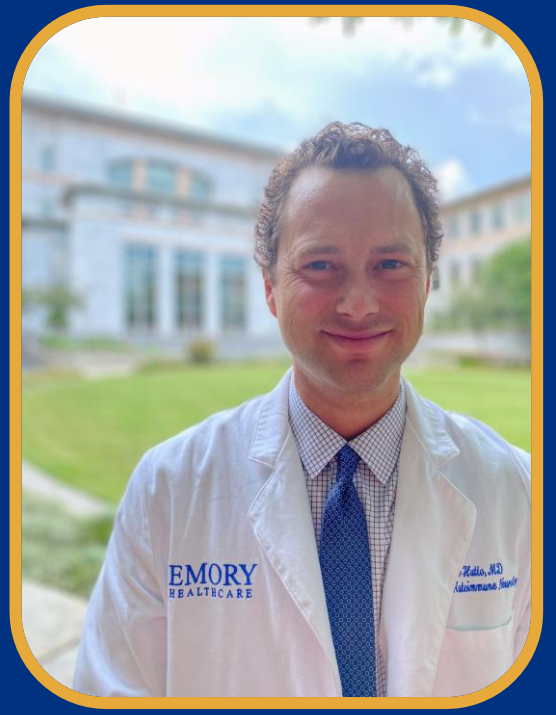
Neuroimaging Spectrum of Neurosarcoidosis

Spencer K. Hutto, MD
Assistant Professor of Neurology
Associate Program Director, Neurology Residency
Director, Emory Neurosarcoidosis Clinic
Emory University School of Medicine



1/18/2026

EMORY UNIVERSITY SCHOOL OF MEDICINE

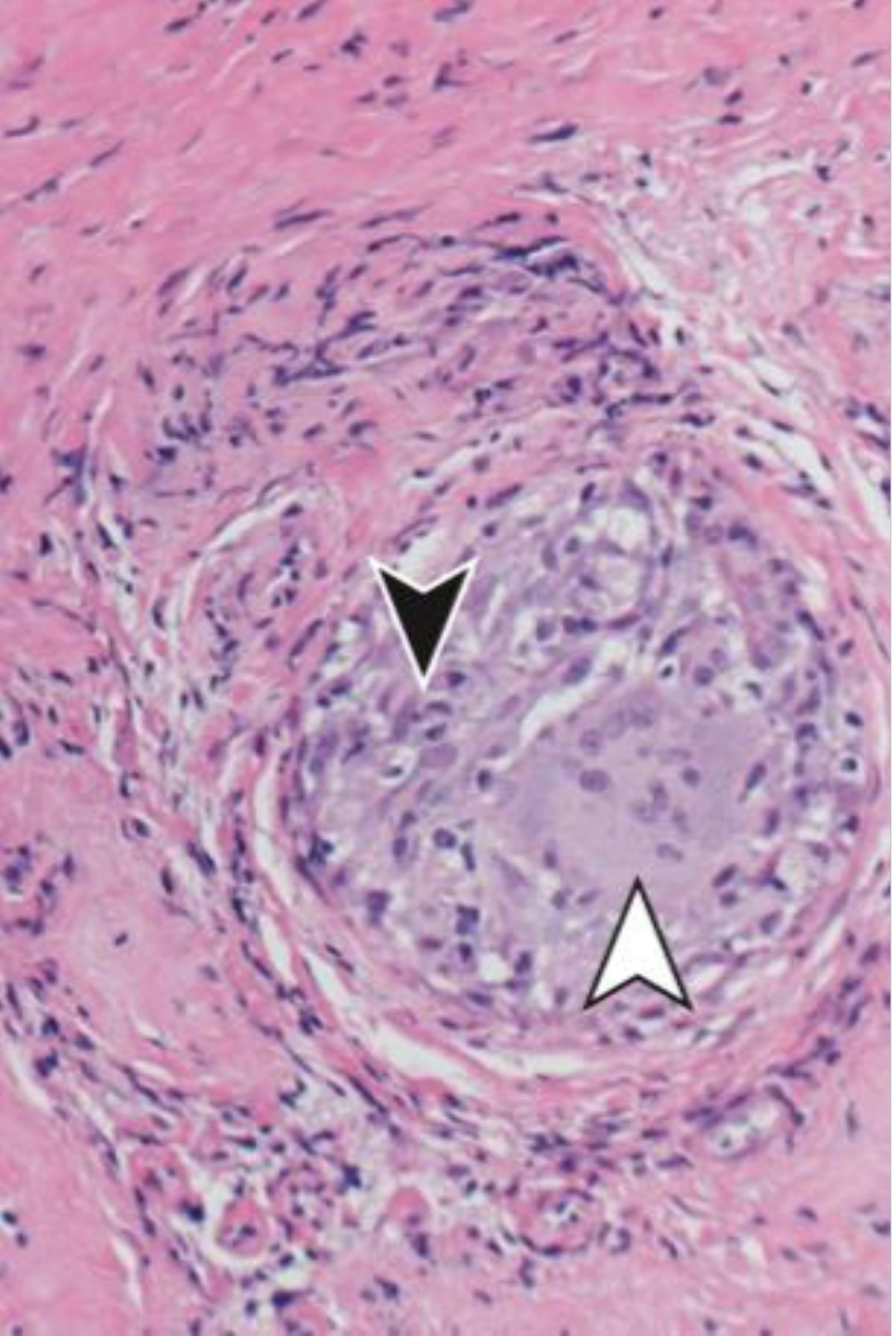
Department of Neurology

Disclosures

- None

Objectives

- Discuss the critical role of neuroimaging in diagnosis
- Develop a framework for understanding the manifestations of neurosarcoidosis
- Outline the principal radiographic phenotypes of neurosarcoidosis
- Recognize the potential for the clinicoradiographic phenotype to inform clinical course, treatment selection, and prognosis



The Challenge

Stern et al. JAMA Neurol 2018.

Box. Proposed Diagnostic Criteria for Central Nervous System and Peripheral Nervous System Neurosarcoidosis

Possible

1. The clinical presentation and diagnostic evaluation suggest neurosarcoidosis, as defined by the clinical manifestations and MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system and after rigorous exclusion of other causes.
2. There is no pathologic confirmation of granulomatous disease.

Probable

1. The clinical presentation and diagnostic evaluation suggest neurosarcoidosis, as defined by the clinical manifestations and MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system after rigorous exclusion of other causes.
2. There is pathologic confirmation of systemic granulomatous disease consistent with sarcoidosis.

Definite

1. The clinical presentation and diagnostic evaluation suggest neurosarcoidosis, as defined by the clinical manifestations and MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system after rigorous exclusion of other causes.
2. The nervous system pathology is consistent with neurosarcoidosis.
   Type a. Extraneural sarcoidosis is evident.
   Type b. No extraneural sarcoidosis is evident (isolated CNS sarcoidosis).

Abbreviations: CSF, cerebrospinal fluid; EMG, electromyogram; MRI, magnetic resonance imaging; NCS, nerve conduction study.

Stern et al. JAMA Neurol 2018.

Box. Proposed Diagnostic Criteria for Central Nervous System and Peripheral Nervous System Neurosarcoidosis

Possible

1. The clinical presentation and diagnostic evaluation suggest neurosarcoidosis, as defined by the clinical manifestations and MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system and after rigorous exclusion of other causes.
2. There is no pathologic confirmation of granulomatous disease.

Probable

1. The clinical presentation and diagnostic evaluation suggest neurosarcoidosis, as defined by the clinical manifestations and MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system after rigorous exclusion of other causes.
2. There is pathologic confirmation of systemic granulomatous disease consistent with sarcoidosis.

Definite

1. The clinical presentation and diagnostic evaluation suggest neurosarcoidosis, as defined by the clinical manifestations and MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system after rigorous exclusion of other causes.
2. The nervous system pathology is consistent with neurosarcoidosis.
   Type a. Extraneural sarcoidosis is evident.
   Type b. No extraneural sarcoidosis is evident (isolated CNS sarcoidosis).

Abbreviations: CSF, cerebrospinal fluid; EMG, electromyogram; MRI, magnetic resonance imaging; NCS, nerve conduction study.

Clinical features and ancillary tests (MRI, CSF, EMG/NCS) suggest neurosarcoidosis:

Definite: neurologic pathology

Probable: systemic pathology

Possible: no pathology

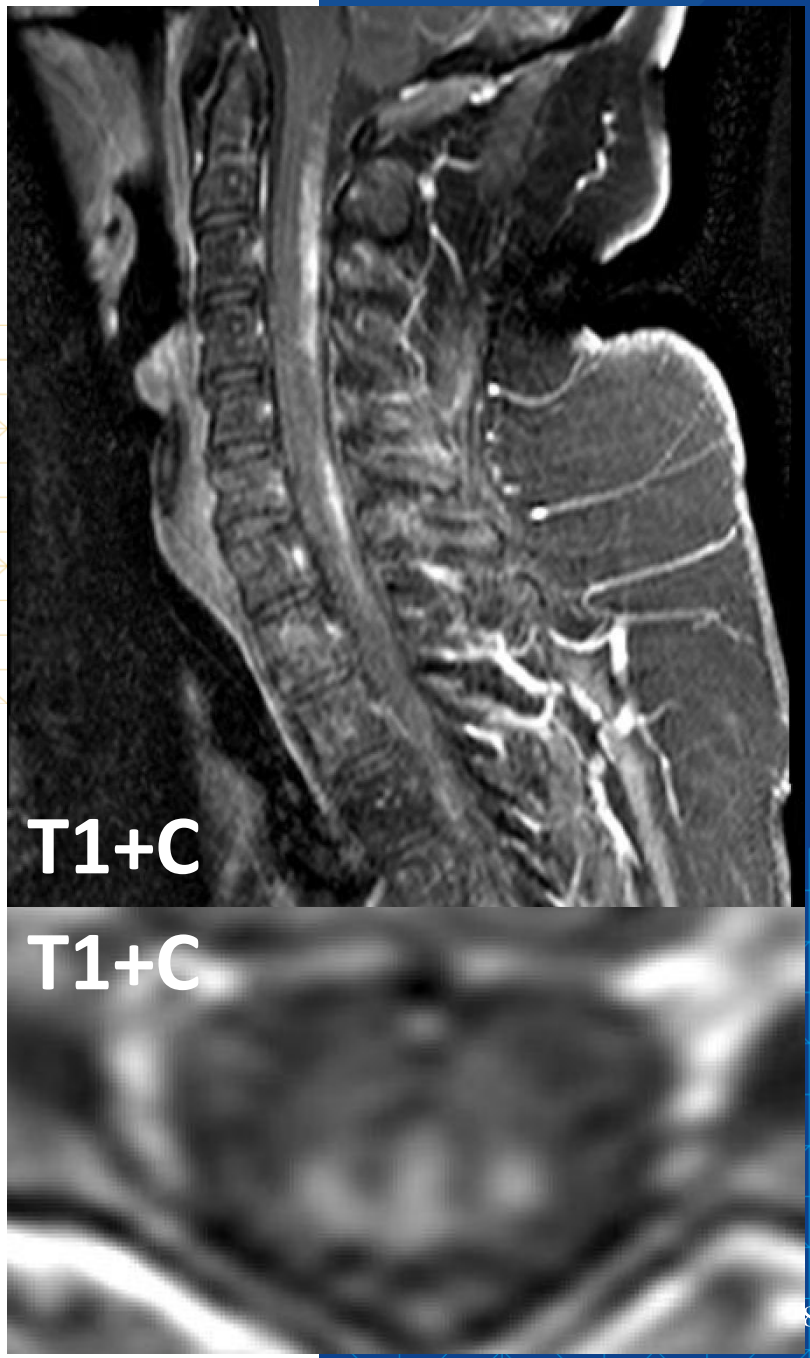
Stern et al. JAMA Neurol 2018.

