches, with stress on the different anatomic variations of surgical importance encountered in this complex region.

Material & Methods:

The study was conducted on 40 temporal bones and 25 fresh frozen cadavers. The infratemporal fossa type A approach was performed and the distances between the important structures was recorded. The occipital condyle was drilled and the condylar emissary vein as well as the hypoglossal canal were studied. The lateral wall of the jugular bulb was resected to study the veins draining into it. The lower cranial nerves were studied at the level of the upper neck, at their exit at the skull base, and in the jugular foramen. An extreme lateral approach was also performed in the fresh cadavers and the different landmarks for identification of the vertebral artery were assessed.

Results:

The shape of the jugular bulb dome was either rounded (80%) or flat (20%). In about two thirds of specimens, the inferior petrosal sinus drained by more than one opening in the bulb. The most common arrangement was that of the sinus passing between cranial nerve IX above and lateral and nerves X and XI below and medial. Less commonly, the sinus passed medial and inferior to cranial nerves IX through XI (20%), while in only 7.5%, the sinus emerged superiorly and travelled lateral to all the nerves. In 4 specimens (10%), the inferior petrosal sinus had no connection with the bulb, terminating only in the internal jugular vein. In 28 specimens (70%) the jugular foramen was divided into two compartments separated by bone or fibrous tissue septa. In 27 of these (67.5%), nerve IX passed in the anterior compartment while the jugular bulb and cranial nerves X and XI passed in the posterior one. In the remaining specimen (2.5%), all three nerves ran in the anterior compartment. In 10 specimens (25%), a single common compartment was found, lodging nerves IX through XI anteriorly and the jugular bulb posteriorly. The condylar emissary vein was identified in 70% of specimens. The transverse process of atlas constituted an important landmark for identification of the internal jugular vein, XI nerve and vertebral artery. Other important landmarks for the vertebral artery where C2 nerve root and the superior and inferior oblique muscles.

Conclusions: The lower skull base is an area of complex anatomy. Proper knowledge of surgical anatomy as seen through the surgical approach is mandatory before embarking on surgery.

Tympanic Bone: Small neglected bone with extreme anatomical importance in the Lateral skull base surgery

Golda Grimblat

Hillel Yaffe Medical Centre, Technion Faculty of Medicine, Hadera, Israel.

The tympanic portion presents the smallest portion of the temporal bone. Nevertheless, we are of the belief that this bone has not received enough attention in the published literature up to date, as its removal easily reveals and controls more medially situated important neurovascular structures. In the present article we would like to stress the anatomical importance of the tympanic bone and its role as a “key structure” in the lateral skull base surgery, namely Infratemporal fossa approach type A and in removal of tumors of this site, in particular, tympanojugular paraganglioma (TJP).

Why does the tympanic bone have such an important role? Because our experience of the largest series of the TJP in English written literature demonstrates the infiltration of the tympanic bone in virtually all C3 and C4 cases, about 70% of C2 and about 40 % of C1 tumors. Laboratory research on 20 formalin-prepared temporal bones was performed in order to demonstrate the tremendous anatomical importance of the tympanic portion with a styloid process in surgery of TJP, conducting one to perform its complete removal. The consequence of complete tympanic bone elimination has a two-fold meaning: removal of tumor-infiltrated tympanic bone and gaining complete control of nearby neurovascular structures, such as jugular bulb and lower cranial nerves in the lateral skull base and vertical internal carotid artery in the neck after removal of the styloid process.

Paragangliomas involving the temporal bone: histopathology and its surgical implications

Mancini F., Sacchi M., Vasconi A., Papotti M.G., Cureoglu S.

Gruppo Otologico – Torino, Italy

Temporal Bone Banks and their Otopathology Laboratories are an outstanding source of information for various diseases affecting the ear and the surrounding structures. Otology has made exciting progress thanks to anatomy, pathology, pathogenesis, and genetics studies carried out in these facilities.

The aim of this study is to explore temporal bone laboratories and banks searching for specimen with temporal bone paragangliomas. Only three Otopathology Laboratories and Temporal bone banks are active at these times all over the world: University of Minnesota Otopathology Lab. (Minneapolis, USA), NIDCD temporal Bone Lab. at The House research Institute at the UCLA (Los Angeles, USA), and Otopathology Lab.

At the Massachusetts Eye and Ear Infirmary (Boston, USA). The objective of our search is the study of possible surgical implications in relation to the behavior of tumor growth. The most important structures found in the temporal bones and usually invaded, surrounded, or compressed by the tumor growth are the jugular bulb, the internal carotid artery, the lower cranial nerves, the facial nerve, and the labyrinth. Also well-known is the bony structure of the skull base with cellular bone and several bony sutures that facilitate the growth and invasion of areas surrounding the temporal bone. Very few cases of Paragangliomas (less than 10 in active Laboratories and few more from inactive collections) were found, therefore we extended our study to Laboratories where histopathology studies had been carried out on surgical specimens.

Observations on temporal bones affected by large tumors saved in temporal bone banks are often in contrast with operative findings. The intrapetrous internal carotid artery has been found surrounded by tumor in several cases but neither the adventitia nor the intima of the artery were invaded by tumor cells. On the contrary during surgery these tissues were often found deeply involved by the disease forcing the surgeon to sacrifice the structure instead of conservative procedures (stents). These findings have been confirmed by surgical specimen. We know that genetic mutations might influence the tumor's malignity or aggressiveness. Some different behaviors seen during our observations could conceals different types of tumors.

We will present some preliminary results obtained by immunohistochemical techniques in the search of markers that may be helpful in diagnosis and follow-up of patients with paragangliomas involving the temporal bone and the skull base.

Pre-Operative Work-Up Of Tympanic And Tympanojugular Paragangliomas

Enrico Piccirillo, Caterina Kihlgren, Mario Sanna

Gruppo Otologico, Piacenza, Italy

The pre-operative work-up of tympanic and tympanojugular paragangliomas consists first of otoscopy and imaging, which allow to make diagnosis and staging. It is important to assess the secretion of catecholamines, perform genetic/family evaluation, and identify any multiple lesions and differential diagnosis.
Petrous bone CT and MRI with and without gadolinium is essential for preoperative work out, diagnosis, staging and surgical planning. The degree of bony erosion is often underestimated radiographically and dural involvement and intradural invasion are sometimes difficult to assess. A clear intradural involvement significantly decreases the possibility of preserving the lower cranial nerves' function.

Close examination of the medial wall of the jugular bulb and bone surrounding the mastoid segment of the facial nerve can help in estimating the likelihood of neural conservation, even in the setting of normal preoperative function. Moreover, it is fundamental to assess venous and arterial involvement with MRA, MRV and Angiography. In any case, detailed clinical and radiological assessment and work-up is essential in tympanomastoid and tympanojugular paragangliomas.

Surgical Management Of Tympanojugular Paragangliomas: Historical Perspectives

Mario Sanna[1], Giuseppe Fancello[1,2]
1. Gruppo Otologico, Piacenza, Italy
2. Department of Otorhinolaryngology, Careggi University Hospital, Florence, Italy.

The first report of paraganglioma in literature dates back to 1762, when Heller introduced the term «glomus tumor».

The name paraganglioma wasn't first used until the early 1900s. Among these tumors, the tympanojugular subtypes are characterized by bone infiltration, erosion and by a close relationship with critical structures such as cranial nerves and internal carotid artery. For these reasons, their management has always represented a tough challenge. Rosenwasser (1945) made the first effort to remove the entire glomus tumor. As a result of the introduction of the microscope in the microsurgery of the meddle and inner ear, the use of bipolar diathermy during surgery and the arteriography, W. House (1964) was able to carry out his surgical revolution, the release of CT scan allowed the advancement of surgical techniques. Fisch published a systematized plan for the treatment of C class tumors in 1978. The development of preoperative embolization in the 1980s and the introduction of balloon occlusion test, or definitive closure of the Internal Carotid Artery (ICA), provided additional assistance to the surgical treatment of this pathology. Magnetic resonance imaging (MRI) with contrast enhancement became available in 1999.

In 2006 we reported the first series using ICA intraarterial stents for the management of tympanojugular paragangliomas.

The surgical refinements, the evolution of radiotherapy techniques with the introduction of radiosurgery, and the proper use of follow-up (in case with ICA involved or in cases considered inoperable) have led to a wide range of options in the management of this disease.

Microsurgical Removal of Class A Paragangliomas: The Gruppo Otologico Algorithm

Alessandra Russo

Gruppo Otologico, Piacenza, Italy

Tympanomastoid paragangliomas (TM PGLs) are tumors confined to the middle ear and the tympanomastoid cavity. According to the modified Fish and Mattox classification, Class A1 TM PGLs present margins clearly visible on otoscopic examination, whilst Class A2 have margins not visible on otoscopy, that may extend anteriorly to the Eustachian tube and/or to the posterior mesotympanum.

In this subgroup of paragangliomas, surgery represents the gold standard treatment, with the goal of completely eradicating the lesion and preserving the hearing.

The surgical approaches formulated according to the algorithm designed by Gruppo Otologico included transcanial approach (TC) for Class A1 and retroauricular transcanal approach (R-TC) with the glove finger flap technique for Class A2. In selected cases, the procedure can be performed under local anesthesia in day surgery.

Up to date 96 patients affected by Class A1-A2 TM PGLs underwent surgical treatment between 1983 and 2023 at Gruppo Otologico, Piacenza, Italy. 41% were classified as A1 and 59% as A2 tumors. Complete tumor removal was achieved in all of them. Three patients developed a recurrence, treated with revision surgery. The postoperative facial nerve function was graded as HB I in all the patients. Overall, the hearing levels remained stable or improved.

According to our results, it is possible to microscopically eradicate class A1 and A2 TM PGLs with excellent outcomes. In our opinion the use of the endoscope doesn't add any advantages.

Management Of Class B Paragangliomas: The Gruppo Otologico Algorithm

Antonio Caruso

Gruppo Otologico, Piacenza, Italy

Paragangliomas are tumors derived from sympathetic paraganglia. In terms of their location, they are categorized as tympanic, jugulotympanic, vagal, and carotid.

Fisch classified temporal bone paragangliomas into four classes. Subsequently, at Gruppo Otologico, we modified the classification by dividing the timpanomastoid paragangliomas into Class A, which includes tympanic paragangliomas, and Class B, comprising hypotympanic or mastoid paragangliomas.

Class A paragangliomas are further divided into Class A1 and A2. Class A1 tumors are of limited size and entirely visible on otoscopy, while Class A2 tumors have margins that are not visible on otoscopy.

Class B paragangliomas are tumors limited to the tympanomastoid compartment without erosion of the jugular bulb. They are further divided into B1, B2, and B3 categories. B1 tumors are confined to the middle ear with an extension into the hypotympanum. B2 tumors involve the middle ear with extensions into the hypotympanum and mastoid. B3 tumors involve the tympanomastoid compartment with erosion of the carotid canal.

This classification is mandatory for surgical management. The aim of this presentation is to introduce the Gruppo Otologico algorithm for the surgical management of Class B paragangliomas.

In the case of B1 paragangliomas, the surgical approach involves canal wall up mastoidectomy with posterior tympanotomy, while for B2 paragangliomas, subfacial recess tympanotomy is also indicated. In the case of B3 tumors, subtotal petrosectomy with middle ear obliteration will be the surgical approach.

We will present the steps of these surgical approaches using intraoperative videos and photos.

Algorithm of Surgical Management of Paragangliomas Class A and B

Kh.M. Diab, O.A. Pashshinina, P.U. Umarov, O.S. Panina, D.A. Zagorskaya

Federal State Budgetary Institution «The National Medical Research Center of Otorhinolaryngology of the Federal Medico-Biological Agency of Russia», (Director - Professor N.A. Davkhes), 123182, Moscow, Russia

Objective:

To present different surgical strategies in patients with paraganglioma type A and B and their clinical outcomes.

Materials and Methods:

During the period from December 2014 to October 2022 172 patients with temporal bone paraganglioma were examined and underwent surgical treatment on the base of NMRC of Otorhinolaryngology (Moscow, Russia). Patient demographics, type of the lesion, functional status, surgical approach; other intraoperative findings; anatomical and functional results after surgeries were evaluated. There were 27 type A; 29 - type B1; 25 – type B2; 38 – type B3 tumors. The retroauricular transcanal approach was performed in cases of type A and B1 paragangliomas; CWU with posterior tympanotomy in all cases of primary B2 neoplasms and CWD in 7 cases of resurgeries (after other clinics); retroauricular transcanal approach removing the entire tympanomeatal flap with widen canaloplasty of the anterior wall of EAC was performed in 80% of type B3 tumors. In half of the cases True-Blue laser was used. In the end of the surgery tympanoplasty with ossicular chain reconstruction (if necessary) was performed in all cases. In 14 cases of B3 paraganglioma with obturation of EAC, deficit of skin of the anterior wall of EAC was revealed and free skin flaps were used for reconstruction. Main outcome measures were assessed in the quality of tumor resection; auditory and facial nerve status in the postoperative period. The period of observation was from 3 month to 5 years.

Results: All performed approaches allowed to totally remove tumors and get good visualization of the middle ear structures. There were no complications intraoperatively. In type A and B1 tumors anatomical results were similar to normal ear, hearing was preserved on the preoperative level or improved. There were no cases of significant hearing deterioration. Ossicular chain was preserved in 62 cases. In type B3 paraganglioma in 7 patients with obturation of EAC neotymapic membrane lateralization was revealed postoperatively, 4 of them had progressive hearing loss. FN function was preserved in 112 cases, in 9 cases there were different degrees of FN paralysis (secondary treated tumors after other clinics) that needed procedures from decompression (n=6), to graft reconstruction (n=1).

Conclusion: Presented surgical algorithm of surgical treatment of patients with paraganglioma type A&B allowed us to perform safe removal of the tumor with preservation of hearing and FN function in most of the cases.

Surgical alternatives for tympano-mastoid paragangliomas

Miguel Arístegui

ENT Department, Hospital General Universitario Gregorio Marañón, 28007 Madrid, Spain.

Tympanomastoid paragangliomas (TMPG) include a wide range of conditions that may be resolved by purely follow up in very small tumors in elderly patients, to more complex cases invading the middle ear cleft, the mastoid or even the protympanum deep in the infratemporal fossa. Those who are candidates for surgery may be managed by otologic approaches that go from purely transcanal approaches to more complex cases who may require subtotal petrosectomy approaches. Tympanomastoid paragangliomas involving the hypotympanic space could be managed through an extended facial recess approach as described by William House decades ago.

We include an alternative to this approach, an ***Extended anterior Hypotympanotomy approach*** which avoids scarifying the chorda tympani, provides better access to the jugular bulb-internal carotid artery interface and depending on the extention of the TMPG, may be performed through an endaural or a retroauricular approach. We will show videos of TMPG managed through different techniques and discuss on the appropriateness of each technique on view of the results.

Minimally invasive surgery for early-stage temporal bone paragangliomas with the use of endoscopy

Prof. Romain Kania, MD, PhD

Tenured Professor in Otorhinolaryngology, Head & Neck Surgery
Lariboisière University Hospital, Greater Paris University Hospitals APHP, Paris University

This presentation focuses on the application of minimally invasive surgery utilizing endoscopy for the treatment of early-stage temporal bone paragangliomas from stage A to B1 according to the Fisch classification. The advent of endoscopic techniques has revolutionized the field by providing a less invasive and more precise approach to these tumors. This presentation discusses the advantages of endoscopic surgery, including improved visualization, reduced morbidity, and shorter hospital stays. The technical aspects of endoscopic surgery for temporal bone paragangliomas will be elucidated, including patient selection, surgical planning, and the step-by-step procedure. The benefits of endoscopic-assisted tumor resection, preservation of normal structures, and the management of potential complications will be highlighted.

Endoscopic and microsurgical management of glomus tympanicum tumors: a case series of 10 patients

CAI Xinzhang, WU Hong, LIU Xing, WU Xuewen, WU Lisha, JIANG Lu, JIN Yi, HE Chufeng, MEI Lingyun, SONG Jian*

Department of Otorhinolaryngology Head and Neck Surgery, Xiangya Hospital, Central South University; Hunan Provincial Key Laboratory of Major Otorhinolaryngology Diseases; National Clinical Research Center for Geriatric Diseases, Xiangya Hospital, Changsha 410008, China
Email: zeiss93@csu.edu.cn

Aims/Objective:

To provide a comprehensive summary of the clinical characteristics associated with glomus tympanicum tumors, as well as to investigate surgical techniques and strategies for preserving auditory function.

Materials/Methods:

Ten cases of glomus tympanicum tumors were collected from the Department of Otolaryngology Head and Neck Surgery at Xiangya Hospital, Central South University between August 2014 and February 2022. All patients underwent endoscopic or microscopic surgery to achieve complete tumor removal, followed by a follow-up period ranging from three months to eight years. We summarized and analyzed the clinical characteristics of these cases, compared preoperative and postoperative hearing levels, and conducted a retrospective summary.

Results:

Ten female patients, aged (49.50±8.00) years old, were included in the study with medical histories ranging from 15 days to 6 years. Seven of these patients reported pulsatile tinnitus and 80% (8/10) of affected ears exhibited varying degrees of hearing loss. Glomus tympanicum tumors were classified according to the modified Fisch & Mattox classification system, with A1 present in three ears (30%), A2 present in two ears (20%), and B1 present in five ears (50%). In all 10 cases (ears), the hearing of the operated ear was improved in 3 cases, maintained at preoperative levels in 6 cases, and slightly decreased in one case. After the operation, 7 ears showed an A-B gap of 0-10 dB and 3 ears showed a gap of 10-20 dB. There was no significant difference in average air conduction hearing threshold, bone conduction hearing threshold, or A-B gap before and after the operation (all $P>0.05$). All cases had successful postoperative healing without complications or recurrence during follow-up.

Conclusion: Glomus tympanicum tumors are prone to bleeding, posing a challenge for achieving complete tumor resection while preserving hearing function during surgery. Type A and B1 tumors can be fully excised without compromising the integrity of the tympanic membrane or ossicular chain, thereby maintaining or even improving postoperative auditory acuity. Endoscopic surgery is a viable alternative to microsurgery for glomus tympanicum tumors, provided that appropriate cases are selected.

Technical Considerations in Endoscopic or Endoscopic-Assisted Removal of Paragangliomas

Michael CF TONG, Wai Tsz CHANG

Department of Otorhinolaryngology, Head and Neck Surgery, and Institute of Human Communicative Research, the Chinese University of Hong Kong

Introduction:

Since 2015, we have utilized otoendoscopy for the removal of paragangliomas, ranging from glomus tympanicum to intracranial advanced stage tumors. This paper focuses on the technical considerations associated with achieving total or near-total resection of these tumors using endoscopic ear surgery techniques, including endoscopic-assisted ear surgery and the use of the 3-D exoscope.

Methods and Results:

We classified our approaches into three categories based on a consecutive series of patients:

1. Total transcanal endoscopic removal: for glomus tympanicum with extension to attic, antrum, and hypotympanum;
2. Combined exoscopic (or microscopic)/ endoscopic removal: for extensive mastoid involvement and/or hypotympanic involvement;
3. Management of intracranial tumors with combined transcanal/transmastoid access.

We also discuss the use of TruBlu lasers and pre-operative angiography with or without embolization.

Discussion and Conclusion: In the era of otoendoscopic ear surgery, our surgical management principles for paragangliomas remain focused on safe and adequate removal of the disease while preserving function. The use of endoscopic ear surgery techniques may allow for better preservation of normal anatomy and reduce residual disease. Additionally, digital enhancement and fiberoptic lasers provide new means of advancing surgical resection.

Pre-Surgical Management of ICA in Head and Neck

Roberto Menozzi, Giulia Capurri

Department of Neuroradiology, AOU Parma, Parma, Italy

Presurgical endovascular management of the internal carotid artery (ICA) is indicated in very extensive tympano jugular, vagal and carotid paragangliomas enveloping, stenosing, eroding the ICA canal and which are vascularized by ICA hypertrophic afferents. It is characterized by two types of procedures. The first is the permanent balloon occlusion of the ICA following an occlusion test; the second, in absence of adequate compensation, is represented by the reinforcement of the vessel wall with a stent. In AOU Parma, we've treated 156 patients between January 1992 and December 2022.

116 of these patients underwent ICA occlusion with balloon, coil, or plug, while the remaining 40 underwent ICA stenting. We had five complications. Two of these were intraprocedural, the first occurred in the first patient treated because of ICA dissection with thromboembolism in the middle cerebral artery (MCA); the other was a thromboembolism of a branch of the MCA without permanent sequelae. We had an early complication due to ischemic hemodynamic suffering. The last two were late, one after more than a year caused by platelet aggregates formed in the residual ICA segment upstream of balloon placement, leading to a minimal thromboembolism; the other was a ruptured anterior communicating artery aneurysm due to flow alteration. All patients with complications underwent ICA occlusion; patients treated with ICA stenting, on the other hand, presented no complications.

Title: Technical Considerations in Endoscopic or Endoscopic-Assisted Removal of Paragangliomas

Tympanojugular Paraganglioma: Perioperative Management

Kh.M. Diab[1, 2], N.A. Daikhes[1], O.A. Pashchinina, Umarov P.U. [1], O.S.Panina[1], D.A. Zagorskaya[1]

[1]Federal State Budgetary Institution «The National Medical Research Center for Otorhinolaryngology of the Federal Medico-Biological Agency of Russia» (Director - Professor N. A. Daykhes), 123182, Moscow, Russia
[2]Department of Otolaryngology, Faculty of Postgraduate education, Pirogov Russian National Research Medical University, 117197, Moscow, Russia

Objective:

The purpose of the study is to increase the effectiveness of treatment of patients with jugular foramen parganglioma (JFP) type C by using new protocols of preoperative management (transcatheter particle embolization, transvenous coil embolization) and additional equipment on intraoperative stages (use of photoangiolytic laser).

Methods:

The article presents our five-year experience of surgical treatment of JFP for the period from December 2014 to December 2022 on the base of the National Medical Research Center of Otorhinolaryngology (Moscow, Russia). Out of 172 paraganglioma tumors there were 24 patients with type C1, 32 patients with type C2, 8 patients with type C3; 5 patients with type D process. Of these, 60 were male and 112 were female aged from 2 to 82 years. All patients were divided into two groups: in the main group, n=38, endovascular intervention was performed on preoperative stage (among them there were patients, 79%, who underwent sole transcatheter particle embolization and those, 21%, who underwent additionally transvenous sigmoid sinus blockage), in the control group, n=26, only microsurgical JFP removal was performed. Superselective embolization of tumoral feeders coming off distal branches of ECA was performed with PVA foam particles (500 µm) mixed in a 1:1 ratio with contrast adopting a pulse pattern of injection until cessation of flow with no reflux of contrast along the microcatheter under real time magnification and collimation fluoroscopic modes. Transvenous sigmoid sinus embolization was performed using detachable coils above superior border of the tumor by navigating through the contralateral JB, SS, transverse sinus. The inferior petrosal sinus (IPS) was blocked also through contralateral IPS to the cavernous sinus. In C1-C2 tumor retrofacial approach; in C3-C4 parganglioma infratemporal approach was performed. Main outcome measures were assessed in volume of intraoperatively blood loss, the quality of tumor resection, time of the surgery; auditory function, the function of the facial nerve and lower cranial nerves in postoperative period.

Results:

In the 1st group post-embolization angiography revealed significant reduction of JFP blood supply and absence of tumoral blushes. The intravenous blockage of the area was performed only in cases of total JB tumor obturation on preoperative MRI scans with gadolinium enhancement. We did not observe any major complications after endovascular stage, in 3 cases we faced with postembolization syndrome (fever, transient facial pain). Volume of blood loss in this group varied from 40 to 400ml. Reduction in tumor size, blood loss improves the likelihood of a technically successful resection and result in a shorter operation time. Volume of blood loss in the 2nd group varied from 900 to 2500ml. In all cases performed approaches were enough to have good visualization of the jugular bulb (JB), internal carotid artery (ICA), control of VII, IX-XI pairs of cranial nerves. In 31 cases on stage of removal of the tumor in hidden areas and from the wall of ICA we additionally used photoangiolytic laser and endoscopic assistance.

Hearing was preserved in 18 cases. Temporary FN dysfunction (from III to V House-Brackmann stage) was noted in 37 cases with full improvement during the first 4 months of observation after surgery. In 2 cases of FN end-to-end anastomosis facial function was improved to II-III degree; in 3 cases of suralis graft reconstruction to III-IV stage. In 5 cases we faced with IX c.n deficits; in 3 cases patients noted increase of tongue and arm volume movement postoperatively. We can not exclude residual tumor tissue adjacent to ICA in 5 cases recidivism was detected on MRI postoperatively in 4 cases.

Conclusion: In patients with invasive jugular paragangliomas such as Fisch class C and D tumors, the use of selective angiography, super-selective embolizations, transvenous coil embolization in restricting vascular supply to JFP can have a significant pre-operative therapeutic role to reduce tumor volume, decrease intraoperative bleeding and facilitate tumor resection. The use of laser and microsurgical techniques with endoscopic assistance during the operation allows to avoid damage of the vital structures of the lateral skull base.

Direct Embolization of Tympanojugular Paragangliomas

Nicola Limbucci

Dept. of Interventional Neuroradiology – Careggi University Hospital, Florence, Italy

Introduction:

Embolization of tympanojugular paragangiomas is often performed before surgical resection in order to reduce intraoperative bleeding and help complete removal of the lesion. Moreover, embolization has also been proposed as the sole treatment for large unresectable tumors or in case of patients with surgical contraindications. Embolization of paragangliomas is traditionally performed by transarterial approach with particles or liquid embolics. However, percutaneous embolization by direct puncture of the tumor is another option, that has been increasingly used for carotid paragangliomas, as they can be easily punctured by ultrasound guidance. However, direct puncture embolization can be an interesting option also for tympanojugular paragangliomas.

The access for percutaneous embolization of tympanojugular paragangliomas is usually the space between the mastoid and the ascending mandibular branch, however accessing the lesion may be difficult because of the limited space and the presence of bony structures and vessels. More uncommonly, large tympanic tumors can be embolized by transtimpanic puncture. Ultrasound guidance is not an option, because of the deep location of the tumors, but the puncture can be performed by fluoroscopic guidance under angiographic road mapping assistance. Recent advancements in cone-beam CT technology with modern angiographic system, make possible a precise image guided access to skull base lesions with the aid of dedicated softwares. These tools create fusion imaging of live fluoroscopy with volumetric data, which are previously acquired by conventional CT or by cone-beam CT performed with the angiographic system. The fused images are used to trace the needle track at the workstation and then perform the puncture under live guidance.

After conventional angiography, necessary to study the vascularization of the tumors, the normal vessels and to identify any dangerous anastomosis,we access to the lesion with a 19 or 20 G needle under cone-beam CT live guidance. Then, we inject contrast to obtain a map of the tumor and the venous drainage. Finally, EVOH based non adhesive embolic material is slowly injected with the conventional technique. If necessary, multiple needles can be used to reach various compartments of the lesion.

The potential advantage of the direct percutaneous approach, over transarterial embolization, is the more precise injection of the embolic material inside the pathologic intratumoral vessels. Therefore, there is a reduction of the risk of cranial nerve ischemia or stroke due to migration of the embolic agent in the cerebral vasculature. The procedure is faster than transarterial embolization with particles, which sometimes requires many microcatheterizations and injections to embolize multiple tumoral compartments.

In our experience, the direct embolization with cone-beam CT guidance has become the standard approach for tympanojugular paragangliomas. In all cases the devascularization of the tumor was satisfactory with low intraoperative blood loss and improved resection of the tumors. In very selected patients, we also used this technique as a palliative treatment in patients with contraindications to surgery (age, comorbidities).

Protective endovascular carotis stent in surgery of tympanojugular paragangliomas

Riccardo Di Micco[1], Frederich Götz[2], Thomas Lenarz[1]

[1]ENT Department, Medizinische Hochschule Hannover, Hannover, Germany
[2]Neuroradiology Department, Medizinische Hochschule Hannover, Hannover, Germany

In the surgery of tympanojugular paragangliomas one of greatest challenge remains the mobilization and preparation of the tumor from the carotis interna, especially in its more fragile horizontal intrapetrosal segment, avoiding a catastrophic vascular injury. Of assistance is the application of an endovascular stent to protect the vessel and allow a higher degree of radicality without sacrifice of the ACI. After almost two decades from its introduction in the lateral skull base surgery, its indications and results should be critically assessed.

Methods:

Between 2009 and 2023, we preoperatively treated 23 patients affected by tympanojugular paraganglioma involving the vertical and horizontal segment of the carotis interna with an endovascular stent three months before surgery. The preoperative findings, the intraoperative complications and the final surgical results were analyzed. The median follow up is 5 years.

Results:

No complication was registered during the stenting procedure. In all cases, it was possible to completely mobilize the carotis interna and perform a complete subadventitial dissection of the paraganglioma without vascular injury. A complete extirpation of the tumor was possible in 22 patients. We did not experience clinical or radiological recurrence to date.

Conclusion:

The preoperative application of a carotis stent facilitates the vessel mobilization and tumor dissection allowing to completely preserve the ACI without risk of vascular damage. The use of the vascular stent is especially indicated in case of revision surgeries, circumferential involvement of the vessel including the horizontal intrapetrosal segment and insufficient intracerebral cross-flow. A standardized procedure reduces the risk of complications and helps the surgeon in such complex operations.

Application of internal carotid artery stent in skull base surgery of paraganglioma

Prof. Zhengnong Chen

Department of Otolaryngology-Head and Neck Surgery, Building 15, No.600 YiShan Road, XuHui District, Shanghai City, China

Objective:

To report the experience of the application of internal carotid artery stent in skull base surgery of paraganglioma and clarify the important role of internal carotid artery stent in skull base surgery.