The Problems

- CNS biopsies: easier said than done
- Granulomas in the body don’t necessarily equal CNS granulomas
- No specific guidelines on what scenarios actually suggest neurosarcoidosis
- No differential diagnoses offered or minimum testing recommended

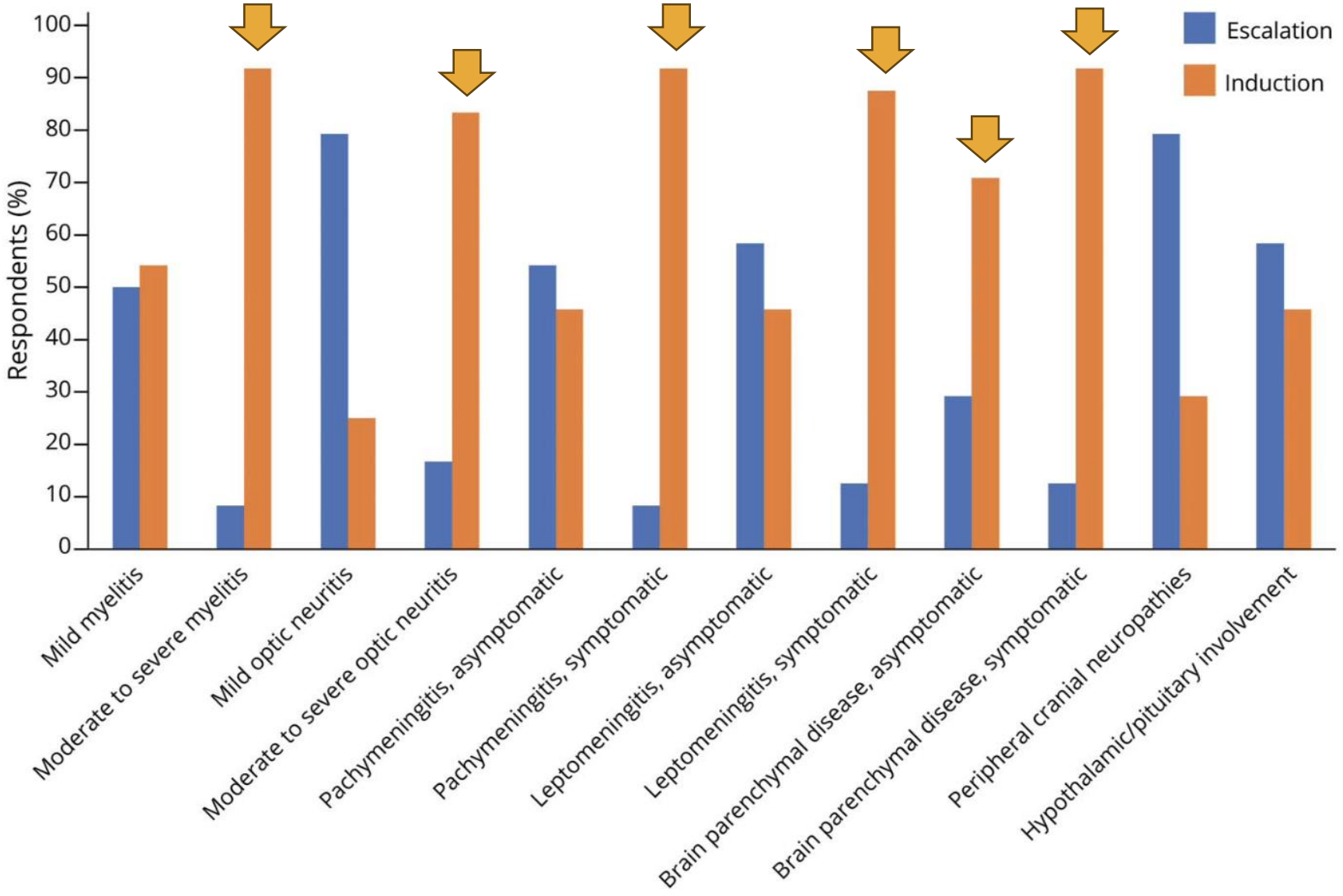
Value of Neuroimaging

- Critical in diagnosis and defining the clinicoradiographic phenotype
- May at some point feature more specifically in diagnostic criteria
- Informs treatment selection and response
- Caution: no findings are proven to be pathognomonic



Stern et al. JAMA Neurol 2018.
Manzano et al. Neurol Clin Pract 2025.

Figure Recommendation of Escalation vs Induction Treatment Approach by Phenotype and Severity of Neurosarcoidosis



Manzano et al. Neurol Clin Pract 2025.

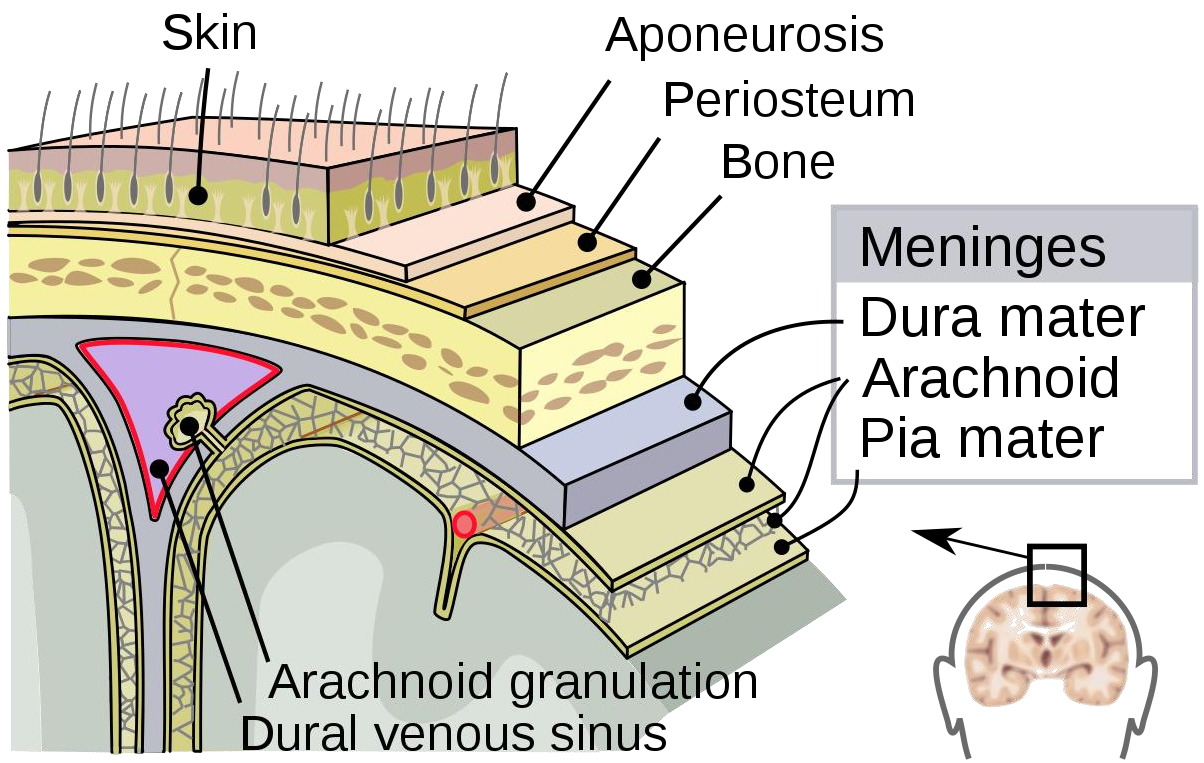
GRANULOMATOUS ANGIITIS OF THE MENINGES IN SARCOIDOSIS

JOHN S. MEYER, M.D.
JOSEPH M. FOLEY, M.D.
AND
D. CAMPAGNA-PINTO, M.D.
BOSTON

From the Neurological Unit and the Mallory Institute of Pathology, Boston City Hospital.

Meningovascular Infiltration

- Meningeal
  - Leptomeningitis
  - Pachymeningitis
  - Cranial neuropathies
  - Infundibulum -> pituitary & hypothalamus
  - Hydrocephalus
  - Seizures
  - Cauda equina
- Subpial/perivascular
  - Brain parenchyma
  - Spine parenchyma
  - Strokes



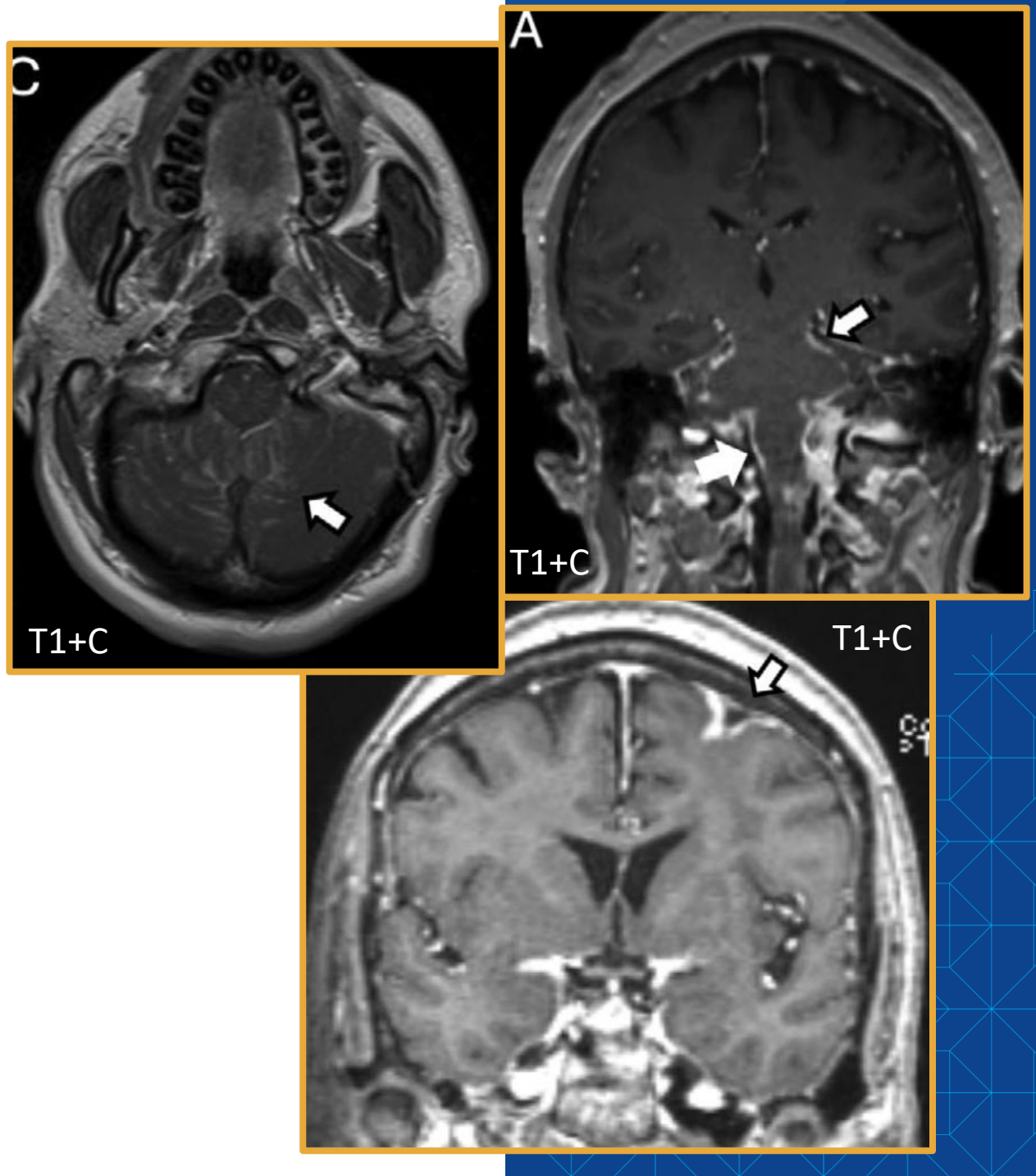
Courtesy Mysid. Wikimedia.