Methods:

A retrospective study of 12 cases with paraganlioma implanted with internal carotid artery stents in the Department of ENT Head and Neck Surgery at the Sixth People's Hospital affiliated with Shanghai Jiao Tong University between 2019 and 2022.

Results:

12 patients underwent digital subtraction angiography and internal carotid artery stents before surgery. Tumor tissue was found to surround the internal carotid artery to varying degrees. The tumors of all patients were completely removed, and there was no involvement of the deep edge (the inner surface of the adventitia) tumor after the resection, and no intraoperative and postoperative complications occurred. The postoperative follow-up was 5 months to 2 years, and all patients had no complications such as spontaneous bleeding and pseudoaneurysm. There were no signs of stenosis or occlusion of the internal carotid artery stent segment in all cases.

Conclusions:

For patients with skull base tumors such as paraganglioma, preoperative imaging indicated extensive involvement of the internal carotid artery, and internal carotid artery stent implantation before surgery is a safe and effective treatment.

Open Issues In Tympano-Jugular Paragangliomas

Roberto Pareschi MD[1], Davide Lepera MD[2]

[1]Dipartimento di Neuroscienze, Ospedale Nuovo di Legnano, Milan, Italy
[2]Dipartimento di Otorinolaringoiatria, Ospedale Nuovo di Legnano, Milan, Italy

The treatment of choice for tympano-jugular paragangliomas is still controversial. High rates of morbidity, incomplete resection, and the aggressive behavior of these tumors are the main arguments for advocates of primary radiotherapy. However, Radical surgery is the only treatment that offers the complete and immediate resolution of the disease with low recurrence rate. With current techniques, large lesions, tumours involving cranial nerves, or complex glomus jugulare tumors that were deemed inoperable in the past are being safely and totally resected.

Between 1993 and 2014 we diagnosed 257 glomus tumors of the temporal bone. Of these patients, only 170 had a class C lesion (tympano-jugular paragangliomas) and were included in this study; 142 of these patients underwent surgery, 36 of whom had intracranial extension of the disease; 28 (10.9%) underwent RT or a wait-and-scan policy because of their age (> 65) and/or poor general status, or because they refused surgery. The overall radical resection rate was 91 % with a recurrence rate of 7.8% after total resection.

Facial nerve function at 1 year was House–Brackmann grade I to II in 76% of patients and grade III or better in 84 % of patients. Hospitalization was shorter than 14 days in 89 % of the cases. All patients with pharyngolaryngeal palsy had sufficient compensation at discharge. Thirty-two vocal cord Teflon injections were performed after surgery to reduce hoarseness and aspiration. There were no cases of intra or postoperative death.

The management of jugular paragangliomas is challenging, highly controversial and evolving. Radical surgery represents our choice in patients with small tumors (C1). For more advanced lesions (C2, C3, C4, D1, D2) we discourage surgery only in patients in precarious general conditions and or older than 65 years old. Over the last decade there has been a shift to partial resection with staged radiosurgery, or to exclusive radiosurgery, but there is a need for more adequate follow-up.

Surgical management of tympano jugular paragangliomas: about 18 cases

Farid Boudjenah[1], Houssem Eddine Bouraba[1], Yacine Moussaoui[1], Tewfik Boutiba[1]

[1]Otolaryngology department of Beni Messous Teaching Hospital, Algiers, Algeria

Aim:

This study aims to relate our experience in the management of temporal paraganglioma at our center.

Material and methods:

A retrospective case review, of 18 patients with the diagnosis of tympano jugular paraganglioma Fish class C and D, that were managed surgically in the period extending from January 2018 and December 2022 at our center. The main approach was the infratemporal fossa approach type A. In 8 patients, the bridge technique was used, in order to preserve the facial nerve function. No preoperative embolization was used.

Results:

There was no perioperative mortality. There were 3 cases of cerebrospinal fluid leak, that was managed conservatively. We observed lower cranial nerve impairment in two cases. There was no residual tumor in the MRI conducted at 6 months of follow-up in 15 cases. The facial nerve was resected in 5 cases.

Conclusions:

Total surgical excision a is the main treatment modality for tympano jugular paraganglioma. However subtotal resection could be considered in cases of advanced age.

Treatment of Temporal Bone Paragangliomas: An Experience from A Single Center in China

Prof. Shixun Zhong

Department of Otolaryngology, The First Affiliated HospitalChongqing Medical University, Chongqing, China

Objective:

To review the outcome of surgical treatment of tympanomastoid paragangliomas (TMP) and tympanojugular paragangliomas (TJP).

Material and Methods:

Fifteen patients with tympanomastoid paragangliomas and tympanojugular paragangliomas were managed surgically between June 2019 and December 2022. The records were retrospectively reviewed. The surgical strategy, outcome and influence factors were studied.

Results:

There were 7 patients with TMP, and 8 with TJP. The TMPs were managed microscopically or endoscopically or in combination. The TJPs were managed microscopically with infratemporal fossa type A approach. Gross-total tumor removal was achieved in all cases. Based on the degree of tumor involvement, facial nerve was managed with various techniques such as Fallopian bridge technique, rerouting of facial nerve and reconstruction with graft. No recurrence was found during the period of follow-up. There was one case of postoperative cerebrospinal fluid leak who recovered with conservative therapy. One case with postoperative hoarseness improved gradually.

Conclusion: TMP and TJP can be successfully managed microscopically or endoscopically or in combination. Surgery is the primary treatment of choice for vast majority of these tumors with high control rate and low complications rate.

Our strategy and results in management of extensive jugular foramen paraganglioma

Hao Wu, Zhanyan Wang

1. Department of Otolaryngology, Head & Neck Surgery, Shanghai Ninth People's Hospital, affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China
2. Ear Institute, Shanghai Jiaotong University School of Medicine, Shanghai, China
3. Shanghai Key Laboratory of Translational Medicine on Ear and Nose Diseases, Shanghai, China

Objective:

Jugular foramen paraganglioma (JFP) is a highly vascular lesion. The primary therapeutic option for JFP is complete excision of tumor with preservation of vital neurovascular structures. The infratemporal fossa type A (IFTA-A) approach has been advocated as the classical surgical management of JFP which required facial nerve rerouting and resulted in different degrees of permanent facial palsy in most patients. The purpose of this study was to present the outcomes of the IFTA-A and the modified IFTA-A in different JP classes, and to discuss their indications.

Methods:

We retrospectively reviewed 136 patients with JFP Fisch type C/D operated at our center between January 2017 and December 2021 using IFTA-A (FN total anterior rerouting) or modified IFTA-A (FN partial anterior rerouting or fallopian bridge technique). The treatment outcomes of JP treated with IFTA-A and modified IFTA-A were compared.

Results:

The modified IFTA-A was used for C1/C2/partial C3 (the beginning of horizontal ICA involved) tumors (76.5%,104/136), and IFTA-A is used for the other partial C3 (the distal part of horizontal ICA involved)/C4 tumors (23.5%,32/136). The average follow-up duration was 40.5 months (13-72months). Gross total tumor removal was achieved in 96.3% (131/136) patients, near-total removal in 3.7% (5/136) cases, and there was evidence of recurrence in 4.4% (6/136) of the JFP. There was no perioperative mortality. The patients who received a modified IFTA-A presented significantly better HB I-II FN function (95.2%,99/104) at 1 year after surgery than those with the IFTA-A (62.5%,20/32, $P < 0.05$). The other main results of modified IFTA-A and IFTA-A were compared and no significant differences were observed in tumor recurrence, lower cranial nerve dysfunction and CSF leak.

Conclusion: Modified IFTA-A is a safe and effective surgical treatment for C1/C2/partial C3 JFP. Compared with the standard IFTA-A, this approach brings significantly better results in terms of facial nerve function after surgery, and its indication mainly depends on the extent of tumor invasion of ICA.

Key words: Jugular foramen, paraganglioma, surgical management, IFTA, facial nerve.

Surgical treatment and effect evaluation of tympanojugular paraganglioma with 34 cases report

Prof. Zhaohui Hou

The Chinese PLA General Hospital, Beijing, China

Introduction:

The aim of this study was to show our experience in the management of tympanojugular paraganglioma.**Methods:** This was a retrospective study of paragangliomas diagnosed between 2016 and 2022. A total of 34 patients with 36 tumours were analysed. The cases of paragangliomas included in this group were totally jugulotympanic tumours.

Results:

Mean age at diagnosis was 43.1 years; 19 patients were female (55.8%) and 15, male (44.2%). Multifocality was present in 3 patients (8.8%). Surgery was performed on 36 isolated paragangliomas: these were 7 tympanic, 29 jugular paragangliomas. Of class C1, C2, C3, and C4 tumors, we found 4 (11.1%), 20 (55.5%), 3 (8.3%), and 2 (5.5%), respectively. 12 (33.3%) tumors had intracranial extensions and 1 (2.7%) involved the vertebral artery. A single-stage procedure was adopted in all 36 (100%) tumors. The transcanal endoscopic approach was used in all tympanic paragangliomas cases, And the infratemporal fossa type A approach was used in all jugular paragangliomas cases. In 1 patients (2.9%), an intra-arterial stenting of the internal carotid artery was performed. Total tumor removal was achieved in 32 cases, and Gross-total tumor removal was achieved in 2 cases (5.5%). Postoperative cranial nerve deficits in isolated jugular paragangliomas were 34.1%. Nerve deficit was found more frequently in tumours with intradural extension (100%) than in extradural tumours (32.2%).

Conclusions: Management of tympanojugular paraganglioma may need a logical decision-making process, and benefits and potential risks of all treatment options should be taken into consideration for every individual patient.

Keywords: facial nerve; infratemporal fossa approach; lower cranial nerves; tympanojugular paragangliomas.

“Rerouting or not rerouting” the facial nerve in jugular paragangliomas

Miguel Arístegui

ENT Department, Hospital General Universitario Gregorio Marañón, 28007 Madrid, Spain

In 1989 Ugo Fisch described the Infratemporal Fossa Approach Type A for the management of Jugular Paragangliomas (YPG). Since then, the need of rerouting the facial nerve has been a matter of debate in the surgical community. Those against rerouting the facial nerve argued that you can obtain enough internal carotid artery (ICA) control without doing so. And those defending rerouting reply that there is not enough control not only of the ICA but of the apical and clival extension of the tumor and so there is a higher risk of residual. We believe that ***anterior partial permanent rerouting of the facial nerve*** is necessary in many cases of YPG. But acknowledge that there may be cases in which rerouting may be avoided and help obtaining a better functional result.

We would like to discuss the topic through selected videos from certain cases and open a debate that is still going on.

Surgical innovations in management of paraganglioma in the jugular foramen

Chunfu Dai

Department of Otorhinolaryngology, Fudan University Eye and ENT Hospital, Key Laboratory of Auditory Medicine of the National Health Commission, Shanghai, 200031, China

Background:

Intraoperative inferior petrous bleeding and postoperative facial paralysis are great challenge to skull base surgeons in surgical management of patients with paraganglioma in the jugular foramen. In addition, radiographic definition of extrabulbar tumor of paraganglioma is not established. To compare the safety and effectiveness of surgical treatment of jugular paragangliomas (JPs) following the application of our innovation surgical techniques.

Methods:

In our clinic practice, tension free anterior facial nerve rerouting and tunnel packing of the inferior petrous sinus were applied. Fifty-six patients with JPs were analyzed for tumor classification, surgical outcomes, and intratumor blood vessels.

Results:

MRI TW1 and MRI with enhancement sequences were statistically significant in the diagnosis of tumor growth patterns in term of ROC curve analysis(Area=0.833, P＜0.05). The gross total resection in C1-2 (100%) was significantly greater than that in C3 and D (66.7%). The presence of postoperative good facial nerve (FN) function House-Brackmann (HB) I-II in C1-2 (89.5%) was not significantly different from C3 and D (93.3%) (P =0.694). The presence of preoperative and postoperative lower cranial nerve (LCN) deficits was correlated with the Fisch classification of tumors (P<0.05), and more intraoperative blood loss was demonstrated in advanced tumors (P=0.050). Further study showed that the cross-sectional area of intratumor blood vessels was positively associated with intraoperative blood loss (P<0.001).

Conclusions: Recognition of extrabulbar or intrabulbar growth patterns preoperatively are essential to design optimal surgical strategy and minimize postoperative complications. Surgical excision of JPs is a safe and effective strategy, and early surgical treatment is a good option for patients with C1-2 tumors without surgical contraindications.

Surgery of D3 intradural tympano-jugular paraganglioma

E. Zanoletti, D. Cazzador, D. d'Avella, A. Mazzoni

Section of Otorhinolaryngology-Head and Neck Surgery, Department of Neurosciences, University of Padova, 35128 Padova, Italy

Objective:

Surgery of large intradural tympanojugular paragangliomas (TJ-PGs) into the cerebellopontine angle is a surgical challenge, representing an infrequent condition with extensive involvement of vessels and brainstem. These tumors are often deemed as inoperable, but the current classifications lack accuracy for defining the operability or inoperability of large intradural TJ-PGs. In this work we retrospectively revised some large intradural T-J PGL, which were classified as D3 and operated on but could otherwise have been judged as inoperable. Operability criteria, treatment strategies, and resection techniques are herein discussed to face this infrequent condition. METHODS: Over a series of 65 class Di (intradural) TJ-PGs operated on between 1975 and 2015, the cases with large D3 intradural tumors were retrospectively reviewed. The strategy of treatment was reappraised to focus on how large intradural tumors and at-risk surgery could be modified into a feasible although demanding procedure. The surgical outcome at long term F UP was analyzed. RESULTS: Seven patients over 65 intradural Tj-PGL presented with large intradural tumors, ranging from 4 cm to 5.5 cm in diameter. These cases were treated either via a petro-occipital trans sigmoid approach in a single-stage resection (4 patients) or via a petro-occipital approach as a second-stage surgery after a previous infratemporal fossa approach on the extradural tumor (3 patients). The intradural large tumor presented critical contact, in one case dubious encasement, with the vertebral artery. Complete tumor resection was obtained in 5 cases, residual tumor was in the remaining two. No new postoperative cranial nerve losses were observed. The surgical procedure was aborted in 2 cases because of cerebellar edema and carotid artery tear, respectively, with no sequalae. DISCUSSION AND CONCLUSION: These few cases over a larger series of intradural TJ PGL offer the possibility to evidence and discuss the surgical strategy on large and otherwise-deemed-inoperable tumors, which applied a fundamental principle of skull base surgery. A wide surgical extradural approach was performed, through extensive removal of the petro-occipital skull base and exposure of the dural root of the tumor. The dural root and the extradural component are known to carry the main blood supply to the intradural tumor and the preemptive hemostasis of the extradural and dural roots allowed to proceed, in the same stage or in a staged-procedure, with the resection.

Staged Removal of Intradural Paragangliomas: The Gruppo Otologico algorithm

A. Taibah, G. Fancello, M. Sanna

Gruppo Otologico, Piacenza, Italy

Paragangliomas are rare, vascular, slow growing tumors that arise from the paraganglionic system associated with vascular and neuronal adventitia. The majority of paragangliomas are benign, locally agressive tumors and they tend to infiltrate into the adjacent tissues. Depending on origin, the route of spread are highly variable.