Imaging Keys to Identifying Neurosarcoidosis

- “Outside-in” neuroimaging phenotypes
  - Dorsal subpial enhancement (trident sign) in myelitis
  - Pachy- or leptomeningeal involvement
  - Parenchymal lesions often adjacent to meningeal inflammation with perivascular infiltration
- Peripheral clues for sarcoidosis
  - Hilar lymphadenopathy (thoracic spine MRIs)
  - Parotid involvement (cranial MRIs)

Cranial Leptomeningitis

- Basal > convexal
- Often invasive and destructive
- Brainstem syndrome (1/3) or encephalopathy (2/3)
- Hydrocephalus and adjacent parenchymal involvement possible
- Steroids alone are insufficient



Hutto & Bou. Clinical Neuroimaging 2025.
Kidd DP. J Neurol 2018.
Kidd DP. Pract Neurol 2020.
Ungprasert P, Matteson EL. Rheum Dis Clin N Am 2017.

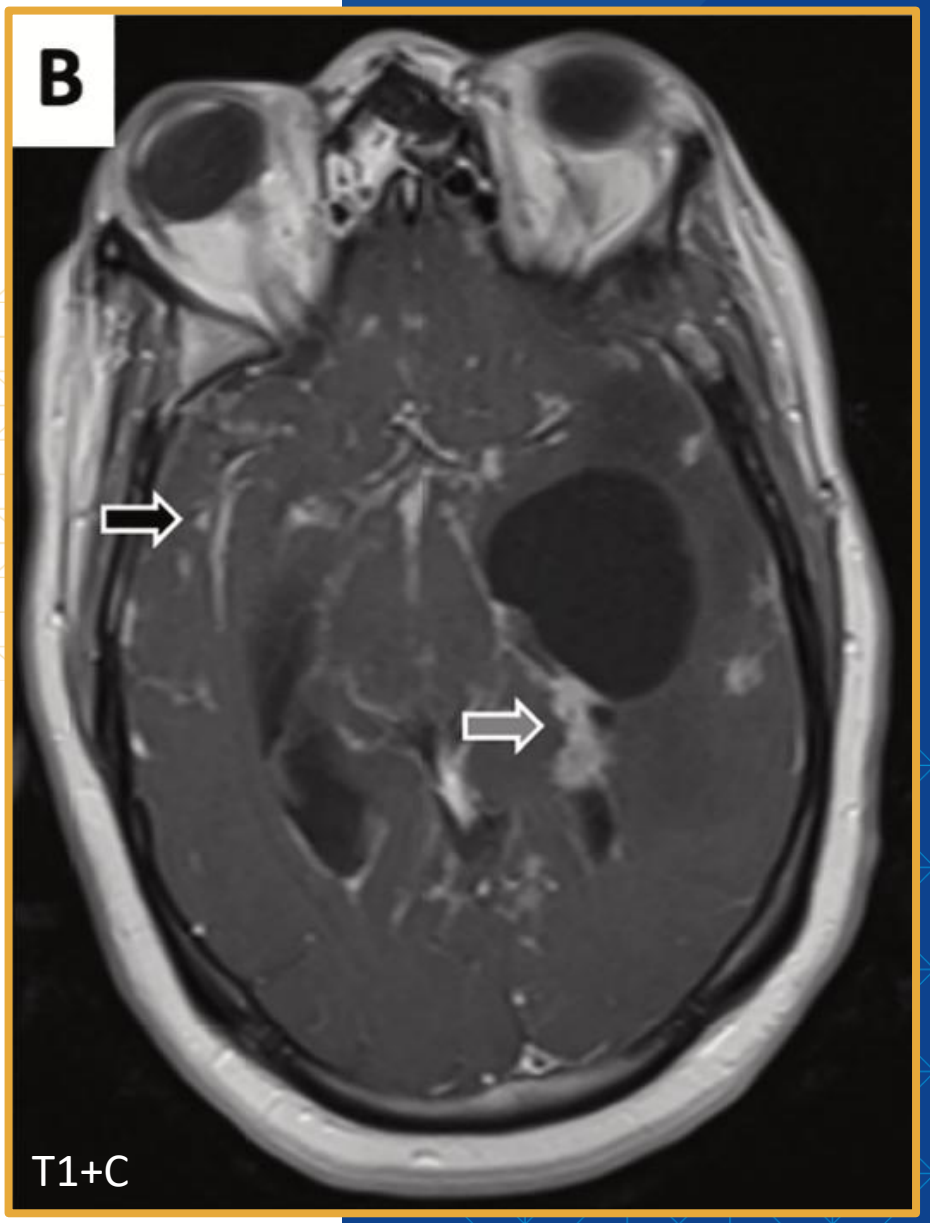
Spinal Leptomeningitis

- Can be asymptomatic or overshadowed by a more significant manifestation
- Extension of basal leptomeningitis along the course of the cervical spine
- May be associated with radiculitis or cauda equina disease

Hutto & Bou. Clinical Neuroimaging 2025.

Hydrocephalus

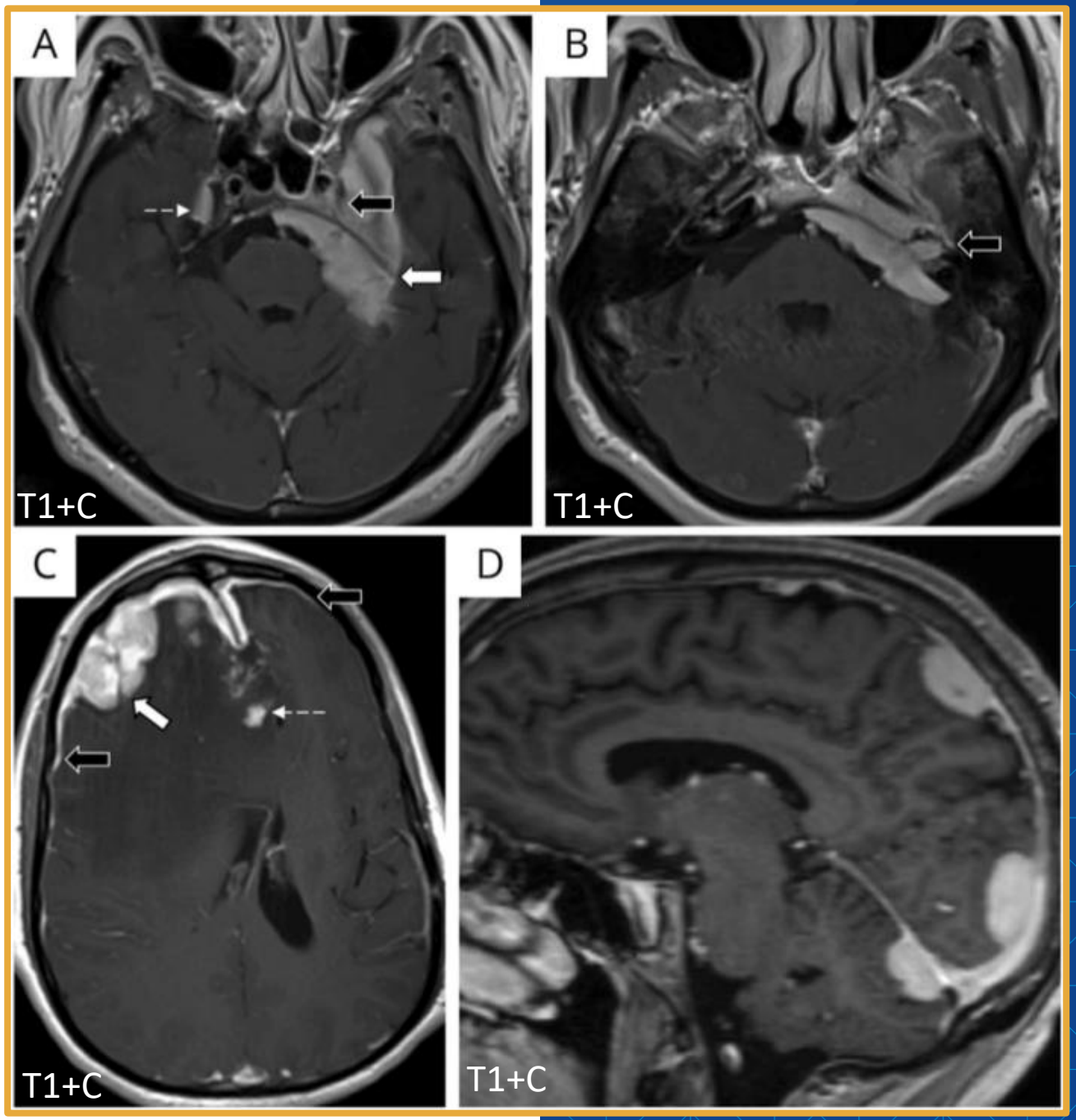
- Less common (7-14%)
- Communicating and obstructive types seen
- Accompanied by meningoventricular inflammation, usually of the posterior fossa (fourth ventricle, basal cisterns)
- CSF diversion may be required
  - No definite impact of steroids on ability to wean from EVD
- Significantly disabling with risk for mortality



El Sammak et al. MSRD 2023.
Ten Dam et al. J Neurol 2022.

Pachymeningitis

- Falx, anterior/middle cranial fossae, or tentorium
- Variable morphology: mass-like or *en plaque*
  - No holocephalic smooth lesions
- Single (42%) or multiple (58%)
- “Dural tails” in 15%



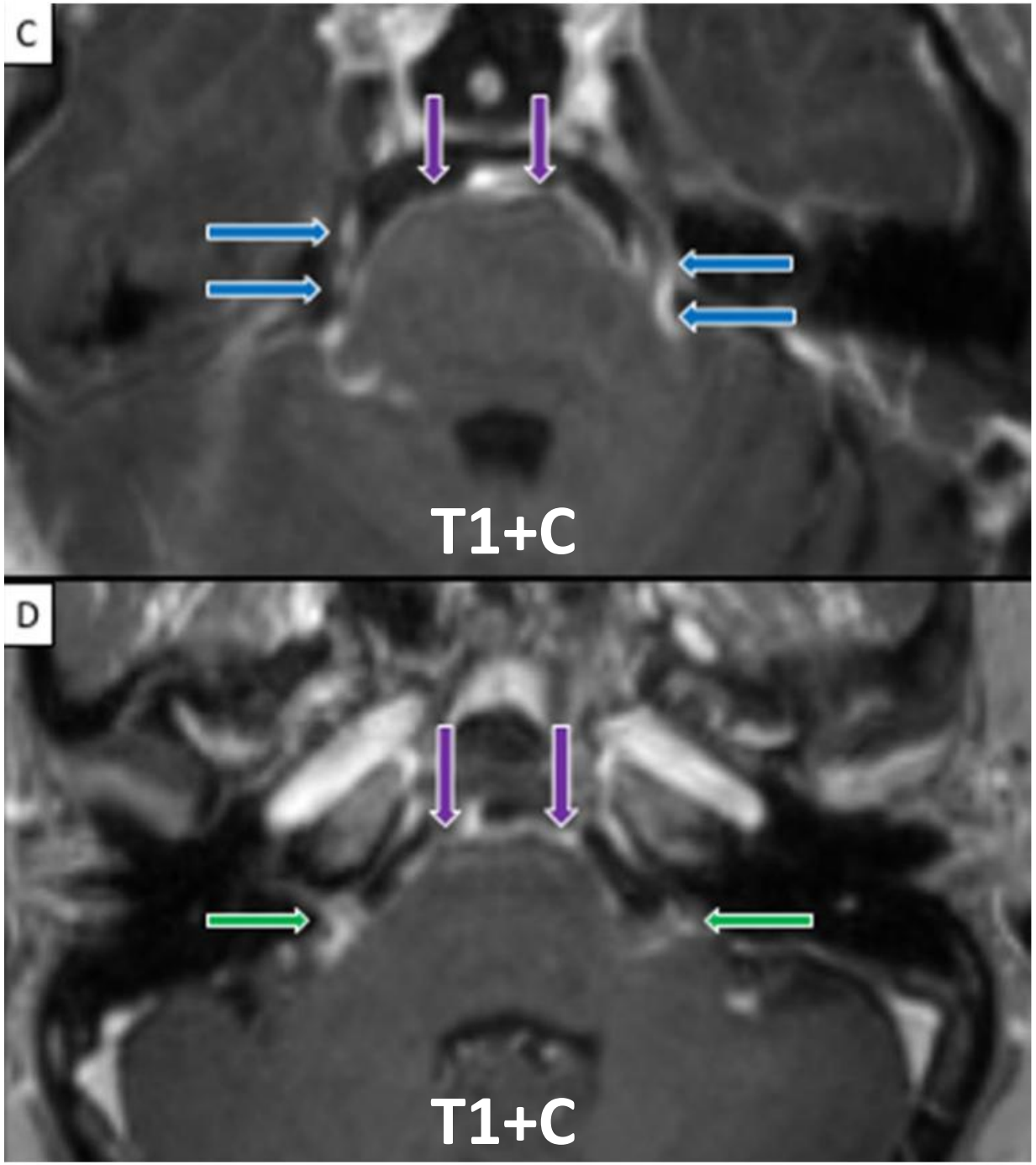
Kidd DP. J Neurol 2018.
Kidd DP. Pract Neurol 2020.
Chakales et al. Neurol Neuroimmunol Neuroinflamm 2022.

Facial Neuropathy

- May be inaugural manifestation
- Bilateral possible (concurrent or sequential)
- Third occur as multiple cranial neuropathies
- Facial nerve enhancement in 40%
- Complete recovery in 64-85%

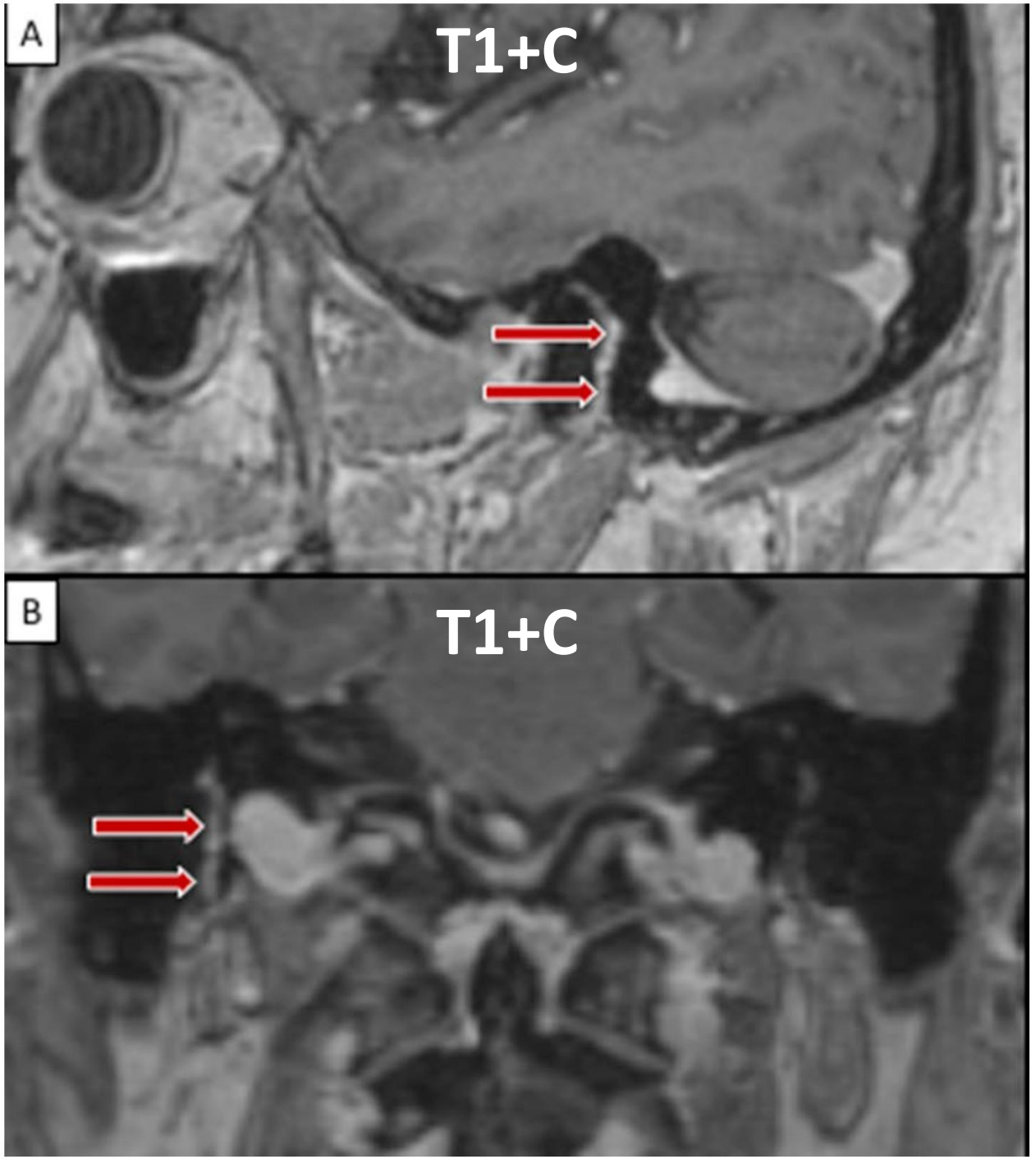
Kidd DP. J Neurol 2018.
Kidd DP. Pract Neurol 2020.
Webb et al. J Neurol Sci 2021.
Nwebube CO et al. J Neurol 2022.

Green: facial
Blue: trigeminal
Purple: pontine surface



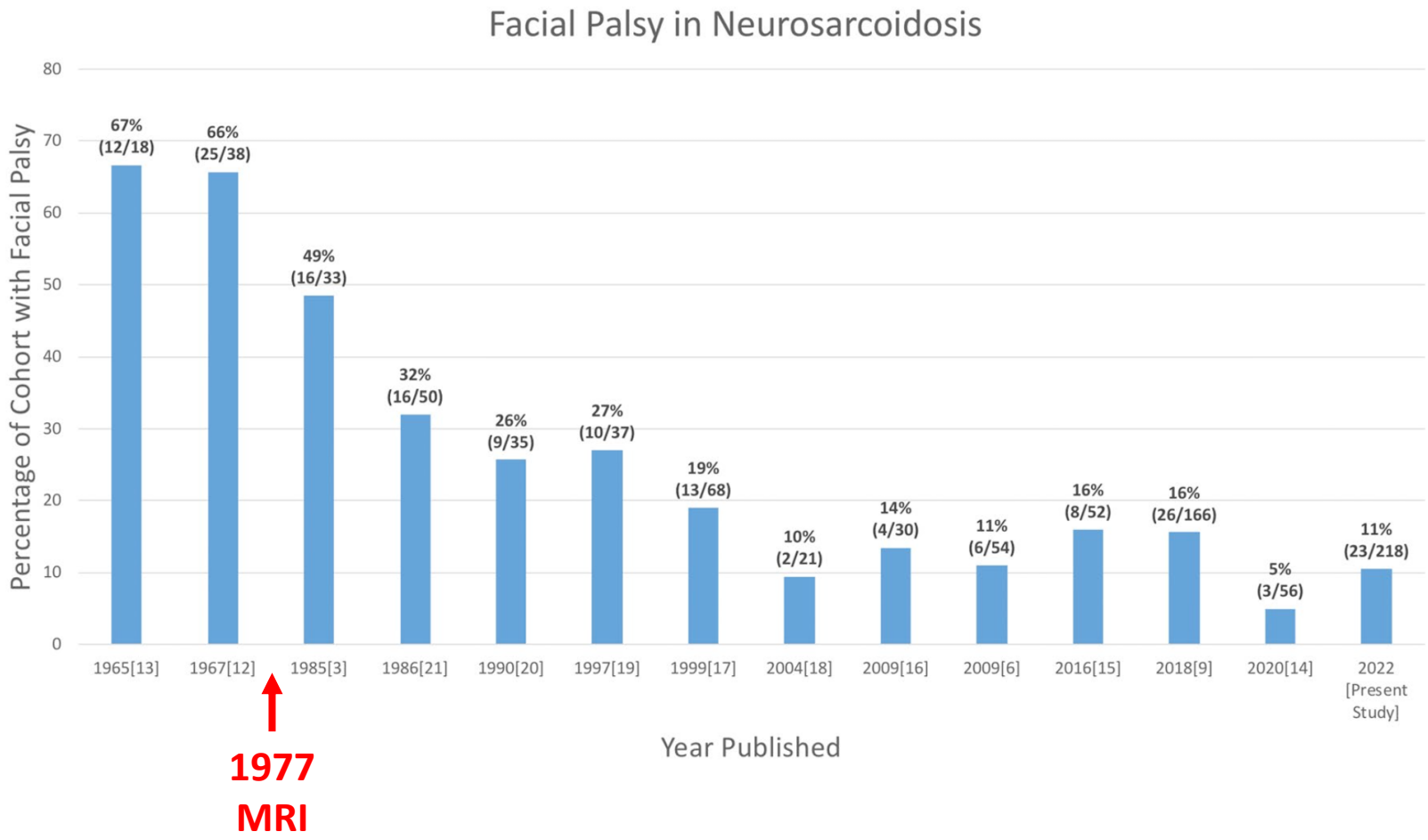
Facial Neuropathy

- MRI abnormalities may extend beyond the subarachnoid space
- Example of the facial nerve enhancing in the mastoid segment
  - A: Sagittal plane
  - B: Coronal plane



Nwebube CO et al. J Neurol 2022.

Frequency of Facial Neuropathy in NS Cohorts

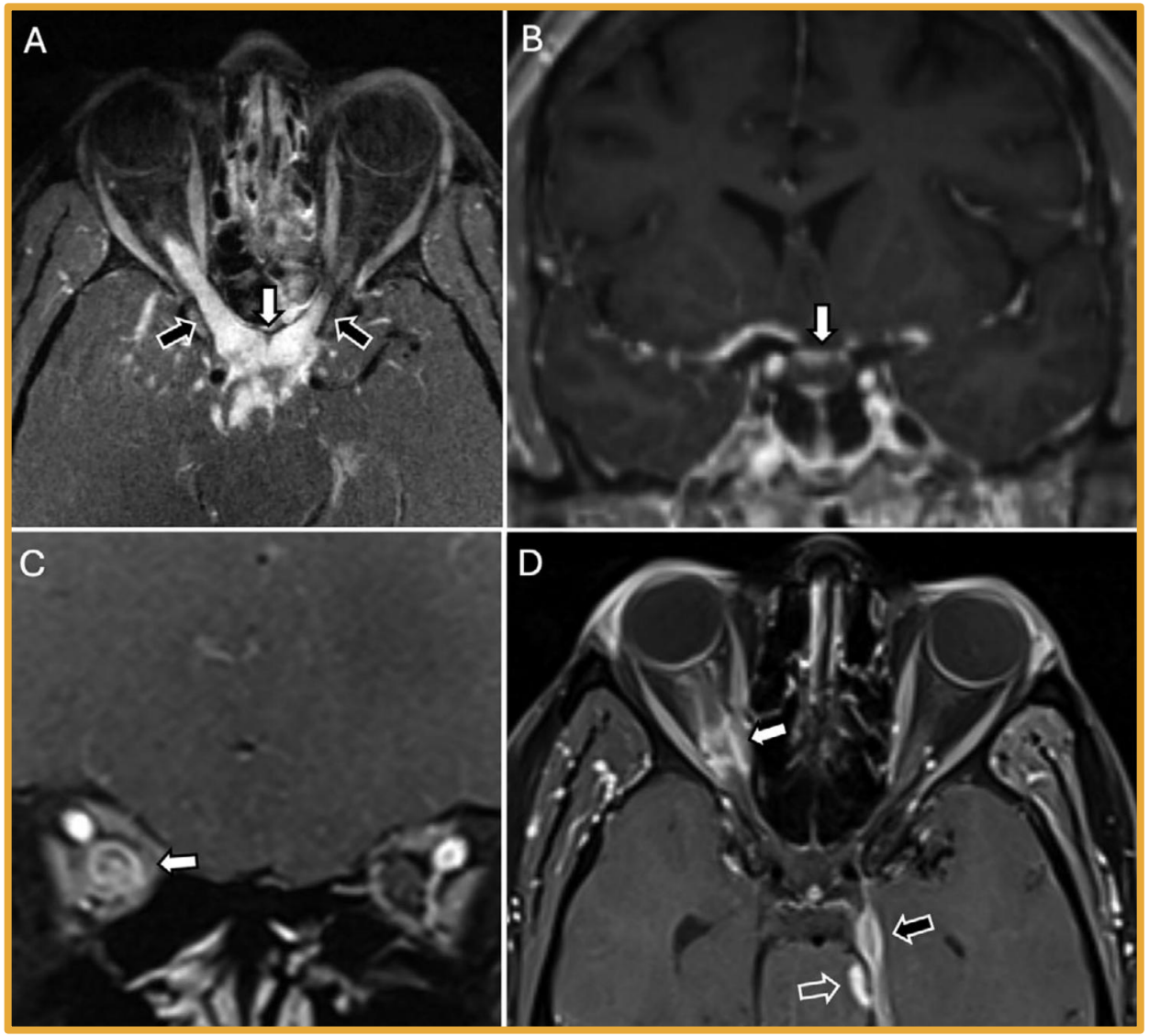


Nwebube CO et al. J Neurol 2022.