The tympanojugular paragangliomas were divided into class C and D (FISCH classification), were C indicated the carotid artery involvement by the tumor and D its intracranial extension, De (extradural) and Di (intradural). The intradural component was further divided according to tumor size into Di1< 2cm, and Di2> 2cm.

Some authors advocate that, with a multidisciplinary approach and meticulous closure, resection should be performed in a single stage regardless of the size of the intradural tumor.

We have a different opinion regarding this statement, since we staged the surgery in 48% of our Di2 cases. In this study we present our algorithm on When? and Why? a staged procedure is performed.

Management of the So-Called Inoperable Tympanojugular Paragangliomas: The Gruppo Otologico Experience

Mario Sanna

Gruppo Otologico, Piacenza, Italy

Head and Neck Paragangliomas are rare tumors that, due to anatomic location and the close relationship with neurovascular structures, pose significant challenges to surgical treatment. In the last decades, we assisted in the continuous progress of surgical techniques, particularly in Skull Base Surgery, which allows the treatment of tumors previously regarded as inoperable.

Over the years, the Gruppo Otologico has built a considerable experience in the surgical management of tympanic, tympanomastoid and tympanojugular paragangliomas, with over 450 cases operated up to date.

A thorough study of the tumor characteristics has allowed us to modify the Fisch classification and develop a new management algorithm, with the aim of guiding the surgeon in the decision-making process. Moreover, the standardization of surgical approaches has made complete excision of the tumor possible, with a higher rate of facial and lower cranial nerve function preservation.

In our clinical practice, we have also introduced, the management of the internal carotid artery as a crucial part of pre-operative work-up. Nowadays, by means of stent positioning through interventional radiology procedures, it is possible to perform a safe and complete removal of paragangliomas involving the internal carotid artery, in the past considered unresectable, avoiding life-threatening hemorrhage and carotid blowout.

During the lecture, the management of “so-called inoperable” tympanojugular paragangliomas would be illustrated step-by-step.

Infratemporal Type "A" approach: Refinements and Surgical Technique

Maurizio Falcioni

Department of Otorhinolaryngology and Otoneurosurgery, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy

Introduction of the Infratemporal type A approach by Hugo Fisch in the 80s has revolutioned the approach to the jugular foramen area. With time some steps of the approach have been progressively refined and modified with the target to make the approach easier and reduce the surgical risks. In the presentation the Author will discuss the following steps: blindsac closure of the external auditory canal; facial nerve rerouting; closure of the sigmoid sinus; dissection of the jugular vein; intra-bulbar tumor dissection. The final technique presently adopted at the ENT and Otoneurosurgical Department of Parma, is slightly different from the original Fisch description and is a combination of the experience acquired from the Author in his years spent at the Gruppo Otologico of Piacenza and some refinements personally adopted in the last years in Parma.

Tumor Progression in Tympanojugular Paragangliomas: The Role of Radiotherapy and Wait and Scan

Giuseppe Fancello[1,2], Virginia Fancello[1,3], Gianluca Piras[1], Mario Sanna[1]

3. Gruppo Otologico, Piacenza, Italy.
4. Department of Otorhinolaryngology, Careggi University Hospital, Florence, Italy.
5. Ear Nose and Throat & Audiology Unit, Department of Neurosciences, University Hospital of Ferrara, Ferrara, Italy.
6. Audiology Unit, Department of Specialistic Surgical Sciences, IRCCS Cà Granda Foundation, Policlinic of Milan, Milan, Italy.

Tympanojugular paragangliomas (TJ PGLs) are rare tumors characterized by bone infiltration and erosion and a close relationship with critical structures such as cranial nerves and internal carotid artery. For these reasons, their management represents a tough challenge. Since the fifties, radiotherapy (RT) has been proposed as an alternative treatment aimed to avoid tumor progression. However, the indolent nature of the tumor, characterized by slow growth, is a crucial factor that needs to be considered before offering radiation.

This study aims to examine tumor progression in RT patients through a systematic review of literature. In addition, we reviewed the cohort of TJ PGL patients who underwent solely wait and scan at Gruppo Otologico.

The rate of tumor progression identified in the RT and wait and scan groups were 8.9% and 12.9% respectively. These outcomes suggest the innate slow growth of PGLs. However, it is not possible to draw certain conclusions because of the wide heterogeneity of the studies. Thus, when complete surgical excision of TJ PGLs is not feasible, appropriate counseling and patient selection, including comprehensive tumor classification, should be performed before proposing RT for controlling tumor progression, since wait and scan may represent a reasonable option in selected cases.

Clinical outcomes for patients undergoing radiotherapy to head and neck paragangliomata: single institution retrospective review

Fatima Ali, Gemma White (joint first authors), Anand Velusamy, Paul Carroll, Barbara McGowan, Phil Touska, Fahim-Ul Hassan, Louise Izatt, Rupert Obholzer, Mary Lei (last author for correspondence)

Neuroendocrine Tumour Multidisciplinary Team, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom

Aims/Objectives:

Surgical excision of head and neck paragangliomas (HNPGL) is associated with a risk of permanent cranial nerve dysfunction. Highly conformal radiotherapy (RT) techniques have facilitated improvements in treatment morbidity, with radiation becoming increasingly utilised for this indication. We report outcomes for patients with HNPGLs treated with RT at a large tertiary referral centre.

Methods:

Data from patients with HNPGL treated with RT between 2010 and 2022 were collated. All cases had been reviewed by a specialist neuroendocrine tumour multidisciplinary meeting. Patient demographics, tumour characteristics, RT treatment and outcomes were extracted from medical records.

Results:

Data were collected for 45 patients with 54 HNPGLs who received RT. Demographics, presentation, tumour, and RT details are summarised in Table 1. Median (range) follow-up since RT was 45 (6-221) months. Stereotactic radiosurgery (SRS) was delivered by linac (23 patients) and gamma knife (2 patients). The remaining 23 patients received conventional fractionated intensity modulated radiotherapy (cIMRT). One-year follow-up imaging was available for 36 patients with 45 tumours: maximal tumour diameter was stable in 20/45 (44%), reduced in 24/45 (53%) and increased in 1/45 (2%). Of the 24 tumours that reduced in size, 9/24 (38%) had received SRS and 15/24 (63%) received cIMRT.
Symptomatic improvement was reported in 50% of patients (SRS 60% and cIMRT 43%).
Acute and late adverse effect (AE) data were collated. 16/45 (36%) had at least one grade 2 acute AE. The most frequent grade 2 acute AEs were dysgeusia (8/45, 18%), anorexia (7/45, 16%) and throat pain (6/45, 13%). No grade 3 acute AEs were observed. 10 patients (10/45, 22%) experienced at least one late AE persisting 3 months following RT. The most frequent late AEs were xerostomia (9/45, 20%) and dysphonia (4/45, 9%). One patient (2%) developed osteoradionecrosis following previous extensive surgical excision involving major vessels. No patients treated with SRS experienced late AEs.

Conclusion: RT delivered as either SRS or cIMRT can provide local tumour control with symptomatic improvement and acceptable treatment-related morbidity. RT should be considered as an alternative to surgical excision, particularly in the context of slow-growing tumours, advancing age or patient preference. Patients with HNPGL benefit from management delivered by a multidisciplinary team including both surgical and oncological expertise.

Table 1

Characteristic	Patients (n=45)	
	Number	%
Male	12	27
Female	33	73
Age (years): median (range)	50 (26-82)	
Family history HNPGL	11	24
Mutation	19	42
SDHB	9	20
SDHC	3	7
SDHD	7	16
Presenting symptoms		
Tinnitus	20	44
Dysphonia	16	36
Neck mass	13	29
Hearing loss	12	27
Multiple tumours	5	11
Total tumours	54	
Carotid body	7	13
Vagal	18	33
Jugular	19	35
Jugulotympanic	8	15
Skull base	2	4
Tumour size (mm): median (range)	31 (12-88)	
Radiotherapy intent		
Primary treatment	35	78
Following surgical resection (median 13 (range 1-24) years since surgery	10	22
Radiotherapy indication		
Growing tumour	18	40
Symptomatic	16	36
Risk of surgery to nerve function	13	29
Radiotherapy technique		
SRS	25	56
cIMRT	23	51

Stereotactic Radiosurgery for Temporal and Neck Paragangliomas: a Single-Center Retrospective Experience over 25 years

Lorenzo Yuan, MD; Antonio Meola, MD, PhD, Wei Deng, Rong Lu, PhD; Elaheh Shaghaghian, MD; Kuan-Nien Chou, MD; Matthew Fitzgerald, PhD; Nikolas Blevins, MD; Steven D. Chang, MD

Clinical Assistant Professor of Neurosurgery, Clinical Assistant Professor of Otolaryngology, Head and Neck Surgery (by courtesy), Department of Neurosurgery, Stanford University, School of Medicine

Aims and Objectives:

Temporal and Neck Paragangliomas (TNPGs) are rare, mostly benign neuroendocrine tumors traditionally treated with surgery. Stereotactic Radiosurgery (SRS) is non-invasive highly-focused radiation treatment widely used to treat tumors of the head and neck. The present study aims to determine the long-term clinical and radiological outcome of TNPGs treated at a single institution.

Materials and Methods:

After Institutional Review Board approval, a single-institutional retrospective study was conducted including 44 patients with 50 TNPGs, treated with Cyberknife (Accuray, Sunnyvale, CA) SRS between 1998 and 2022. In the cohort, 30 patients (68.2%) were females, 5 (11.4%) had genetic syndromes, 2 (4.5%) had catecholamine secretion. SRS was performed for recurrent or residual TNPGs, in 3 (6.8%) and in 5 (11.4%) patients, respectively. The most frequent presenting symptoms were tinnitus in 26 (59.1%) patients, lower cranial nerve dysfunction in 17 (38.6%) patients, and vertigo in 7 (15.9%) patients. Facial function was intact in 43 patients (97.7%). Hearing function was AAO-HNS class A in 32 (72.7%) patients. TNPGs included 33 tympanojugular (TJP), 13 carotid body (CBP) and 4 glomus vagale (GVP) paragangliomas. SRS was delivered by a median margin dose of 20 Gy in a median of 2 fractions to a median target volume of 8.6cc, with a median isodose line of 79%. The median clinical and radiological follow-up was 69.8 and 73.3 months, respectively.

Results:

Local tumor control was achieved in 49 (98%) TNPGs, without statistically significant difference between TJP and neck paragangliomas. Size decreased in 41 (82%) TNPGs, with a median volumetric change speed of -1.3 cc/year. Progression occurred in 1 CBP (2%) with a volumetric change speed of 0.7 cc/year, but no further treatment was required. The median progression-free survival (PFS) was 72.4 months. The median overall survival (OS) was 71.9 months. Adverse Radiation Effects (ARE) occurred in 2 tumors, although were asymptomatic and further treatment was not required. Symptomatic control, including improved and stable symptom severity, was achieved in 92.3% of cases with tinnitus, in 100% of cases with lower cranial nerve dysfunction and in 85.8% of cases with vertigo. Facial nerve function remained intact in 42 (95.5%) patients, while hearing function remained AAO-HNS class A in 33 (75%) of patients.

Conclusions: Hypofractionated SRS allows for excellent local tumor control (98%), sustained over long-term follow-up. The symptomatic outcome is excellent in terms of tinnitus, vertigo, and lower cranial nerve dysfunction. Hearing and facial nerve function remains preserved in most cases. ARE were extremely rare, asymptomatic and did not require treatment.

Radiotherapy of head and neck paragangliomas: treatment differences based on extension and localisation

Viola Salvestrini [1,2]

[1] Radiation Oncology Unit, Cyberknife Center, Istituto Fiorentino di Cura e Assistenza, Florence, Italy
[2] Radiation Oncology Unit, Azienda Ospedaliero-Universitaria Careggi, University of Florence, Florence, Italy

Paragangliomas (PGs) are slow-growing neoplasms accounting for less than 0,5% of all head and neck tumors. PGs are commonly benign entities which usually affect young patients. Carotid body tumors are the most common type among head and neck PGs, followed by jugular, tympanic, and vagal PGs. The optimal management of PGs depends particularly on the patient's characteristic, size and location of PG. Historically, surgery has been the main approach even if it is associated with high morbidity caused by the common proximity of the PG with critical neurovascular structures. Furthermore, definitive radiation therapy (RT) or subtotal resection followed by adjuvant RT or stereotactic radiosurgery (SRS) is a feasible and effective treatment option which demonstrates high rates of local control and may preserve neurological function. Although no randomized trials have compared these two approaches, RT is usually performed as an alternative option to surgery with the purpose to stop the progression of symptomatic disease. Indeed, conventional fractionated external beam RT has been adopted for treatment of benign head and neck PGs since 1950, with 95% of local control rate with minimal morbidity and low complication rate. Overall, SRS showed a local tumor control rate of approximately 94% with no difference in terms of SRS technique. However, there is limited data based on large cohorts of patients that could guide the treatment algorithm of head and neck PGs due to the rarity of these tumors. Hence, the purpose of this lecture is to provide an overview of RT of PGs and to report on a single-center case series of patients treated with robotic SRS.

Stereotactic Radiosurgery Outcomes for Jugulotympanic Paragangliomas and Treatment Algorithm

Olivia Kalmanson, MD, MS; Emily Bacalao, MD; Madeline Olson, BA; Olivia Ovard, BS; and Stephen Cass, MD

Department of Otolaryngology, The University of Colorado School of Medicine, 12631 E 17th Ave, Aurora, CO 80045, United States

Objective:

To evaluate outcomes of stereotactic radiosurgery (SRS) outcomes for treatment of jugulotympanic paragangliomas (JT PGL).

Methods:

IRB approval and informed consent were obtained. A prospective study of patients with JT PGL undergoing SRS by a single surgeon, at a single institution 2003-2020 was performed. Patient demographics, SRS parameters, tumor characteristics, audiologic examinations, and clinical symptoms were collected.

Results:

A total of 29 patients underwent single-session SRS for JT PGL during the time period, 21 female, 8 male. The average age at treatment was 56±12y (35-83). Up-front SRS was performed in 20 patients (69%) and salvage in 9 (31%), with an average dose 15.1±0.4Gy (14-16, n=28). All patients had Fisch C (82.8%) or D (17.2%) tumors with an average volume of 6.13±2.88cc (2.45-13.62, n=28). With radiographic follow up of 68±50mos (9-211, n=24), 87.5% of tumors never exhibited radiographic growth after SRS, 12.5% demonstrated enlargement at some point, and 0% demonstrated progressive or sustained growth. There was no significant difference between Fisch C and D tumor stability over time. Clinical failure occurred in 1 patient, characterized by progressive facial nerve paresis requiring surgical intervention. With clinical follow up of 77±54mos (1-212, n=19), 9 patients (47.3%) exhibited pulsatile tinnitus pre-SRS. Of those 9 cases of pulsatile tinnitus, 8 (88.9%) resolved post-SRS, while 1 (11.1%) persisted. The median time to pulsatile tinnitus resolution was 15mos. Eleven patients had serviceable hearing pre-SRS with audiologic follow up of 99±63mos (9-204). Hearing was preserved in the treated ear for an average of 63.2±45.7mos (0-137). Hearing declined over time after 5 years in the treated ear, but the decline was not statistically significantly different from that of the untreated ear. Hearing preservation appears better than published results for SRS treatment of vestibular schwannoma despite higher cochlear doses.