Optic Neuropathy

- Clinical
  - Can be an inaugural manifestation
  - Bilateral in 30-53%
  - Nadir 20/200 or worse in 24%
- Enhancement patterns:
  - Intrinsic 25%
  - Perineural 44%
  - Both 31%

- Locations
  - Apex 72%
  - Canalicular 69%
  - Prechiasmatic 50%
  - Orbital 47%
  - Chiasm 25%
  - Optic tracts 22%
- Long (>50% of optic nerve): 28%

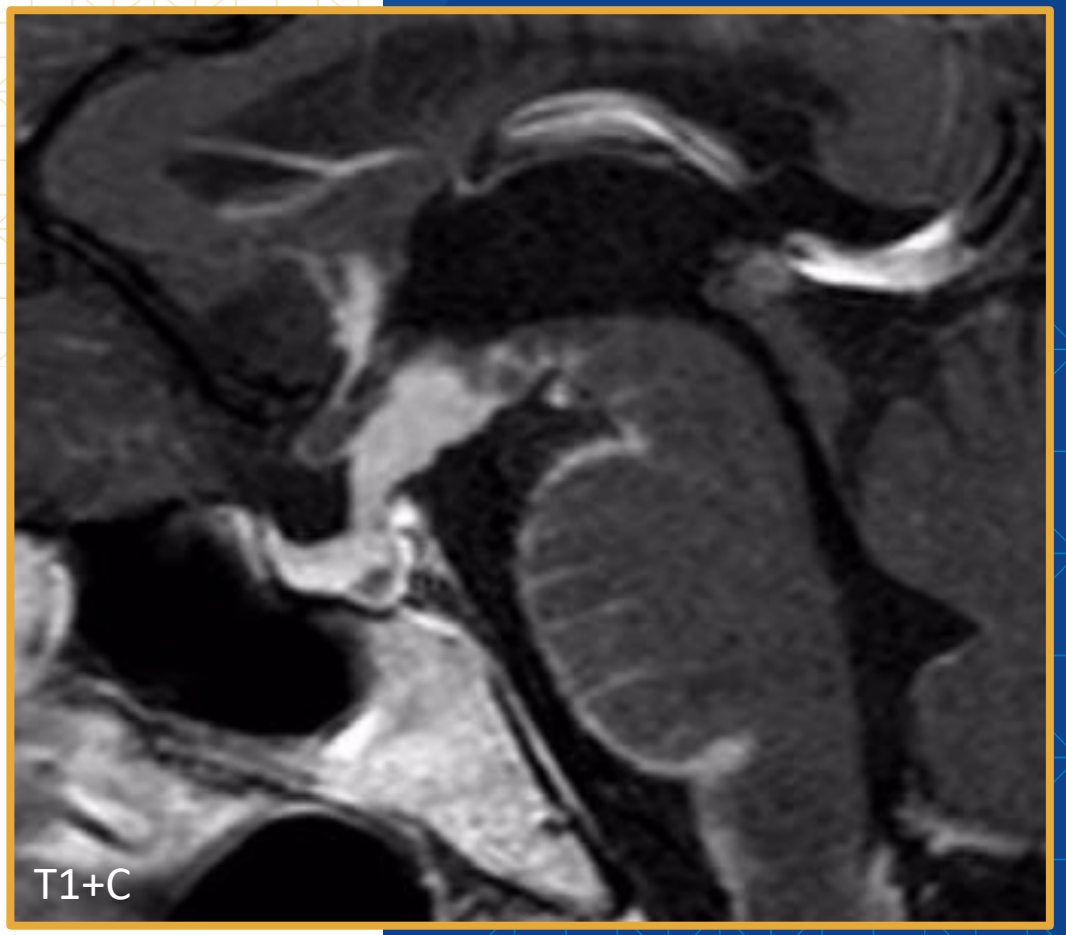


Kidd DP. J Neurol 2018.
Kidd DP. Pract Neurol 2020.
Webb et al. J Neurol Sci 2021.

Frohman et al. J Neuro-ophthalmol 2003.
Hutto & Bou. Clinical Neuroimaging 2025.
Nakirikanti et al. J Neuroimmunol 2025.

Hypothalamus, Pituitary Gland & Stalk

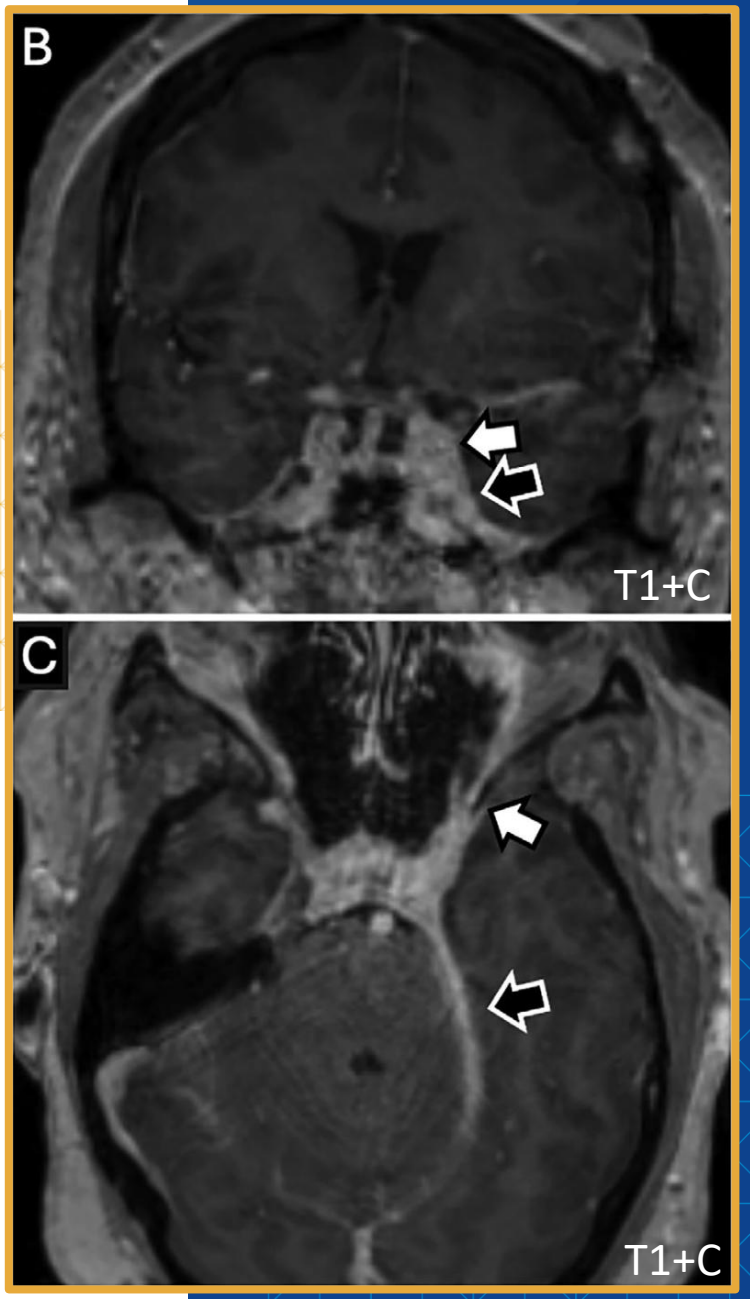
- Neuroendocrine symptoms
- Imaging abnormal in most
  - Stalk > gland
  - Concurrent optic nerve, leptomeningeal, and cavernous sinus disease
- Endocrine testing
- Most do not completely recover
  - Though they may radiologically improve



Kidd DP. Pract Neurol 2020.
Ungprasert P, Matteson EL. Rheum Dis Clin N Am 2017.

Cavernous Sinus

- 8% in one skull base series
- May extend anteriorly or posteriorly
  - Orbital apex
  - Meckel's cave
  - Pachymeninges
  - Tentorium
- Vascular complications are possible
  - Ischemic stroke related to vascular disease



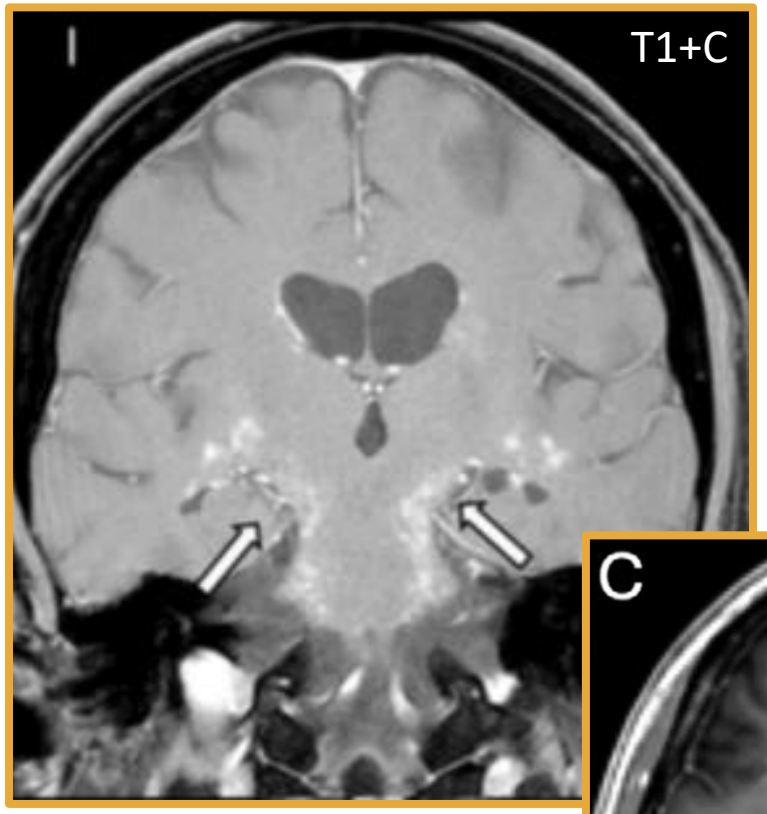
Hutto et al. Neurol Sci 2024.
Carlson et al. Otol Neurotol 2015.
Hutto & Bou. Clinical Neuroimaging 2025.