Conclusion: SRS is an effective treatment for JT PGL resulting in radiographic tumor stability, improvement in pulsatile tinnitus, and hearing preservation. Our results support the growing body of literature on JT PGL outcomes which led to the treatment algorithm we use at our institution. This algorithm proposes radiotherapy be the primary treatment modality for Fisch C and D tumors, except in several specific circumstances (SDH B mutation or metastatic tumor, secreting tumor, intracranial mass effect, failed prior RT, pre-treatment facial nerve paralysis).

Radiological Anatomy of Parapharyngeal Space (PPS)

Prof. Roberto Maroldi

Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, ASST-Spedali Civili, Brescia, Italy

The PPS has an inverted pyramid shape with its base against the base of the skull and an inferior apex at the junction of the posterior belly of the digastric muscle and the greater cornu of the hyoid bone. There are two definitions of the PPS in radiological literature, and the radiologist and surgeon at each institute need to understand each other's nomenclature.

The suprahyoid neck spaces are classified by Harnsberger based on the splitting of the layers of deep cervical fascia. The PPS is the fat space lateral to the pharynx (enclosed by the middle layer of cervical fascia and posteromedial to the masticator space (MS). The carotid sheath and the neural structures inside (posterior to the styloid process) are defined as the "carotid space (CS)". According to this view, the PPS contains fat, the pterygoid venous plexus, and the ascending pharyngeal artery.

In the definition by Som and Curtin, the space posteromedial to the MS is divided by the tensor-vascular styloid fascia into two compartments: an anterior pre-styloid compartment and a posteriorly located post-styloid compartment. The pre-styloid compartment contains fat, the deep lobe of the parotid, the ascending pharyngeal artery, and the pterygoid venous plexus. Nodes and muscle are not included in this radiological definition of prestyloid PPS. Neurovascular structures such as the internal carotid artery, internal jugular vein, sympathetic chain and superior cervical ganglion, cranial nerves IX, X, XI, and XII, as well as paraganglionic tissue, are in the post-styloid compartment. The CS in the Harnsberger definition corresponds to the post-styloid or retro-styloid PPS. The stylo-pharyngeus muscle runs in front of the ICA to blend into the constrictor muscle: behind its long sling and medial to the ICA are located the retro-lateral-pharyngeal nodes and the superior cervical ganglion.

Surgical anatomy of the parapharyngeal space

Wenlong Tang MD

Changzhi Medical College Affiliated Heping Hospital, Shenzhen ENT Institute, Changzhi Medical College, China

The parapharyngeal space is divided by the styloid diaphragm in pre- and poststyloid compartments. The poststyloid compartment of the parapharyngeal space (infrapetrosal space) is located behind the styloid fascia, below the petrous bone, and medial to the mastoid process. The foramina in the infrapetrosal space connecting the intra- and extracranial spaces are the jugular foramen, external opening of the carotid canal, stylomastoid foramen, and hypoglossal canal. The extracranial segments of the VII, IX, X, XI, XII cranial nerves are initially contained in this area as well as the sympathetic trunk. The main vascular structures are the internal carotid artery and the internal jugular vein. The classical approach to the infratemporal fossa and parapharyngeal space is performed through a retroauricular incision with different modifications that usually involve mastoidectomy. This session thoroughly reviews the surgical anatomy of these regions through anatomical dissections and the key anatomical landmarks for lateral skull base approaches. Knowledge of these anatomical relationships is of essential importance to approach lesions safely and successfully.

Vagal paraganglioma

Elisabetta Zanoletti, Stefano Concheri, Antonio Mazzoni

Otoneurology and skull base surgery section, ENT Department, University Hospital of Padova

Vagal paragangliomas are rare tumors that develop in the carotid space or retrostyloid compartment of the parapharyngeal space. They arise from islands of paraganglion tissue derived from the neural crest that is located on the vagus nerve, both in its cervical aspect and in the jugular foramen. They account for 5% of all head and neck paragangliomas with an annual incidence of 1 per 100,000 population, with a female predominance. Vagal paraganglioma can be solitary, bilateral, and either unilateral or bilateral associated with multiple paragangliomas. The incidence of multifocal tumors in patients without a family history is around 10%, whereas the incidence of multiple paragangliomas rises to 30 to 40% in those with a positive family history. Familial cases account for 40 to 50% of vagal paragangliomas. Recent studies showed paragangliomas with genetic basis linked to a double mutation occurring in chromosome 11, where the tumor suppressor PGL-1 gene is located. Other PGL-2,3,4 categories have been recently discovered.

The growth of these tumors is very variable: some grow upward toward the skull base while others extend down into the neck. Treatment planning for these patients is challenging and the major dilemma is the choice between surgery and observation. Radiotherapy as a realistic alternative lacks an evidence base. The decision must be based on several factors that include the age of the patient, the preoperative status of the vagus, the size and growth rate of the tumor. There are some basic facts that should be considered before balancing pro and contra of each option:

1. The natural morbidity of and vagal deficits is better tolerated than that caused by surgery.
2. The elderly do not compensate well for vagal deficits.
3. Large tumors may inflict other cranial nerve deficits.

The experience of our group on cervical vagal paraganglioma accounts for 24 primary tumors, and our indications to surgery relate to the afore mentioned categories. Microsurgical technique was always applied and provided excellent results but the vagus nerve preservation.

Surgical Resection of Carotid Body Tumors with and without Embolization

Prof. Dan M Fliss MD Facs

Department of Otolaryngology, Sackler School of Medicine, Tel Aviv University, Israel

Head and Neck Paragangliomas (HNPGL) are a rare and diverse tumor entity arising from non secretory head and neck parasympathetic ganglia. They account for 0.6 % of head and neck tumors. This is in contrast to paragangliomas in other areas of the body, which usually arise from secretory sympathetic ganglia and produce catheocolamines.

HNPGL are classified according to their anatomical location with carotid body tumors (CBT) being the most common location followed by Jugulo tympanic HNPGL and vagal PGL surgery is the gold stand and for curative treatment of resectable CBT's and is recommended in otherwise healthy patients because of the risk of local complications related to the tumors size and a very small but definite risk of malignancy. Because of their high vascularity preoperative selective angiography with embolization may help to reduce tumor size, bleeding and other operative complications thus facilitating resection. However, the need for preoperative embolization remains controversial because most of the tumor many feeding vessels arise from the adventitia of the carotid artery which cannot be adequately embolized.

This topic reviews our own treatment protocol for GPT's with special reference to preoperative Embolization.

The novel method and efficacy of the same-day preoperative embolization and surgical resection of carotid body tumors

Katsunori Katagiri

Department of Otolaryngology Head and Neck surgery, Iwate medical university school of medicine, Morioka, Japan

Objectives:

Carotid body tumor (CBT) locates in close contact to bifurcation of the carotid artery and has hypervascular network supplied by many feeding arteries. These features of the CBT make the surgical resection exceedingly difficult with much blood loss and prolonged operation time. There are some reports about preoperative embolization of CBT, but their interval time from embolization to surgery are mostly more than 24 hours. In our institution surgical resection is carried out routinely within 3 hours following the preoperative embolization. In this study we evaluate the efficacy of our procedure by analyzing the blood loss and duration of carotid body tumor (CBT) surgery following same-day preoperative embolization.

Methods:

We reviewed the medical records of subjects retrospectively. Twenty-one patients with 22 CBTs were enrolled in this study. Our same-day procedure comprises preoperative embolization of the feeding arteries in the morning followed by surgery within 3 hours after the embolization is completed.

Results:

The mean operative time and the mean amount of blood loss were 177 min and 36.9 ml, respectively. Since 4 patients underwent resection of the carotid artery and reconstruction, operation time and blood loss were increased in these patients. We found that 18 CBTs had more than 3 feeding arteries. Almost all the postoperative complications, mainly cranial nerve paralyses, resolved within months after surgery.

Conclusions: Our same-day procedure is a safer and superior alternative to traditional CBT surgery, having good outcomes.

Interventional Neuroradiological Management of the Ica in patients affected by Tympano-Jugular, Vagal and Carotid Paragangliomas

R. Menozzi, G. Capurri

Presurgical endovascular management of the internal carotid artery (ICA) is indicated in very extensive jugular-tympanic, vagal and carotid paragangliomas. These tumors can envelop, determine stenosis and erosion of the ICA canal and are vascularized by ICA hypertrophic afferents.
The endovascular management consists of two types of procedures.
The first is the permanent occlusion of the ICA following an occlusion test; the second, in absence of adequate compensation, is represented by the reinforcement of the vessel wall with a stent.
In AOU Parma, we've treated 168 patients between January 1992 and December 2022.
116 of these patients underwent ICA occlusion with balloon, coil or plug, while the remaining 52 underwent ICA stenting.

Regard ICA permanent occlusion we had five complications. Two of these were intraprocedural, the first occurred in the first patient treated as a consequence of ICA dissection with thromboembolism in the middle cerebral artery (MCA); the other was a thromboembolism of a branch of the MCA without permanent sequelae. We had an early complication due to ischemic hemodynamic suffering.
The last two were late complications, in particular in a case a year later, caused by platelet aggregates formed in the residual ICA segment upstream of balloon placement, leading to a minimal thromboembolism.
Another one was represented by a ruptured anterior communicating artery aneurysm due to flow alteration.
Regarding patients treated with ICA stenting we didn't have any complications.

Microsurgery in Carotid Paraganglioma

Elisabetta Zanoletti, Stefano Concheri, Antonio Mazzoni

Section of Otorhinolaryngology-Head and Neck Surgery, Department of Neurosciences, University of Padova, 35128 Padova, Italy

The aim of this study is to describe the surgical technique for carotid paraganglioma microsurgical excision, developed by our group over more than 35 years, as well as the underlying surgical anatomy. This study also aims to assess the outcomes of such a microsurgical approach in terms of disease control, complication risk and functional results. A cohort of 29 consecutive carotid paraganglioma cases in 25 patients was sorted out of the overall series of 222 cases of head and neck paragangliomas (174 jugular, 29 carotid, and 18 vagal paragangliomas), No perioperative death, carotid injury requiring repair, or stroke was noticed in this series. No surgical injury or postoperative-onset functional damage of the main trunk of cranial nerves VII to XII occurred. The only nerve lesions were the loss of the lateral branch of the superior laryngeal nerve of the vagus and the descending branch of the hyoglossus in Shamblin 2 and 3 cases. From a disease control standing point, no recurrence was observed over the follow-up in this cohort. The small numerosity and the retrospective study suggest a cautious conclusion, that however cannot disregard the view that microsurgery may be a progress on treatment.

Choosing optimal timing of carotid body tumor removal; 20 years single centre experience

A Schepers MD PhD, H. Alimohammad MD, prof J.F. Hamming MD PhD, P. Marang PhD, prof JC Jansen MD PhD

Department of Vascular Surgery, Leiden University Medical Center, The Netherlands
Department of Otolaryngology/Head and Neck Surgery, Leiden University Medical Center, The Netherlands

Aims:

Surgical removal of CBT's can be challenging and accompanied by serious surgical complications. Moreover, since in general these tumors are benign and without symptoms, optimal timing of surgery is of the utmost importance. Besides the necessity for shared decision making in this type of pathology, tumor size and the presence of proven growth of the tumor are dominant factors in opting for surgery. Here we describe our experience with surgical removal of CBT's in a 25 years window. Surgical technique and complications are described. Furthermore, optimal timing is studied by correlating tumor size with risk of complications.

Methods:

All patients that underwent surgery in the last 20 years were included in this study . Tumor size (in three dimensions; anterior-posterior, cranio-caudal, largest perpendicular plane) and Shamblin classification was determined on pre-operative MRI. Postoperative complications were extracted from our prospective complication registry.
Logistic regression was used to assess which variables were independently associated with nerve injury, including age at surgery, Shamblin classification and those dimensions that captured different aspects of tumor size (rather than measuring the same as shown by high correlations) as possible independent variables.

Results:

In all patients our previously described cranial-caudal technique was used. In the period of 2003-2023, 134 CBT resections were performed in 123 patients. Bilateral CBT's were found in 59 patients but only 11 patients underwent bilateral resection. Tumors had a largest diameter of 3.0 cm (1.1- 9.0) and were classified as Shamblin I, II and III in resp 20, 66 and 48 cases. Excessive perioperative blood loss (defined as more than 100 ml) did not occur. Re-exploration due to postoperative hemorrhage was necessary in was 6 patients. Cranial nerve damage resulted was seen in 34 cases (25.3%), of which the majority (n=19) resolved in weeks. Most frequently damaged nerve was the marginal branch of the facial nerve (n=17) Injury of 2 nerves occurred in 6 cases. The risks for nerve injury increased with larger tumor size and Shamblin classification. Logistic regression analysis showed that the anterior-posterior (AP) diameter significantly increased the odds of a nerve injury, a doubling for every 1 cm increase in AP diameter (odds ratio [95%CI] 2.12[1.29-3.48], P-value = 0.003.

Conclusion: This study shows that CBT's can be removed with acceptable risks of postoperative complications. Measured tumor size in AP plane is a strong predictor for postoperative nerve injury of a CBT resection. This predictor can be used in daily clinic to give insight in operative risks and to properly inform patients of periprocedural risks.

Head-Neck Paragangliomas: Surgery Or Wait-And-See? A Very Difficult Decision

Canu L[1,2,3], Zanatta L[1,2], Santoro R[4], Zamengo S[1], Jance B[1], Martinelli S[1,3], D'Amore F[1], Ercolino T[2,3], Mannelli M[1,3], Maggi M[1,2,3], Rapizzi E[5]

Department of Experimental and Clinical Biomedical Sciences, University of Florence, Florence, Italy

Head and neck paragangliomas (HNPGLs) are rare neural crest derived tumors with benign behavior in most cases.

Paragangliomas can arise as sporadic or as familiar forms. As their size increases, they can compress or infiltrate adjacent neurovascular structures causing neurological symptoms. They are characterized by unpredictable, mostly slow growth. Surgery is a therapeutic option,but might cause neurological deficits. Therefore, the clinical management of affected patients is still controversial.

In a recent study we compared the outcome of surgery versus a wait-and-see approach in 72 patients evaluated between 2000 and 2021 in the Endocrinology Unit of Careggi University Hospital in Florence.