Parenchymal Disease

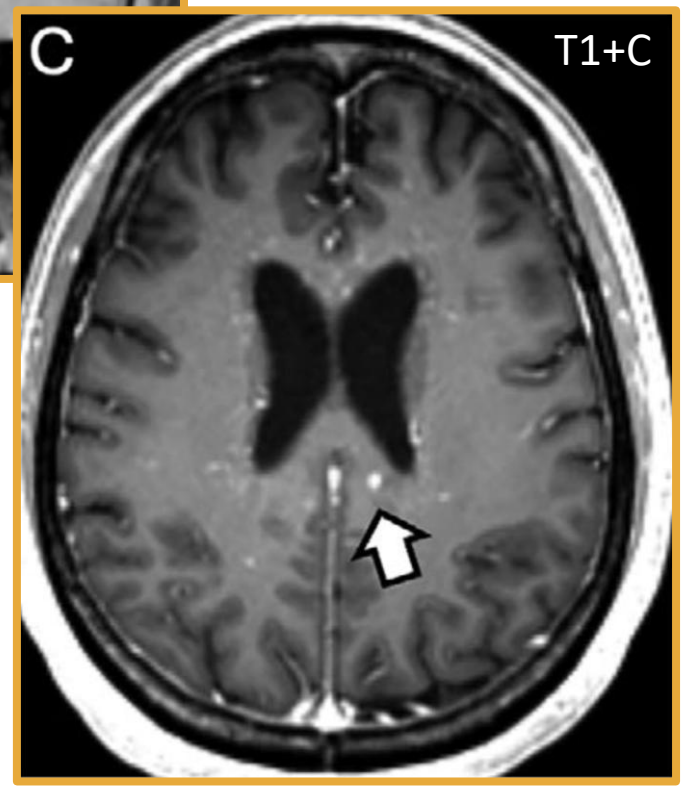
- Solitary or multiple enhancing nodules
  - Usually subpial, lineonodular, and small
  - Tumefactive lesions possible (4-8%)
  - Higher risk for relapse
- Perivascular Radial Enhancement
- Small asymptomatic white matter lesions are common
  - Non-enhancing, non-specific in appearance
  - Cortical or periventricular

Bou et al. J Neurol 2023.
Law et al. Neurology 2019.
Joubert et al. JAMA Neurol 2017.

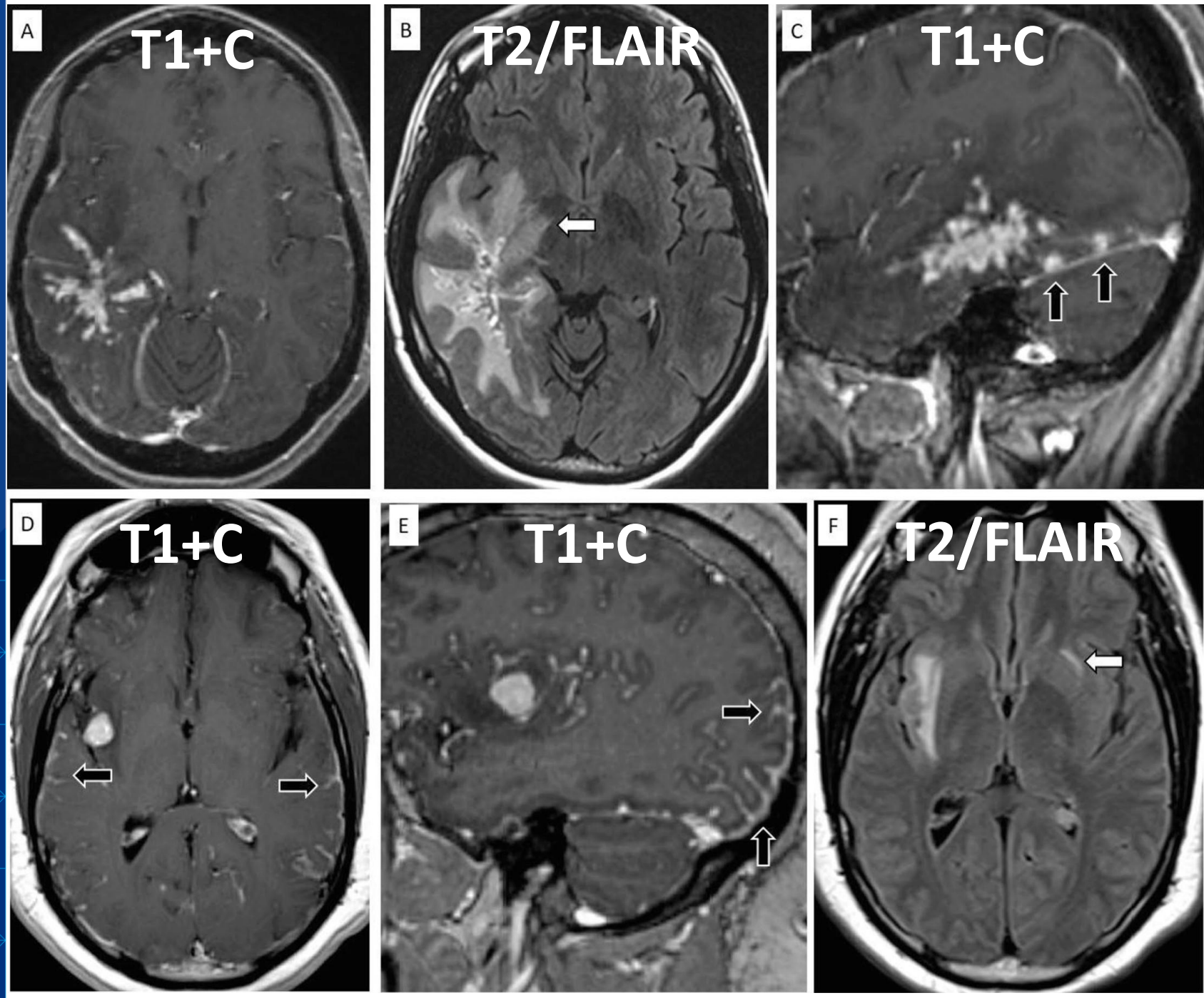
Outside-In Radiographic Patterns



Perivascular Radial Enhancement



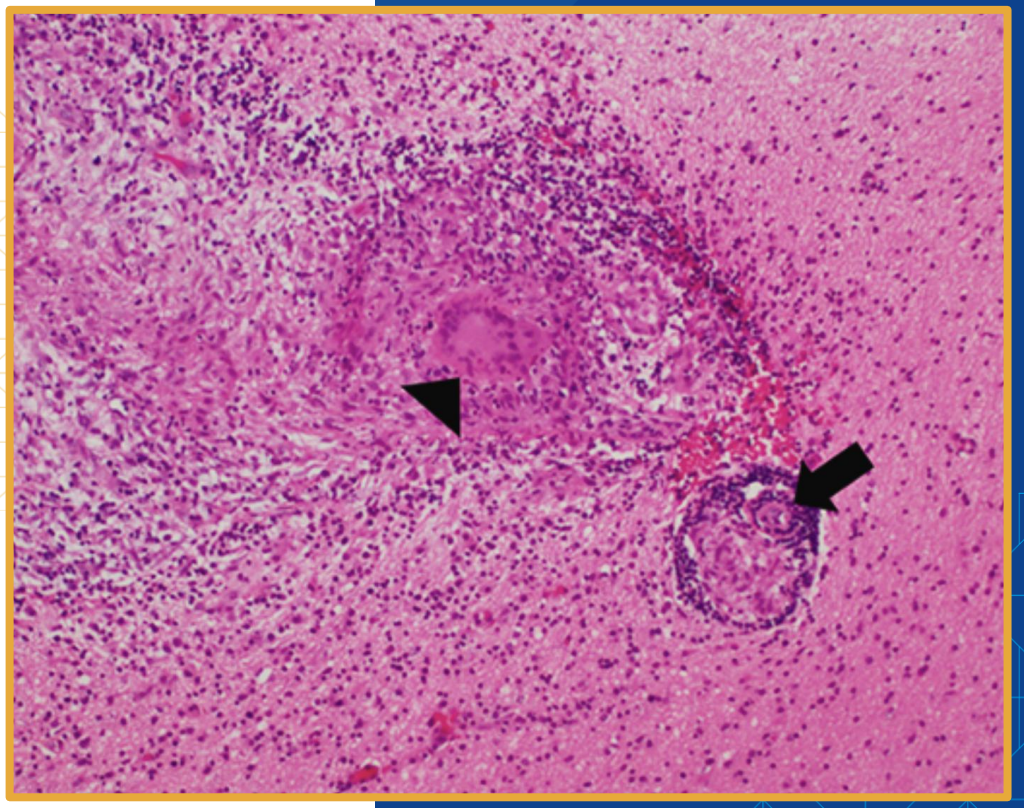
Tumefactive Brain Lesions



Bou et al. J Neurol 2023.

Ischemic Stroke

- Mechanistically
  - Perivascular angiitis
  - Direct vascular involvement (granulomatous vasculitis)
- Caudal-to-rostral distribution
  - Perforating vessels with limited collateral blood flow most vulnerable
    - Pontine perforators
    - Lenticulostriates
  - Posterior-predominant



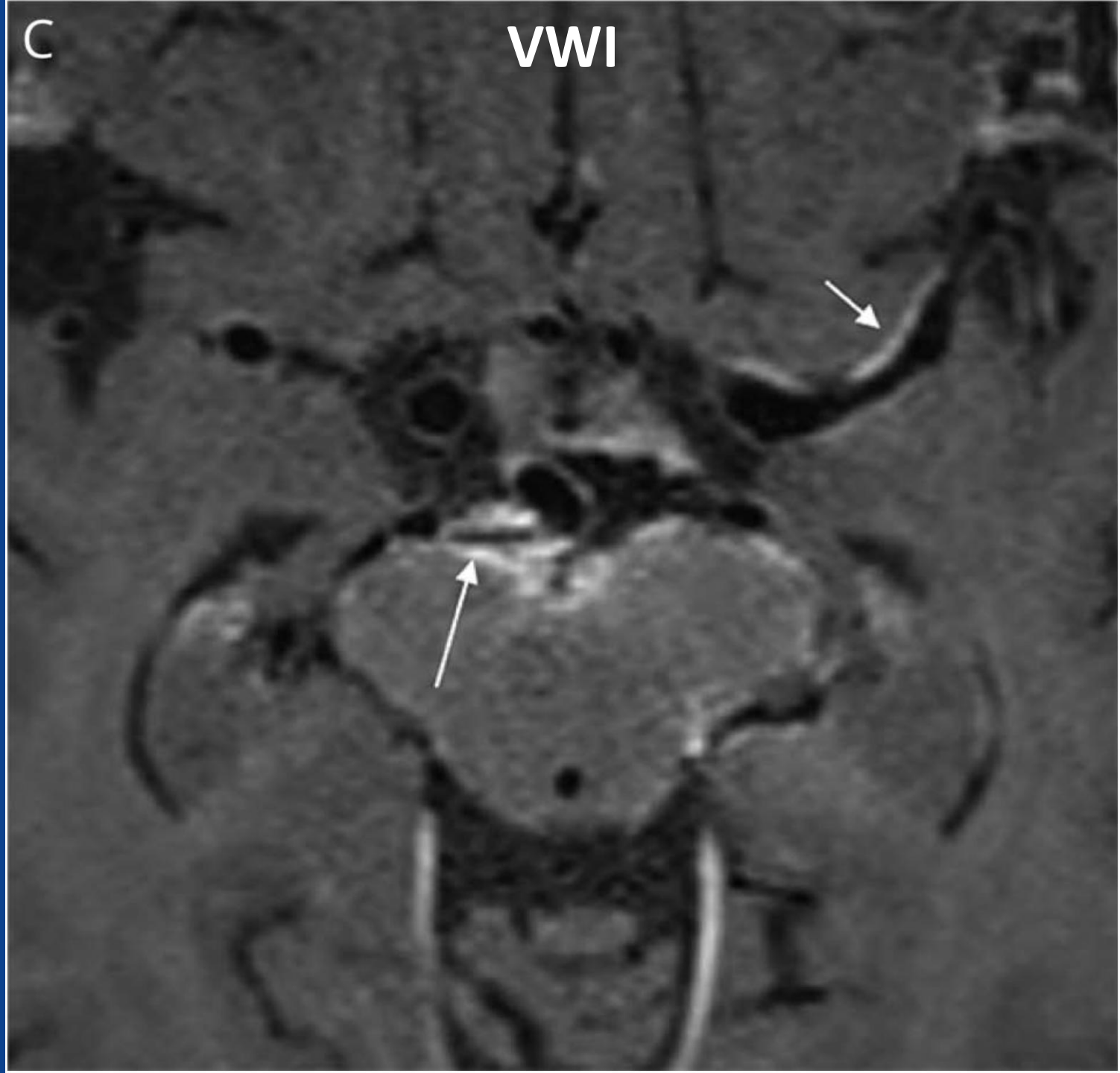
Kidd DP. Pract Neurol 2020.
Hutto et al. Mult Scler Relat Disord 2022.