49 patients (Group A) underwent surgery and 23 (Group B) were followed with a conservative approach. The diagnosis of HNPGLs was made on the basis of lesion characteristics assessed by imaging (CT, MRI and angiography) or by histological examination after tumor removal. All patients also underwent genetic testing for mutations in the susceptibility genes. The presence of functional neurological deficits in speech or swallowing, caused by surgery or by tumor growth in time, was assessed via a dedicated Otolaryngologist visit and by administering three questionnaires evaluating voice (VHI) and swallowing (DHI and MDADI) disability. 32 patients completed also a quality of life questionnaire (EORTC QLQ-H&N35). Mean tumor size did not differ between the two groups. The comparison between group A and group B did not show any significant difference in swallowing as assessed by the MDADI test while a significant difference was observed in the VHI and DHI test, suggesting greater neurological disabilities in patients undergoing surgery, as also assessed at the Otolaryngologist visit.

The results of the EORTC QLQ-H&N35 showed no significant differences between the two groups.

Conclusion: The management of HNPGL patients remains challenging for clinicians. This preliminary study, although conducted on a limited number of patients, seems to suggest that a "wait and see" approach might be sometimes preferable to surgical removal of the tumor especially when the tumor has already grown in size over 34 mm.

Head And Neck Paragangliomas: A 16-Year Experience Of A Single Center In Turkey

Gokce Aydemir, Cuneyt Orhan Kara, Ferda Bir, Fazıl Necdet Ardıç

Department of Otorhinolaryngology, Faculty of Medicine, Pamukkale University, Denizli

Aims/Objectives:

We aim to conduct a comprehensive analysis of head and neck paraganglioma cases treated at our tertiary care hospital over a 16-year span (2007-2023), focusing on demographic variables as well as preoperative and postoperative characteristics.

Materials/Methods:

A total of 44 patients diagnosed with paraganglioma through histopathological examination were retrospectively selected and analyzed. 5 patients were excluded from the study due to limited accessibility, resulting in a final sample of 39 patients. The study encompassed various aspects including demographic information, presenting complaints upon admission, preoperative radiological assessments, paraganglioma types, staging at admission, postoperative complications, and cases of recurrence during the follow-up period.

Results:

The female: male ratio was found as 3.55:1, and the mean age of the patients was 54 years. Out of the total cases, 35.9% were identified as carotid body paraganglioma, 25.6% as tympanomastoid paraganglioma, 23.1% as tympanojugular paraganglioma, 10.2% as vagal paraganglioma, 5,2% as other head and neck paraganglioma. Except for 1 case, all cases (97.4%) were benign and non-functional. Over a three-year follow-up period, recurrence was observed in 1 case of tympanomastoid paraganglioma and 5 cases of tympanojugular paraganglioma, accounting for a recurrence rate of 15.4%.

In cases of carotid body and vagal paraganglioma, the most common complaint was the presence of painless mass in the neck, while hearing loss and pulsatile tinnitus in cases of tympanomastoid and tympanojugular paraganglioma. According to the Shamblin staging system for carotid body tumors; Postoperative cranial nerve palsy was observed in 1 patient in stage 2 and 4 patients in stage 3, while none of the patients in stage 1 had nerve palsy. In addition, intraoperative internal carotid artery (ICA) anastomosis was required in 1 patient in stage 3. According to Glasscock-Jackson classification for tympanojugular paraganglioma cases; type 1 and type 2 cases have no postoperative complication while type 3 and 4 cases have higher rate of CN paralysis in the postoperative period. In addition, postoperative vocal cord paralysis was observed in all cases of vagal paraganglioma.

The first of the other head and neck paraganglioma cases was the patient who underwent orbital exenteration and maxillectomy due to paranasal sinus squamous cell carcinoma, and a paraganglioma was found incidentally in the orbital tissue. The second case involved a functional paraganglioma that was initially identified as a neck mass who have also concurrent diagnoses of adrenal gland cancer and lung cancer. Subsequently, it was determined to be a metastatic paraganglioma.

Conclusion: We observed that the average age and male-female ratio were consistent with the findings reported in existing literature. However, we found that carotid body paragangliomas were the most frequently encountered type of paraganglioma in our cases. The location of the tumor plays a crucial role in determining the presenting complaint. Additionally, higher-grade paragangliomas and those located in the vagal region were associated with an increased risk of postoperative cranial nerve palsy. Consequently, it is imperative to utilize preoperative imaging to accurately identify the type and stage of paraganglioma, as this information is essential for predicting potential complications that may arise during the surgical intervention.

Recommendation for the management of head and neck paragangliomas (temporal bone, carotid body and vagal)

Prof Romain Kania MD PhD

Tenured Professor in Otorhinolaryngology, Head & Neck Surgery Lariboisière University Hospital, Greater Paris University Hospitals APHP, Paris University

This presentation provides concise recommendations for managing head and neck paragangliomas, specifically in the temporal bone, carotid body, and vagal according to the latest issues in the literature, the Dutch recommendation and the experience of our institution, Lariboisière University Hospital. It synthesizes current evidence and expert consensus to guide clinicians in treatment, and follow-up. Topics include initial evaluation, diagnostic workup, surgical approaches, and adjuvant therapies. Emphasizing a multidisciplinary approach and personalized care, these recommendations aim to optimize patient outcomes and improve the management of these rare tumors.

Change of paraganglioma treatment in the head and neck

Konrad Schwager[1], Philipp Heine[1], Adnan Moalem[1], Katrin Schulze[2], Nicole Buhl-Heinrichs[3]

[1]Department of Otorhinolaryngology, Head and Neck Surgery, Klinikum Fulda gAG, Academic Teaching Hospital Philipps University of Marburg, Pacelliallee 4, 36043 Fulda
[2]Department of Radiooncology-Radiotherapy, Klinikum Fulda gAG, Academic Teaching Hospital Philipps University of Marburg, Pacelliallee 4, 36043 Fulda
[3]Department of Diagnostic and Therapeutic Nuclear Medicine, Klinikum Fulda gAG, Academic Teaching Hospital Philipps University of Marburg, Pacelliallee 4, 36043 Fulda

The treatment of paragangliomas of the head and neck is very challenging. There is no doubt early disease is the domain of surgery. But most challenging are tumors of the categories C and D according to Fisch classification. Surgical treatment often is accompanied with cranial nerve dysfunction, the facial nerve, and the lower cranial nerves. Swallowing and aspiration following lower cranial nerve dysfunction are major problems postoperatively. We present an algorithm of diagnostic and therapeutic procedures we follow at the Head and Skull Base Center Klinikum Fulda, University Medicine Marburg. In the tumors underwent surgical therapy total resection was achieved for Glomus caroticum 100%, Glomus vagale 90% and Glomus jugulotympanicum type A according to Fisch in 100%, type B 83%, type C 67% and finally the most extended stadium type D in 62%. According to our interdisciplinary concept, watchful waiting, following with MRI-scans, radiation therapy and recently nuclear medicine treatment (peptide receptor radionuclide therapy; PRRT) get increasing importance beyond the aim of total or near total surgical resection. We think that paragangliomas of the head and neck should be more recognized as a chronic disease that should and can be treated. Physicians together with the patient should figure out the personal and individualized treatment modality considering control of disease and quality of life.

The proper role of imaging in staging and surveillance in the management of paraganglioma

Robert Lorenz

Cleveland Clinic, Head and Neck Institute, Cleveland, Ohio, Usa

The recommendations for the frequency of imaging in both paraganglioma cases, as well as succinate dehydrogenase enzyme mutations, has changed significantly over time due to the earlier identification of both gene mutations and smaller tumors. The uses of imaging are multiple, including screening for tumors in the case of gene positivity, detecting progression of disease at the untreated primary site, checking for recurrence of treated tumors, detecting a second primary tumor, as well as both regional and distant metastases. More conservative recommendations have become more prevalent recently. This presentation will focus on new literature from the speakers' group in Cleveland, Ohio, produced for observation data from hundreds of paraganglioma and SDH mutation patients with serial imaging over decades.

Follow up of paragangliomas

Jeroen Jansen, Erik Hensen, Abbey Schepers on behalf of the Paraganglioma Group Leiden

Paraganglioma Group, Leiden University Medical Center, Leiden, The Netherlands

There are 3 reasons to follow patients with head and neck paragangliomas:

1. genetic predisposition
2. current paragangliomas
3. post-surgery

1. Most patients with a genetic predisposition for paragangliomas have a SDHx mutation. The penetrance of the disease is age dependent and very variable. With a lifetime risk of 100%, carriers of a paternally inherited SDHD mutation have the highest risk. However, paragangliomas develop slowly and do not need immediate treatment when diagnosed. We consider MRI of the head and neck and mediastinum, with a 5-year interval, sufficient for follow up of parasympathetic paragangliomas. Alternatively, screening when symptoms arise could be promoted in elderly patients or when the access to health care is low. Screening for sympathetic paragangliomas is more complex and in our practice is individualized. Catecholamine excess is currently monitored with annual or bi-annual serum values. Non secreting paragangliomas can be diagnosed with CT-scan, MRI or PET-CT using somatostatin analogues. Because there also is a reason to screen for the rare associated renal cell carcinoma and GIST tumors we usually choose for MRI.
2. Patients with head and neck paragangliomas seldom have an immediate indication for treatment. Most patient will first be followed with annual MRI. If no indication for treatment arises in the first couple of year of follow-up, we will individualize the screening-interval depending on the symptoms, the size and location of the tumor and the need of the patient. In clinical practice this means that many patients with stable, or very slow growing, tumors are followed with longer intervals or even refrain from MRI scans unless they develop symptoms. In many cases however, the risk of developing new paragangliomas is an additional reason to maintain follow-up of the entire head and neck region. We do not routinely screen for metastatic paragangliomas. We do not stop follow-up after radiotherapy, although, in our experience, it often results in a growth arrest.
3. After radical surgery there is no need for follow-up in sporadic cases of paraganglioma. Patients with residual disease are followed according to paragraph 2. Patients that have a genetic predisposition are followed according to paragraph 1.

Functional outcomes of surgery and long-term results in paraganglioma surgery

Thomas Lenarz[1], Riccardo Di Micco[1]

[1]ENT Department, Medizinische Hochschule Hannover, Hannover, Germany

The surgery of paragangliomas of the head and neck remains challenging due to the intimate relationship usually arising between the tumor, the vessels, and the cranial nerves in the skull base. Extensive involvement of the arteria carotis interna is not infrequent. As total gross extirpation should be pursued to avoid recurrence, questions arise on the functional results of radical surgery and its long term results.

Methods

Retrospective cohort study in a tertiary referral center, 67 patients operated between 2009 and 2023 with the diagnosis of paraganglioma of the head and neck were collected. The preoperative clinical and radiological findings, the surgical technique, the intraoperative and postoperative complications and the final surgical results were analyzed. The median follow up is 5 years.

Results

In case of extensive skull base involvement, an infratemporal fossa approach was always mandatory. Complete gross excision of the tumor in the skull base was achieved in all cases, in two case of intradural extension only a partial intracranial excision was possible. A staged procedure was adopted in three cases of bilateral multifocal tumors. The most common intraoperative complication was venous bleeding from the inferior petrosal sinus, while arterial vascular injuries were more common at the carotis bifurcation. At the time of surgery, 35% of patients were already suffering from cranial nerve deficits. 29% of patients developed additional nerve palsy postoperatively, mostly transient facial palsy in tympanojugular paragangliomas and vagus palsy in in glomus caroticum and vagale tumors. We experienced one recurrence. No perioperative exitus was registered.

Conclusion

Although radical excision of skull base paraganglioma is usually achievable, the risk of additional nerve palsies remains high. Vascular damages are rare in expert hands but are usually difficult to manage. The use of a carotis stenting helps the surgeon to mobilize and safely dissect arterial vessels in case of extensive vascular involvement. Although in the long term most patients are disease free, an integrated care concept with long-term follow up is needed, focusing on rehabilitation strategies such as hearing restoration, reanimation of the paralyzed face and dysphagia treatment.

Management of Bilateral Head and Neck Paragangliomas at a Single Institution — Surgical and Clinical Outcomes

Evan L. Tooker, MS; Mana Espahbodi, MD; Anne Naumer, MS; Luke O. Buchmann, MD; Wendy Kohlmann, MS; Hilary C. McCrary, MD MPH; Neil S. Patel, MD

Departments of Otolaryngology-Head and Neck Surgery, University of Utah Health, Salt Lake City, Utah

Objective:

Report the treatment strategies and clinical outcomes of subjects with sporadic and familial bilateral carotid body and/or bilateral vagal paragangliomas.

Methods:

A retrospective review of all patients with bilateral carotid body tumors (CBT) and/or bilateral vagal paragangliomas (VP) between 1987 and 2023 was performed. Age at diagnosis, sex, laterality, type of tumor, succinate dehydrogenase *(SDHx*) pathogenic variant (PV), clinical symptoms at time of diagnosis, clinical symptoms that developed during period of observation, type of treatment, and cranial nerve (CN) outcome data were obtained. Diagnostic interventions included next generation sequencing (NGS), MRI, and metanephrine and/or catecholamine testing. Tumors were treated using stereotactic radiosurgery (SRS), intentional subtotal resection (STR), gross total resection (STR) or multimodality therapy. Cranial nerve outcomes were assessed using clinical documentation of facial, laryngeal, tongue, and shoulder function.

Results:

A total of 21 subjects with bilateral CBT and 3 subjects with bilateral CBT and bilateral VP met inclusion criteria. Subjects consisted of *SDHD* (58%, 14/24) PV, *SDHB* (8%, 2/24) PV, sporadic (17% 4/24), and unknown genetic status (13%, 3/24). Of note, the three subjects with bilateral CBT and bilateral VP were *SDHD* PV. The median age of diagnosis was 36.5 year; 67% (16/24) were women. Only four subjects presented with paraganglioma-related symptoms including hypertension (3/4), palpitations (2/4), dysphagia (1/4), dysphonia (1/4), and cervical lymphadenopathy (1/4); one subject had confirmed functional tumors based on elevated plasma catecholamines. The remaining asymptomatic subjects were detected incidentally (29%, 7/24) or through screening protocols for a family history of *SDHx* (42%, 10/24). Treatment strategies included staged bilateral resection (33%, 8/24), staged bilateral resection plus radiotherapy (13%, 3/24), resection of one tumor and observation of the contralateral tumor (21%, 5/24), and observation of bilateral tumors (33%, 8/24). All three bilateral VP remain under observation. Treatment and observation both had favorable outcomes with 92% (22/24) of subjects presenting with no paraganglioma-related symptoms at last follow-up. The two cases of symptomatic CBT at last follow-up included one case under observation with stable symptoms of dysphagia and one case with baroreceptor reflex failure syndrome. Of note, the latter case of baroreceptor reflex failure syndrome was secondary to multiple bilateral resections and radiotherapy for recurrent, symptomatic, secreting tumors.