Ischemic Stroke

Hutto & Bou. Clinical Neuroimaging 2025.

Vessel Wall Imaging

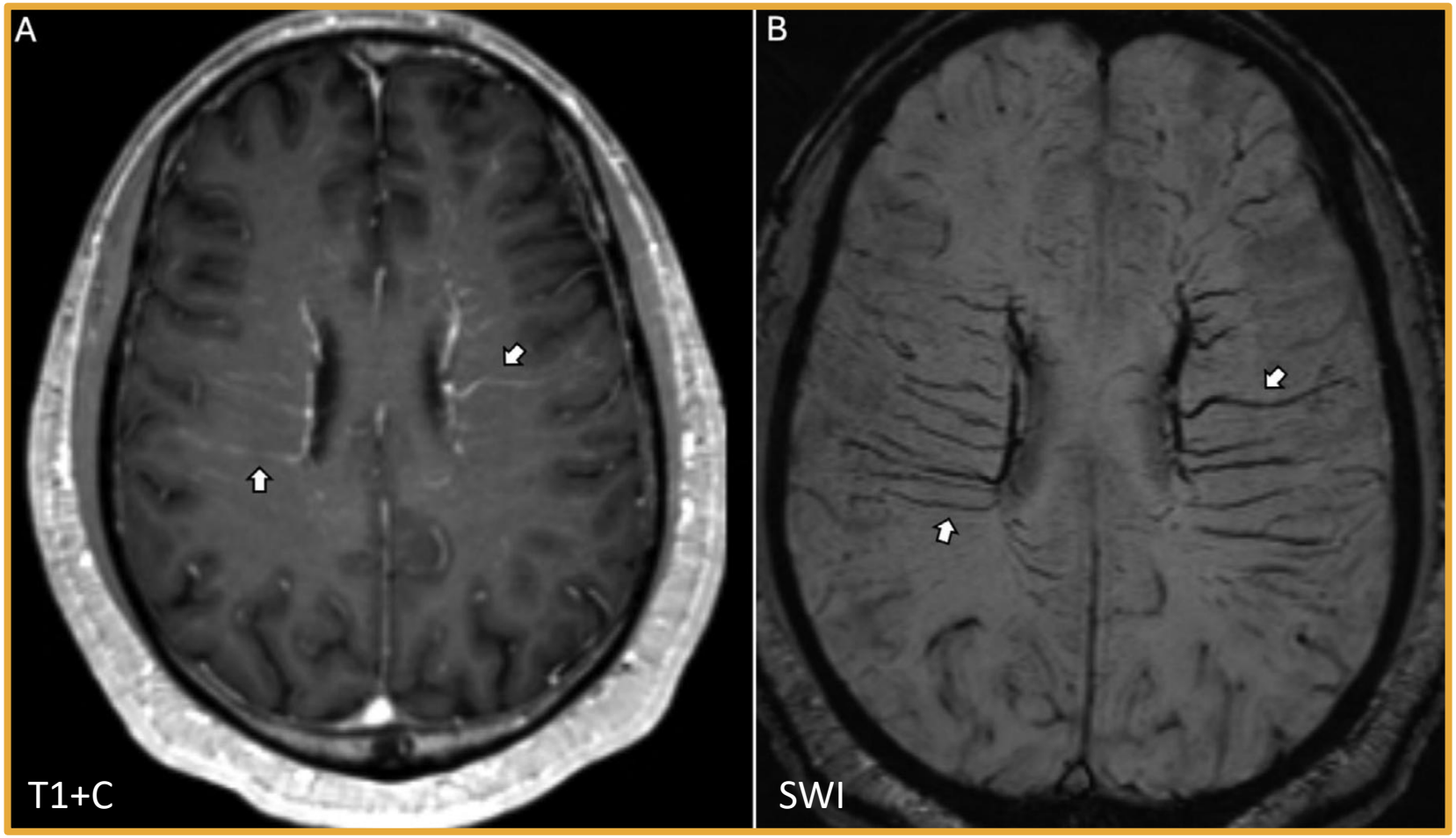
- In unselected patients with CNS sarcoid:
  - Large vessel enhancement: 3/13
    - Circumferential: 2/13
    - Adjacent meningeal: 1/13
  - Lenticulostriate perforators: 6/13
    - Tortuous and/or dilated
  - Medullary veins: 5/13
    - Tortuous and/or prominent



Bathla et al. Neurol Neuroimmunol Neuroinflamm 2021.

Deep Medullary Vein Engorgement

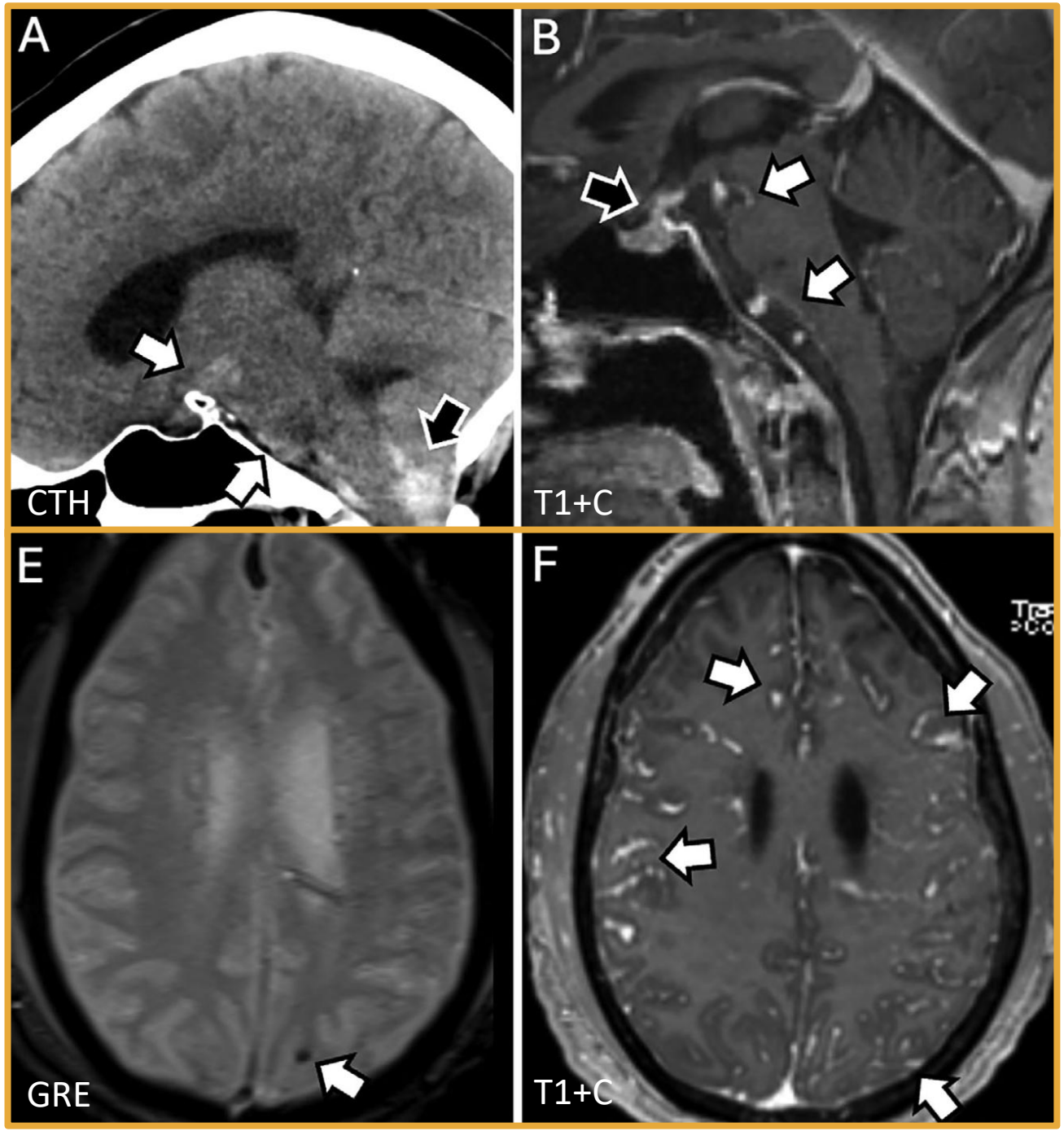
- Best seen on SWI
- Occurs at low frequency (25-33%)
- Can occur in other disorders



Zamora et al. Am J Neuroradiol 2018.
Hutto & Bou. Clinical Neuroimaging 2025.

Intraparenchymal & Subarachnoid Hemorrhage

- Understudied
- Vasculitis & small vessel vasculopathy as possible mechanisms



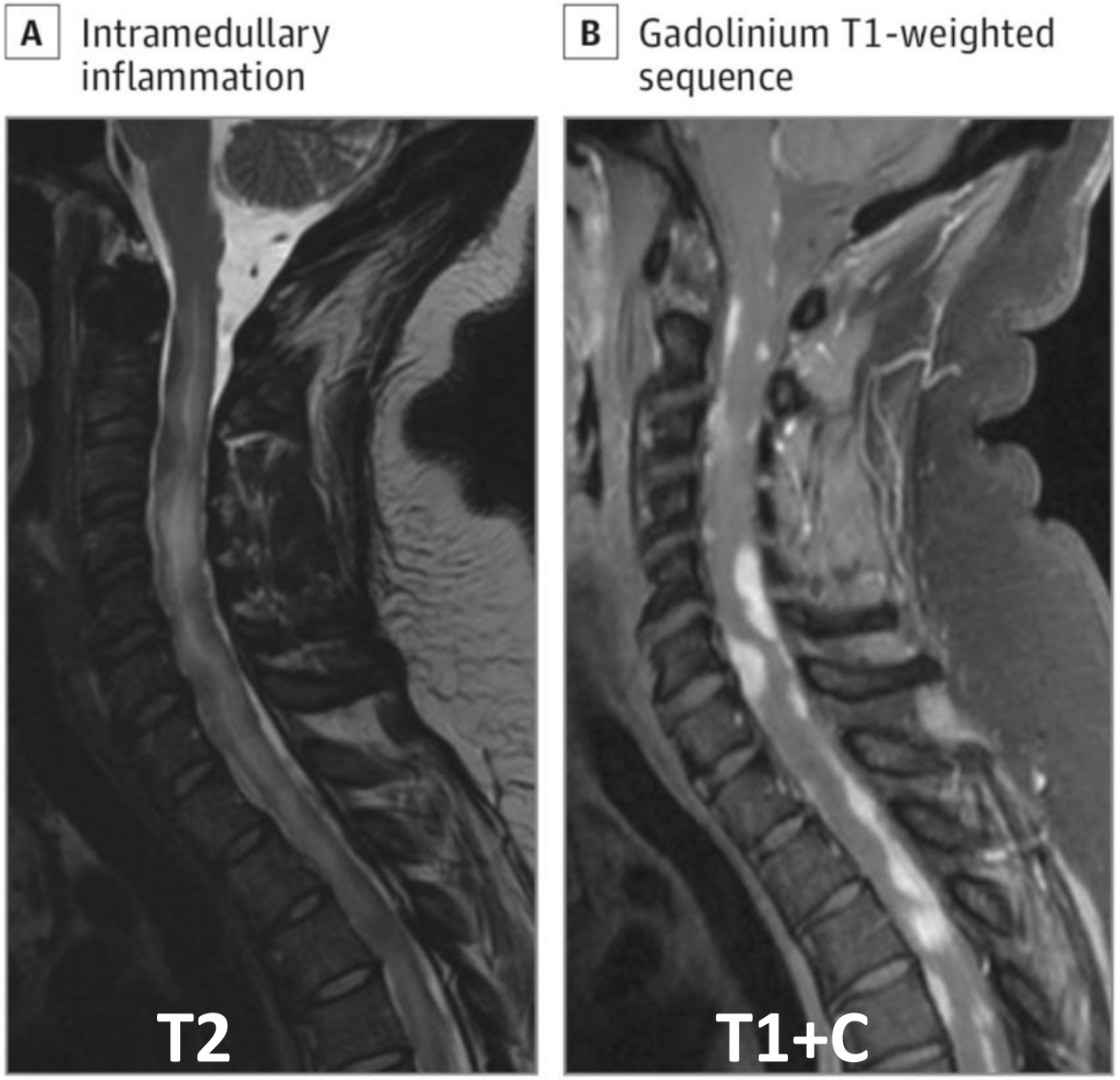
Hutto & Bou. Clinical Neuroimaging 2025.