Conclusions: To the best of our knowledge, this is the second study to report the surgical and clinical outcomes in a cohort of bilateral CBT and bilateral VP. The range of treatment options discussed had comparable and favorable outcomes for tumor and symptomatic control. The morbidity of bilateral vagal neuropathy biases management toward observation or radiotherapy in an effort to preserve function for as long as possible. However, resection of secreting or symptomatic CBT is preferred with a low risk of regional cranial neuropathy. The management of bilateral HNPGL is nuanced, and there is conflicting evidence to support a chosen treatment strategy that balances tumor and patient characteristics and interventional expectations

Post-Operative Outcomes Of Lower Cranial Nerve Function In Tympanojugular Paragangliomas: The Gruppo Otologico Experience

Virginia Fancello[1,2], Giuseppe Fancello[1,3], Giuseppe Santopietro[1,2], Golda Grinblat[1,4], Mario Sanna[1]

1. Gruppo Otologico, Piacenza, Italy.
2. Ear Nose and Throat & Audiology Unit, Department of Neurosciences, University Hospital of Ferrara, Ferrara, Italy.
3. Department of Otorhinolaryngology, Careggi University Hospital, Florence, Italy.
4. Hillel Yaffe Medical Centre, Technion Faculty of Medicine, Hadera, Israel.

Tympanojugular paragangliomas (TJ PGLs) are a complex surgical challenge, because of their invasive nature, high vascularization, and critical position. Despite management advances, the dysfunction of lower cranial nerves (LCNs) continues to affect the outcomes. The IX, X, XI, and XII cranial nerves can be directly involved by TJ PGL expansive growth, hence the preservation during surgical excision is often unfeasible with resultant compromised function.

We performed a retrospective study of all the patients who underwent surgery for TJPs with/without intracranial extensions in the last 20 years (2003-2023) at Gruppo Otologico, Piacenza, Italy.

Limited class C1 and C2 TJ PGLs can be safely removed avoiding lower cranial nerves' dysfunction.

In extended lesions (C3-C4), the natural history of the tumor jeopardized nerve integrity, with around 50% of cases presenting with at least 1 LCN paralysis at diagnosis. In addition, to obtain complete surgical excision nerve sacrifice is often necessary.

Prompt rehabilitation is essential to avoid long-term morbidity. In the case of dysphonia and dysphagia, selected patients can benefit from laryngeal medialization procedures, with the aim to improve airway protection, voice, and thus life quality.

Even young patients can present with extensive TJ PGLs. Surgical excision permits the eradication of the tumor, avoiding further progression. If LCNs deficit occurs, spontaneous compensation in young patients is easier, with good functional outcomes.

Early diagnosis of TJPs is of paramount importance to allow complete tumor removal and reduce the risk of long-term complications.

Facial reanimation in patients with jugular paraganglioma: “Taking the FN out of the equation”

Luis Lassaletta, José Manuel Morales-Puebla, Teresa González-Otero, Javier Gavilán

Facial Paralysis Unit. La Paz University Hospital. Madrid

Patients with persistent or recurrent jugular paraganglioma and partial facial paralysis (FP) who need an additional skull base procedure have an extremely high chance of worsening their facial function. A total gross tumor resection will lead to a total FP in the majority of cases. In addition to the challenging tumor resection procedure due to an already injured FN, the outcome of the facial reconstruction procedure may be impaired by the previous FP.

In these patients with partial facial dysfunction and a paraganglioma requiring additional surgery, we consider an alternative reinnervation procedure, “take the FN out of the equation” before tumor resection. A prophylactic reanimation technique with partial hypoglossal-to-facial and/or a masseter-to-facial transfer before the tumor resection may achieve a facial recovery up to House Brackmann grade III (following an initial grade VI). In this way, facial reanimation is ensured irrespective of the evolution of the tumor. Then, tumor resection can be accomplished with no fear of the FN, as the new facial input is extratemporal.

In this presentation illustrative cases of patients with previous FP undergoing this take the FN out of the equation” in the context of a Facial Paralysis Unit will be shown, emphasizing the tips and tricks of each reanimation procedure.

Treatment of facial nerve palsy in the surgery of Tympanojugular Paragangliomas

Lorenzo Lauda, Enrico Maddalone, Giuseppe Fancello, Virginia Fancello, Mario Sanna

Gruppo Otologico, Piacenza, Italy.

Tympano-Jugular paragangliomas (C1-C4) frequently affect the facial nerve (FN), and their treatment may involve the FN with his possible impairment. In cases where a functional proximal stump cannot be identified and the FN remains intact but with complete palsy, FN anastomosis with another motor nerve becomes necessary to restore innervation to the mimicking musculature. This study presents and compares the outcomes of sural nerve or great auricular nerve grafting anastomosis and the masseterofacial anastomosis (MFA) in patients experiencing facial nerve paralysis following paragangliomas surgery.

Adult patients who experienced complete and permanent facial paralysis following surgery in the paraganglioma's surgery underwent facial nerve reanimation through either sural nerve or great auricular nerve grafting anastomosis, or masseteric transfer anastomosis. The assessment of facial nerve function was based on the House-Brackmann grading system (HB). A comparison of facial function results, extent of disease and surgical technique was conducted at the 6-month mark.

In surgery for tympano-jugular paraganglioma of grade C1-C4, the facial nerve exhibits a degree II-III dysfunction, as per the House-Brackmann grading scale, in 90% of cases, despite its anterior transposition. The presentation highlights that in the presence of facial nerve infiltration, grafting or end-to-end anastomosis represents the standard approach in facial nerve surgery. In cases of unsuccessful recovery, the preferred option is massetero-facial anastomosis.

Labbè operation as an option for facial reanimation in long standing facial paralysis

Davide Rizzo, MD, PhD[1,2], Pierangela Tramaloni[2], MD, Roberto Gallus, MD[3], Francesco Bussu MD, PhD[1,2]

[1] *Department of Medical, Surgical and Experimental sciences, University of Sassari, Sassari, Italy*
[2] *Otolaryngology Division, Azienda Ospedaliera Universitaria, Sassari, Italy*
[3] *Otolaryngology, Mater Olbia Hospital, Olbia, Italy*

Objectives:

The human face is a crucial tool for expression and interpersonal communication, so patients with complete peripheral facial paralysis experience severe problems in social interactions, and from dysfunctions in eye protection, speech articulation, chewing and swallowing. After the onset of facial paralysis, if there is not a clear anatomical interruption of the continuity of the nerve or if it has been surgically reestablished (nerve grafts, nerve anastomosis), spontaneous recovery, independently of the aetiology, is considered possible within 6-8 months after clinical onset. In most of the literature, paralysis is considered long-standing after 18 months.

In these cases, the primary goal for reconstructive surgeons is to reestablish facial symmetry, tone, and coordinated movements of the paralyzed face.

Materials and Methods:

The static procedures are somehow successful at obtaining closure and protection of the eye on the paralyzed side and a certain symmetry of the upper third of the face, but more complex dynamic procedures are definitely preferable for the middle and lower third.

Labbè operation is a true lengthening myoplasty procedure described in 2000 by Labbé and Huault. The temporalis muscle is elongated and the released coronoid tendon of the muscle is transferred to the nasolabial fold and lips, thus preserving a fixed temporal point. It is a dynamic correction since the motor innervation to the temporalis muscle coming from the third branch of the trigeminus is preserved and the muscle normally contracts at the end of the operation. For the treatment of upper third of the face we performend a Paul Tessier's lengthening of the levator muscle of the upper eyelid combined with Krastinova-Lolov's external blepharorrhaphy.

We describe a multi-institutional series of Labbè procedures performed by a single surgeon (FB) in the last 12 years.

Results:

41 patients have been recorded. No major complications occurred after surgery. In one case intraoperative bleeding impeded the completion of coronoid osteotomy and required a second stage to complete the lengthening temporalis myoplasty, which was anyway successfully performed.

All the patients are subjectively satisfied with the results and don't complain drooling any more.

The upper third has always been successfully managed with static procedures.

In 2 cases a recurrence of adenoid cystic carcinomas in the Gasser ganglion compromised respectively 2 and 4 years after the successful procedure the long-term functional results.

Conclusion: The results of lengthening temporalis myoplasty combined with static correction of lagophthalmos appear to be, in our opinion, comparable with the main series in the literature involving free microneurovascular transfers for long-standing peripheral monolateral facial paralysis.

The advantages of the temporalis elongation myoplasty are: only 1 stage, the lower incidence of complications, the markedly reduced operating time, early recovery of movement, immediate static correction, swiftness, the preservation of the native innervation and vascularization of the muscle, which are therefore much more reliable, with negligible risk of flap failure and of loss of innervation.

Hearing Rehabilitation Strategies after Paraganglioma Surgery, more than Baha Implants

JM Morales-Puebla, I Sánchez-Cuadrado, M Calvino, J Gavilán, L Lassaletta

Department of Otolaryngology, La Paz University Hospital, Madrid, Spain

Paragangliomas are tumors that, depending on their extension, can lead to hearing loss, tinnitus, balance problems and lower cranial nerve paralysis by themselves or because of their surgical treatment. Hearing loss after paraganglioma surgery has an important impact on quality of life (QOL). It can be classified as conductive, mixed or sensorineural. Traditionally, bone anchored hearing devices have been the rehabilitation option for conductive or mixed cases and even for single-sided deafness.

Material and Methods:

An assessment on the current possibilities of auditory rehabilitation was carried out and their pros and cons were analyzed.

Results:

For conductive and mixed hearing loss bone conduction implants (BCI), either percutaneous or active transcutaneous, and active middle ear implants (AMEI) can be used. For profound sensorineural hearing loss cochlear implant is the only option to restore hearing. BCI or CROS/BICROS hearing aids can be an alternative in single-sided deafness to lessen the head shadow effect.

Discussion:

Contemporary tumor philosophy management is to resect as much as possible but trying to minimize postoperative sequela in order to maximize post-treatment QOL. The decision on which option to choose to rehabilitate hearing depends on several factors. Among them, the necessity of further treatment of the tumor, and the necessity of postoperative imaging follow up should be considered. For BCI, the main issues addressed include the decision about the optimal position for each patient, the management of dura and sigmoid sinus, and the consequences of having an implant in contact with these structures. For AMEI the advantages of personalizing the coupling method to the clinical situation of the patient must be considered. Difficulties in imaging follow-up due to the artifacts produced by devices with magnets need also to be discussed.

Conclusion: Different strategies of hearing rehabilitation can be considered after paraganglioma surgery in order to improve QOL.

Current hearing rehabilitation strategies after tympanojugular paraganglioma surgery

Rolf Benedict Salcher[1], Riccardo Di Micco[1], Thomas Lenarz[1]

[1]ENT Department, Medizinische Hochschule Hannover, Hannover, Germany

Hearing rehabilitation after paraganglioma surgery remains not standardized and mostly underexplored. As most patients underwent middle ear obliteration as a part of the infratemporal fossa approach, conventional hearing aids are ineffective and more complex solutions are required. In order to assess the current available options and clinical shortcomings a retrospective analysis of the hearing rehabilitation strategies in a tertiary referral center was performed.

Material and methods:

A retrospective analysis of the hearing rehabilitation strategies and results in a tertiary referral center after skull base paraganglioma was performed. Between 2008 and 2023 40 patients received surgery form tympanojugular paraganglioma requiring obliteration of the middle ear. The preoperative and postoperative hearing performances were collected. The proposed and applied hearing rehabilitation strategies and their acceptance from side of the patient were analyzed.

Results:

Of the 40 patient, 11 already suffered from profound hearing loss at time of surgery. 5 of them accepted and profited from a CROS hearing aid. In one case, a cochlear implantation was successfully performed after ruling out recurrence. The remaining 29 patient developed a severe conductive hearing loss after surgery. In two cases, an acoustic implant was used with high gain. Five patients were regularly using a CROS hearing aid. 22 patients were not rehabilitated at time of the last follow-up

Conclusion: The paraganglioma patient is theoretically not different from a single side deafness one, however modern hearing rehabilitation has mostly been sidelined in the follow up. The majority of patients has been directed towards CROS hearing aids, but they are mostly not accepted in the long term. In case of functional inner ear, a bone-anchored hearing aid offers a valid alternative. Should inner ear be insufficient for acoustic implants, cochlear implantation remains a valid option. Considering the current available therapeutically options, a stronger, differentiated approach to hearing rehabilitation should be pursued in the near future as part of the integrated concept of treatment.

Vestibular Rehabilitation in Tympano-Giugular Paragangliomas

Giannuzzi Anna Lisa[1], Rebecchi Elisabetta[1], Santopietro Giuseppe[1,2], Mario Sanna[1]

1 Gruppo Otologico, Piacenza, Italy
2 ENT and Audiology Unit, University Hospital of Ferrara, Italy

Tympano-mastoid and tympano-giugular paragangliomas are usually benign, slowly growing, painless tumors. The common presenting symptoms are pulsatile tinnitus, conductive hearing loss and cranial nerve impairment. Especially in the early stages of the disease, vertigo is a rare presentation. It may be due directly to the pathology, to the pre-operative treatments or to the surgical resection. In any case of vestibular hypofunction it is important to start vestibular rehabilitation as soon as possible in order to improve dynamic visual acuity and passive Vestibulo-Ocular-Reflex gain.

We describe our pre and post-operative vestibular examination and our vestibular rehabilitation personalized protocol.

Iatrogenic Sequelae of Vagal Paraganglioma: Review of the Literature and Therapeutic Options

Giorgio Peretti

Unit of Otorhinolaryngology, Head and Neck Surgery, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Vagal paragangliomas are rare neuroendocrine tumors arising from the paraganglia located in the vagus nerve. The treatment of these tumors can result in iatrogenic sequalae, which are unintended negative outcomes due to medical intervention. The aim of this abstract is to provide an overview of the iatrogenic sequalae of vagal paraganglioma treatment. The most common treatment for vagal paragangliomas is surgical resection, which can result in various complications such as vocal cord paralysis, dysphagia, and Horner's syndrome. In addition, preoperative embolization can lead to cranial nerve injuries, stroke, and myocardial infarction. Radiation therapy, which is an alternative treatment option, can cause long-term side effects such as radiation-induced fibrosis, radiation necrosis, and secondary malignancies. The treatment of iatrogenic sequelae depends on the specific type and severity of the complication. In some cases, the symptoms may be self-limiting and resolve on their own over time. However, in other cases, medical intervention may be necessary. For example, vocal cord paralysis resulting from surgical resection of a vagal paraganglioma may require speech therapy or even surgical intervention to restore normal vocal cord function, in terms of injection laryngoplasty or type I thyroplasty. Injection laryngoplasty can be done in the outpatient clinic, under local anesthesia, using reabsorbable material such as hyaluronic acid; or it can be performed under general anesthesia, in microlaryngoscopy, using long lasting materials such as autologous fat or Vox implant. Dysphagia may be managed with dietary modifications, swallowing therapy, or in some cases, a temporary placement of a feeding tube. To avoid these latter therapeutic options, type A botulin toxin injection in the cricopharyngeal muscle can be useful. The botulinum toxin is a type of neurotoxin that works by blocking the release of acetylcholine, a neurotransmitter that stimulates muscle contraction. When injected into the muscles involved in swallowing, the toxin can weaken or paralyze them, making it easier for the patient to swallow. The injection is typically performed by a trained healthcare professional, such as a gastroenterologist or otolaryngologist. The procedure involves using a thin, flexible endoscope to guide the injection needle to the affected muscles. The dose and location of the injection will depend on the specific cause of dysphagia and the individual patient's needs. Botulinum toxin injections can provide temporary relief of dysphagia, typically lasting several months. The treatment may need to be repeated periodically to maintain its effectiveness.