Myelitis

- Often an initial neurologic manifestation
- Typically cervical but any segment
- Short or longitudinally-extensive
- Thoracic MRI may reveal hilar LAD
- Disabling
  - ~50% ending with mRS 2 or worse
  - Mostly as result of initial attack

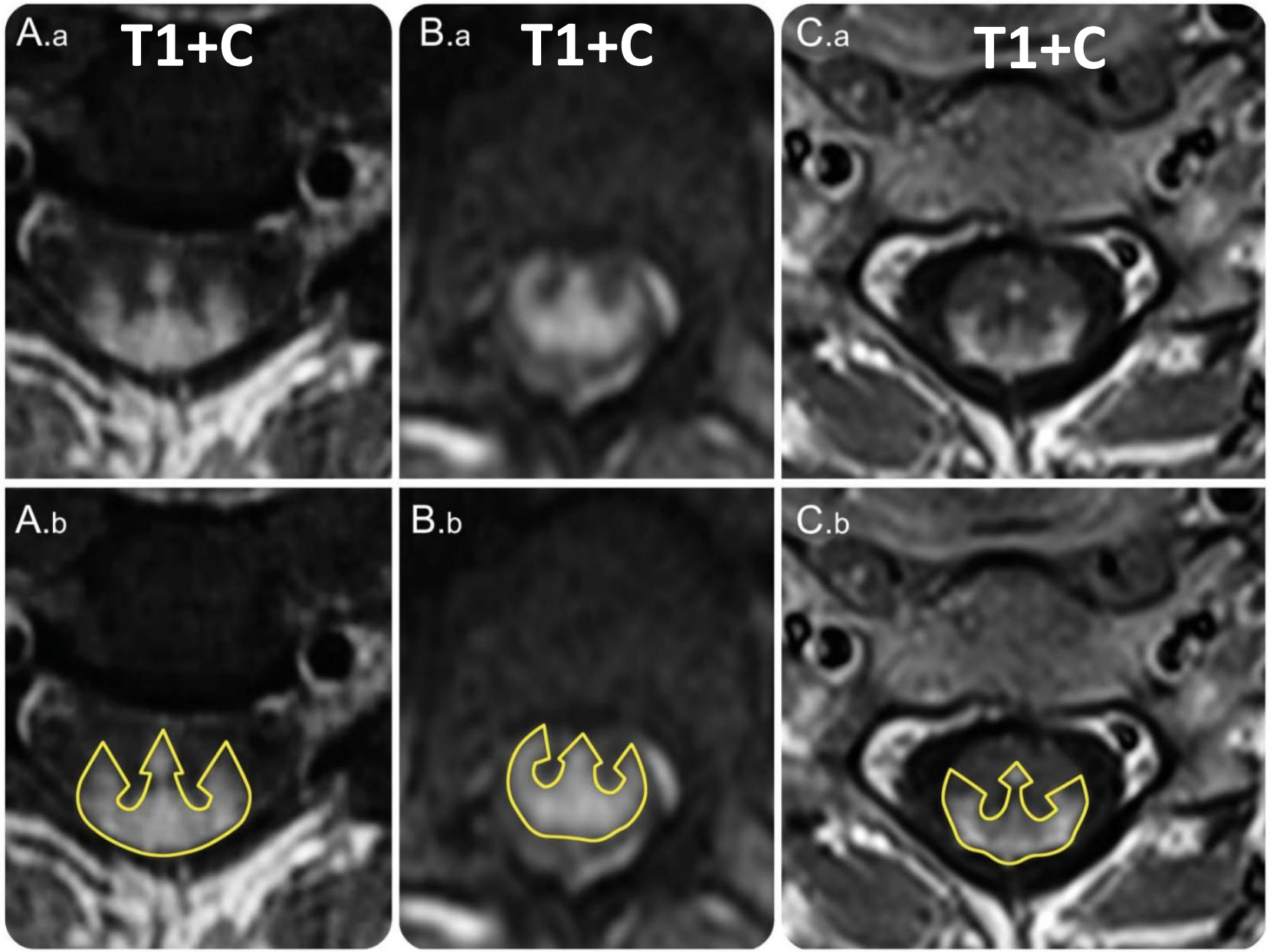
Kidd DP. Pract Neurol 2020.
Stern et al. JAMA Neurol 2018.
Flanagan et al. Ann Neurol 2016.

Outside-In Radiographic Patterns



Dorsal Subpial & Central Canal Enhancement

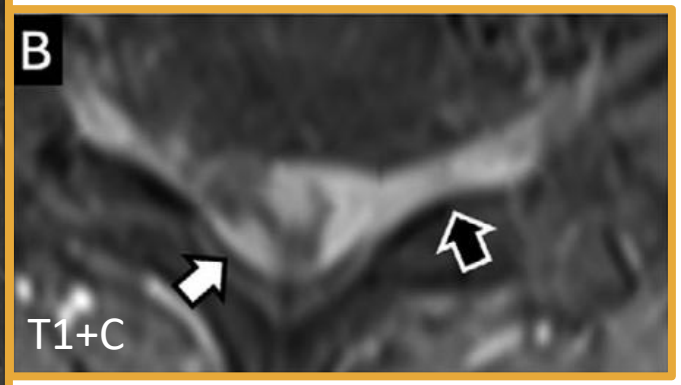
Trident Sign

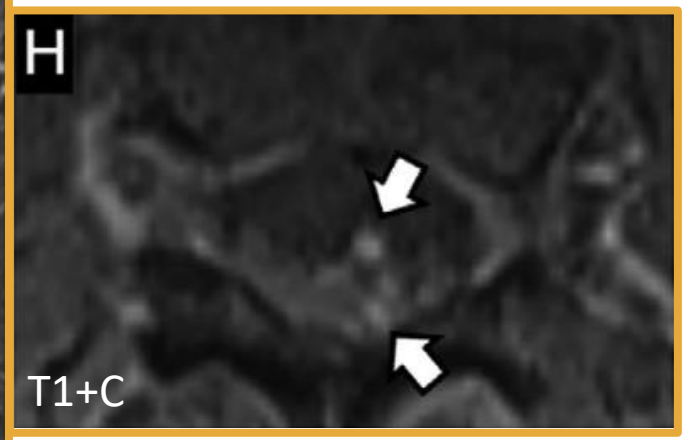


Zalewski et al. Neurology 2016.

Cauda Equina & Spinal Nerve Roots

- Cauda equina
  - 6.5% of patients
  - Nodular enhancement
  - Often co-existent with myelitis
- Spinal nerve roots
  - Often co-existent with spinal leptomeningitis





Hutto & Bou. Clinical Neuroimaging 2025.
Bou et al. Neurol Neuroimmunol Neuroinflamm 2022.
Murphy et al. Neurol Neuroimmunol Neuroinflamm 2020.

Radiographic Differential Diagnosis, Part 1

*No radiographic abnormalities are known to be pathognomonic for neurosarcoidosis

Differential diagnosis by cranial neuroanatomical location	
Leptomeningitis	Bacteria (especially tuberculosis) Fungi (especially Coccidioides and Cryptococcus) Spirochetes (especially syphilis and Lyme) MOG antibody disease Cancers (carcinomas, lymphoma)
Pachymeningitis	Meningioma Systemic metastases Rheumatologic (IgG4-RD, AAV, RA, SLE) Histiocytoses (Erdheim-Chester, Rosai-Dorfman) Tuberculosis
Cranial neuropathies	Bacteria (especially Lyme and syphilis) Viruses (HIV, VZV, CMV) Bell's palsy Rheumatologic (AAV, SLE, IgG4-RD) Inflammatory polyradiculoneuropathies (GBS, MFS) Cancer (carcinomas, lymphoma, leukemia) Diabetes Nutritional disease (B12, copper, thiamine)
Optic neuropathy	Demyelinating disease (MS, MOGAD, NMO) Bacteria (especially Bartonella, Lyme, toxoplasmosis, syphilis) Viruses (CMV, VZV) Ischemic optic neuropathies (arteritic, nonarteritic) Paraneoplastic disease (CRMP5) Cancer (meningioma, optic glioma, lymphoma) Nutritional disease (B12, copper, thiamine)
Ventriculitis	Bacteria Lymphoma CMV
Brain parenchymal lesions	Demyelinating disease (MS, MOGAD, NMO, ADEM) Cancer (carcinomas, lymphoma, glioma) Inflammatory (PACNS, Behçet, CLIPPERS, Susac) Histiocytoses Infection (abscess, encephalitis, PML)
Hypothalamus, pituitary gland, infundibulum	Histiocytoses (Langerhan) IgG4-RD, NMO Tumors (glioma, parasellar meningioma, lymphoma, leukemia, metastases) Developmental (craniopharyngioma, germinoma, hamartoma) Autoimmune (lymphocytic hypophysitis, autoimmune hypothalamitis) Bacteria (syphilis, tuberculosis)
Cavernous sinus disease	Tolosa–Hunt syndrome Vascular disorders (carotid-cavernous fistula, cavernous sinus thrombosis) Cancer (lymphoma, metastases, pituitary adenoma) Viruses (VZV) Fungi (Mucor, Aspergillus) Rheumatologic (AAV, orbital pseudotumor, GCA) Diabetes

Hutto & Bou. Clinical Neuroimaging 2025.

Radiographic Differential Diagnosis, Part 2

*No radiographic abnormalities are known to be pathognomonic for neurosarcoidosis

Differential diagnosis by cerebrovascular and spinal neuroanatomical location	
Ischemic stroke	Cerebral emboli (including due to cardiac sarcoidosis) Small vessel disease Intracranial atherosclerosis
Intracerebral hemorrhage	Vasculitis from other causes Cerebral amyloid angiopathy Hypertension Systemic metastases Hemorrhagic conversion of ischemic infarcts
Vasculitis	Intracranial atherosclerosis Viruses (VZV, HIV, CMV) Fungi (Cryptococcus, Coccidioides, Aspergillus, Histoplasma) Bacteria (syphilis, tuberculosis, Lyme) Rheumatologic (AAV, cryoglobulinemic, Behçet, RA, GCA, SLE) Intravascular lymphoma
Myelitis	Demyelinating disease (MS, MOGAD, NMO) Viruses (HIV, HTLV, VZV, WNV, enteroviruses) Bacteria (syphilis, tuberculosis) Spinal cord infarction Nutritional (B12, folate, copper, vitamin E) Systemic metastases Primary malignancies (ependymoma, astrocytoma)
Cauda equina disease	Viruses (CMV, HSV, VZV) Bacteria (Lyme, tuberculosis, mycoplasma) Cancer (carcinomas, lymphoma) MOG Inflammatory polyradiculoneuropathies (GBS, CIDP)

Hutto & Bou. Clinical Neuroimaging 2025.

Thank You!

Questions? shutto@emory.edu

EMORY UNIVERSITY SCHOOL OF MEDICINE
Department of Neurology