Overall, the treatment of iatrogenic sequelae requires a multidisciplinary approach, involving specialists from various medical fields, such as speech therapy, physical therapy, neurology, and oncology. The specific treatment plan will depend on the nature and severity of the complication and should be tailored to the individual patient's needs.

Trans nasal injection laryngoplasty under local anesthesia

Marco Stacchini

ENT Department, M. Bufalini Hospital, Cesena, Italy

Unilateral vocal fold paralysis (UVFP) is a frequent complication of H&N surgery, as in the treatment of paragangliomas. In case of UVFP glottic insufficiency (GI) often occurs, which causes dysphonia and dysphagia and reduces patient's quality of life. When voice therapy does not provide a positive effect, phonosurgery may be indicated. Several phonosurgical techniques for the treatment of GI due to UVFP have been proposed. These techniques are generally performed using cervical access, under local or general anesthesia (thyroplasty type I, arythenoid adduction, neurorraphy). Injection laryngoplasty (IL) is another widely applied phonosurgical technique, generally performed using trans-oral approach. A relatevely new method of IL under local anesthesia has recently been proposed, which involves a trans-cervical injection under fiberendoscopic guidance. Instead, in our clinical practice we usually adopt a completely trans-nasal fiberendoscopic IL procedure, by local anesthesia, using a high-pressure injection pistol connected to a flexible injection needle, injecting centrifuged autologous fat in the vocal cord. The use of autologous fat reduces the risk of allergic reactions and local granulomatosis that could be caused by synthetic materials. The centrifuged autologous fat as an IL material gives the advantage of less reabsorption compared to other injectable materials like hyaluronic acid, because the stem cells contained in the adipose stroma regenerate new lipocytes which replace the lipocytes deteriorated by the injection procedure.

Non-Selective Laryngeal Reinnervation in the Treatment of Unilateral Vocal Cord Palsy

Virginia Fancello, Kate J Heathcote

Robert White Centre for Voice, Airway and Swallow, University Hospitals Dorset, United Kingdom

Introduction and aims:

Unilateral recurrent laryngeal nerve (RLN) injury is the most common neurological lesion of the larynx and it is associated with dysphonia, dysphagia, aspiration and weak cough.
Non-selective reinnervation (NSR) is a treatment option for unilateral vocal cord palsy (UVCP). The procedure involves the anastomosis of the RLN to the ansa cervicalis. It has the unique quality of restoring muscular tone to the hemi-larynx and is postulated to have several advantages over more established procedures such as type 1 thyroplasty, arytenoid adduction and injection augmentation.

Among 42 patients who have undergone this procedure at the Robert White Centre for Voice, Airway and Swallow, University Hospitals Dorset, UK, 4 presented with vocal cord palsy following treatment for a head and neck paraganglioma (2 tympano- jugular and 2 vagal paraganglioma excision).

Materials and methods:

Pre- and post-operative data were analyzed retrospectively in 42 patients with an age range of 8 to 72 undergoing non-selective reinnervation.
The multidimensional outcome measures used were perceptual voice evaluation, self-reported questionnaire, endoscopic laryngeal findings, acoustic analysis, and electromyography. All patients completed at least 6 months follow up.

Results:

Overall, there was a significant improvement in both objective and subjective measures.

Conclusion:

This case series suggests that laryngeal reinnervation is an effective treatment to improve voice quality in patients with UVCP and represent a feasible technique in the rehabilitation of head and neck paraganglioma sequelae. It can be performed in patients with previous laryngeal framework surgery and does not preclude medialisation procedures in the future If the result is unsatisfactory.

Regenerative Approach to Laryngeal and Velopharyngeal Paralysis

Giovanna Cantarella[1,2], Riccardo Mazzola[3], Luca Morelli[1], Ludovica Battilocchi[1], Mirko Alde'[1,4], Lorenzo Pignataro[1,2]

[1] Department of Clinical Sciences and Community Health, University of Milan, , Milan, Italy.
[2] Otolaryngology and [4]Audiology Units,Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milan, Italy.
[3] Plastic Surgeon, private practice, Milan, Italy

Head and neck paragangliomas may be the cause of lower cranial nerve (CN) deficits, with consequent voice, speech and swallowing impairment, with a severe impact on the patient quality of life. Velopharyngeal and laryngeal unilateral paralysis are among the most common lower CNs encountered deficits, due to IX-X CNs damage. The velopharyngeal paralysis causes velopharyngeal Insufficiency (VPI) resulting in hypernasality and food regurgitation in the nasopharynx due to incomplete closure of the passage between oro- and nasopharynx.. A unilateral laryngeal paralysis causes a breathy voice consequent to defective closure of the glottis during phonation; speech dyspnea and swallowing impairment may also be associated.

Surgical management of VPI aims at improving voice resonance and minimizing the air escape through the nose by restoring a competent velopharyngeal sphincter. In case of mild/moderate VPI, autologous fat transplantation to the velum, posterior pharyngeal pillars and posterior pharyngeal wall has proved to be successful; if one side of the sphincter is paralyzed treatment can be performed on that side only. It is a minimally invasive procedure with respect to major surgery and minimizes the risk of complications.

The treatment of glottic incompetence aims to restore glottic closure during phonation and swallowing. Autologous fat injection has proven to be a reliable, safe and long-term efficient procedure to this aim. Fat is an ideal material to restore volume of vocal folds, as it is vital, does not alter the viscoelastic properties of the vocal fold and avoids the risk of foreign body reaction, extrusion or migration; both vocal folds can be treated at the same time, if needed.

In case of associated paralysis of IX-X CNs, both velopharyngeal and glottic incompetence can be safely treated in the same procedure by fat injections. It has been proven that fat tissue is rich of mesenchymal pluripotent stem cells, cytokines and growth factors.

Fat is harvested from the lower abdomen by liposuction with a blunt-tip cannula connected to a 10-ml Luer-Lok syringe. The plunger of the syringe is retracted to maintain a negative pressure. The lipoaspirate is centrifuged at 3000 rpm for 3 minutes to remove aqueous, hematic, oily components and debris. Then the purified fat parcels are utilized for injection.

For VPI treatment bended blunt cannulas – never needles- must be used to avoid the risk of injecting into the vessels in the posterior and lateral pharyngeal wall; the injected amount is usually 5-8 cc. For the unilateral laryngeal paralysis the paralytic vocal fold is injected 1-2 cc under direct microlaryngoscopy with a bayonet needle; a smaller amount (0.2-0.4 cc) is usually injected in the contralateral moving vocal fold.

Concurrent treatment of both VP and glottic defective closure may favor a more rapid resolution of the speech and swallowing impairment in case of associated paralysis. A second session of fat grafting may be performed to optimize the result, if needed. The use of autologous fat for both procedures allows to exploit its regenerative properties that induce a dynamic remodeling of the treated tissue, preserving and enhancing pliability and vascularity.

	POSTER
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2	**FACIAL NERVE FUNCTION IN IFTa WITH REROUTING: GRUPPO OTOLOGICO EXPERIENCE** Giuseppe Fancello[1,2], Virginia Fancello[1,3], Enrico Maddalone[1,4], Lorenzo Lauda[1], Mario Sanna[1] 1. Gruppo Otologico, Piacenza, Italy - 2. University of Firenze, Italy - 3. University of Ferrara, Italy - 4. University of Insubria, Varese, Italy
3	**ABSOLUTE CONTROINDICATION TO SURGERY: THE SINGLE SIGMOID SINUS** Ida Faralli[1,2], Gianluca Piras[1], Mario Sanna[1] 1. Gruppo Otologico, Piacenza, Italy - 2- University of Insubria and ASST Sette Laghi, Varese Italy
4	**INTERNAL CAROTID ARTERY (ICA) MANGEMENT. REPRESENTATIVE CASES FROM OVER 250 TYMPANOJUGULAR PARAGANGLIOMAS TREATED.** Eleonora Catalano[1,2], Gianluca Piras[1], Mario Sanna[1] 1. Gruppo Otologico, Piacenza, Italy – 2. University of Ferrara, Italy
5	**SURGERY OF TYMPANOJUGULAR PARAGANGLIOMAS IN THE ONLY INTERNAL CAROTID ARTERY** Ida Faralli[1,2], Gianluca Piras[1], Mario Sanna[1] 1. Gruppo Otologico, Piacenza, Italy – 2. University of Insubria and ASST Sette Laghi, Varese Italy
6	**HOW TO AVOID INTERNAL CAROTID BLOW-OUT IN SURGICAL REMOVAL OF C-D TYMPANOJUGULAR PARAGANGLIOMAS** Eleonora Longoni[1,2], Mario Sanna 1. Gruppo Otologico, Piacenza, Italy - 2. University of Cagliari, Italy
7	**INVOLVEMENT OF INTERNAL CAROTID ARTERY IN TYMPANOJUGULAR PARAGANGLIOMAS** Alberto Schena[1], Adriano Zangrandi [1], Carlo Paties [1], Virginia Fancello[2,4], Giuseppe Fancello[3,4], Mario Sanna[4] 1. Pathology Unit, "Guglielmo da Saliceto" Piacenza Hospital, Piacenza, Italy - 2. University of Ferrara, Italy - 3. University of Firenze, Italy - 4. Gruppo Otologico, Piacenza, Italy
8	**NEW CLASSIFICATION OF TYMPANOJUGULAR PARAGANGLIOMAS: THE VERTEBRAL ARTERY** Vittoria Di Rubbo, Mario Sanna Gruppo Otologico, Piacenza, Italy
9	**RESULTS OF FOLLOW UP IN TYMPANOJUGULAR PARAGANGLIOMAS: THE EXPERIENCE OF GRUPPO OTOLOGICO** Diana Ehsani[1,2], Vincenzo Porpiglia[1,3], Mario Sanna[1] 1. Gruppo Otologico, Piacenza, Italy - 2. University of Ferrara, Italy - 3. University of Milano, Italy
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12	**MANAGEMENT OF MULTIPLE PARAGANGLIOMAS** Marco Pollarolo[1], Virginia Fancello[2], Mario Sanna[3] 1. Università degli Studi di Palermo, Italy – 2. Università di Ferrara, Italy – 3. Gruppo Otologico, Piacenza, Italy

13	**RARE GERMLINE SDHAF2 AND VHL MUTATIONS IN THE GRUPPO OTOLOGICO HEAD AND NECK PARAGANGLIOMA SERIES** Diana Liberata Esposito[1,2], Fabio Verginelli[1,3], Giuseppe Fancello[4], Elena Sofia Scialis[5], Elisa Taschin[6], Alberto Schena[7], Rossano Lattanzio[1,2], Virginia Fancello[3], Sara Pagotto[1], Silvia Perconti[1], Simone De Fabritiis[1], Isabella D'Amario[1], Carlo Terenzio Paties[7], Gianluca Piras[4], Lavinia Vittoria Lotti[5], Adriano Zangrandi[7], Mario Sanna[4], Francesca Schiavi[6], Renato Mariani-Costantini[1] 1. Center for Advanced Studies and Technology (CAST), Chieti, Italy – 2. Department of Innovative Technologies in Medicine & Dentistry, *G. d'Annunzio* University, Chieti, Italy – 3. Department of Pharmacy, *G. d'Annunzio* University, Chieti, Italy – 4. Otology and Skull Base Unit, *Gruppo Otologico*, Piacenza, Italy – 5. Laboratory of Ultrastructural Biopathology, Department of Experimental Medicine, *La Sapienza* University of Rome, Rome, Italy – 6. Familial Cancer Clinic and Oncoendocrinology, *Veneto Institute of Oncology IRCCS*, Padua, Italy – 7. Department of Oncology-Hematology, Service of Anatomic Pathology, *Guglielmo da Saliceto* Hospital, Via Taverna 49, 29100 Piacenza, Italy
14	**MULTIPLE PARAGANGLIOMAS: A CASE TO DISCUSS** Lajhouri. M, Ayari. S, Oueslati. I, Frikha. W, Chahed. H, Beltaief. N ENT Department La Rabta Hospital Tunis
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18	**CAROTID BODY PARAGANGLIOMAS: ABOUT 8 CASES** Houssem Eddine Bouraba, Yacine Moussaoui, Tewfik Boutiba, Farid Boudjenah Otolaryngology department of Beni Messous Teaching Hospital, Algiers, Alger
19	**FACIAL NERVE REPAIR: OUR EXPERIENCE** Farid Boudjenah, Houssem Eddine Bouraba, Yacine Moussaoui, Tewfik Boutiba Beni Messous Teaching Hospital, Algiers, Algeria
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	1. Clinic for Otorhinolaryngology and Cervicofacial Surgery, University Medical Centre Ljubljana, Slovenia – 2. Department of Otorhinolaryngology, Faculty of Medicine, University of Ljubljana, Slovenia
21	**OBSERVATION AND PARTIAL TARGETED SURGERY (PTS) IN THE MANAGEMENT OF TYMPANO-JUGULAR PARAGANGLIOMAS: A TREATMENT OPTION** Diego Cazzador, Francesco Benvegnù, Giulia Tealdo, Gioia Martini, Elisabetta Zanoletti, Antonio Mazzoni Otolaryngology Unit, Department of Neuroscience, University Hospital of Padova, via Giustiniani 2, Padova, Italy
22	**METASTATIC MALIGNANT CERVICAL PARAGANGLIOMA: UTILITY OF GA-68-DOTATOC PET/TC** Rosalía Souvirón, Maria Scola, Carolina López Gregorio Marañón Hospital, Madrid, Spain
23	**MANAGEMENT OF CERVICAL PARAGANGLIOMAS: OUR EXPERIENCE** Selima Jouini Nefzaoui S., Romdhane N., Jouini S, Rejeb E., Zoghlemi I., Chiboub D., Hariga I., Mbarek C. ENT Department of Habib Thameur Hospital, Tunis, Tunisia
24	**PRESERVATION OF THE CONDUCTIVE MECHANISM IN JUGULO-TYMPANIC PARAGANGLIOMA SURGERY FOR SELECTED B2, B3, C1, C2 CASES** Th. Somers, T. Van Havenbergh* Skull-base team: ENT-and neurosurgical* departments, Sint-Augustinus Hospital, Antwerp, Belgium
25	**MANAGEMENT OF TEMPORAL BONE PARAGANGLIOMAS TYPE A AND B AT UNIVERSITY MEDICAL CENTRE LJUBLJANA** Manja Hribar[1,2], Aleš Matos[1], Klemen Jenko[1,2], Saba Battelino[1,2], Iztok Fošnarič[1] 1. Clinic for Otorhinolaryngology and Cervicofacial Surgery, University Medical Centre Ljubljana, Slovenia – 2. Department of Otorhinolaryngology, Faculty of Medicine, University of Ljubljana, Slovenia