ENCEPHALITIS

TWO VERY DIFFERENT CASES DURING A WEEK OF HOSPITALIST

Dr Nancy Bozek Feb 5, 2025

CONFLICTS OF INTEREST

- I HAVE NONE TO DECLARE

OBJECTIVES

Describe	Describe the presentation of patients with encephalitis
Develop	Develop an approach to autoimmune encephalitis
Distinguish	Distinguish West Nile from other viral encephalitis

CASE 1 – A 40-50 YEAR OLD MALE

- Presented to his family doctor with a week of viral type symptoms and a rash for 1 day that was non pruritic
- Had 1 day of fever and chills, intermittent myalgias, frontal headache
- Sore throat, rhinorrhea were ongoing, 1 day of diarrhea
- No travel
- Works in construction
- He had a maculopapular rash on his trunk, back arms and forehead
- Temp 37.1
- The rest of his exam was essentially normal

Two days later…

- Present to ER
- Started to feel confused and had weakness of his Rt arm
- Transient diplopia, mild neck pain
- T: 39.6 P:110 RR:16 BP: 131/82
- GCS 14
- Normal neuro exam except for rt arm was totally flaccid

DDX from ER: meningitis vs encephalitis

- Treatment:
  - Ceftriaxone
  - Vancomycin
  - Acyclovir

Meningitis vs Encephalitis

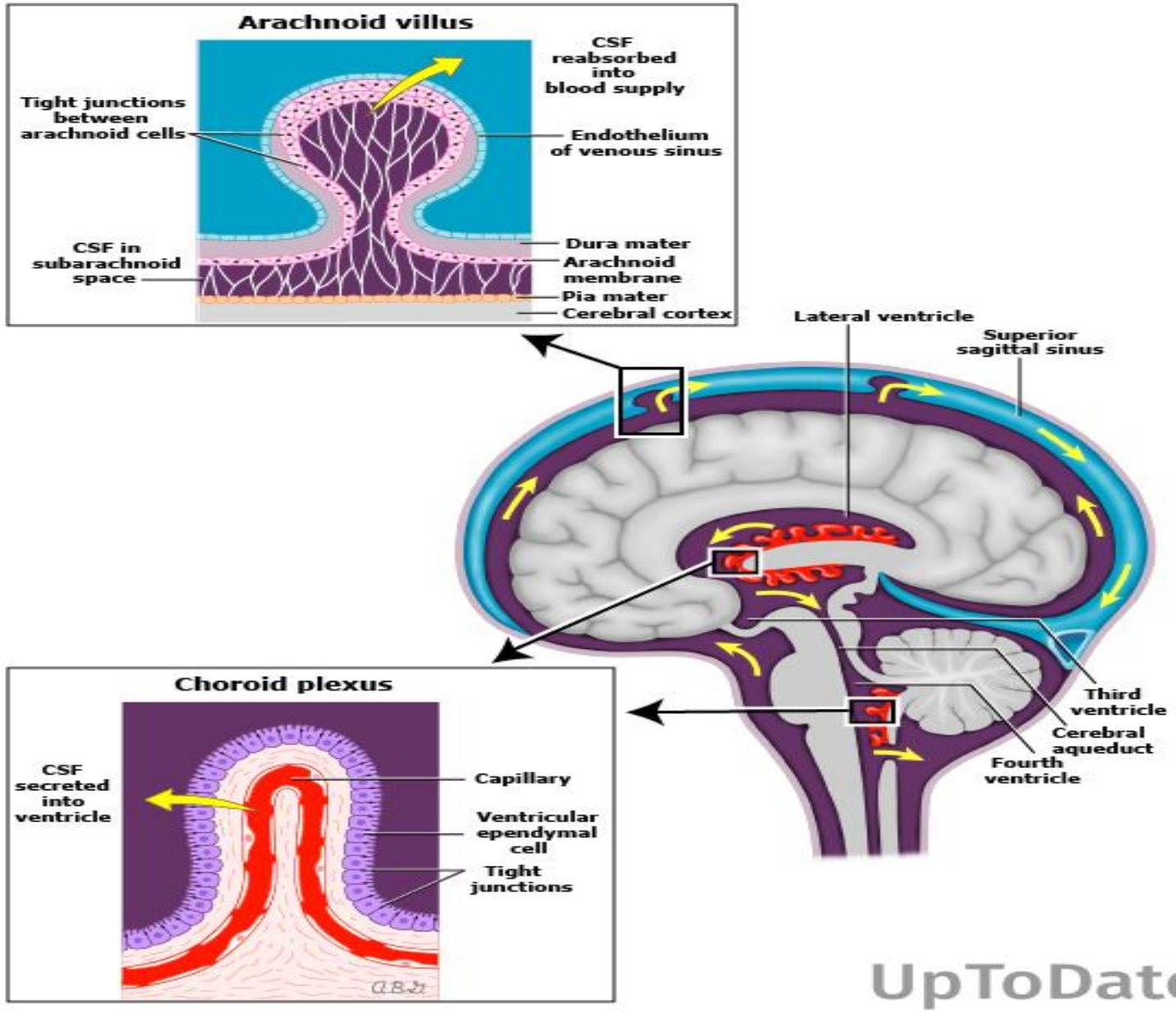
- Patients with meningitis have normal cerebral function
- They may be lethargic

- Patients with encephalitis have abnormalities in brain function
- This includes:
  - Altered mental status
  - Motor or sensory deficits
  - Altered behavior and personality changes
  - Speech or movement disorders
  - Also may include hemiparesis, flaccid paralysis and paresthesias

Investigations

- Cr 117, LFTS and calcium and lytes normal
- CK: 282 (55-170), WBC:11.3 (4.8-10.8), Hgb: 160 (140-180)
- CSF cell count lymphocytes: 93 (40-80)
- CSF neutrophils: 2 (0-0)
- CSF nucleated cells: 127 (0-5)
- CSF protein: 1169 (120-600)
- CSF glucose: 2.9 (2.2-3.9)
- CRP: 21.6 (<8)
- Blood cultures and CSF cultures came back negative

Cerebrospinal fluid (CSF) formation and reabsorption

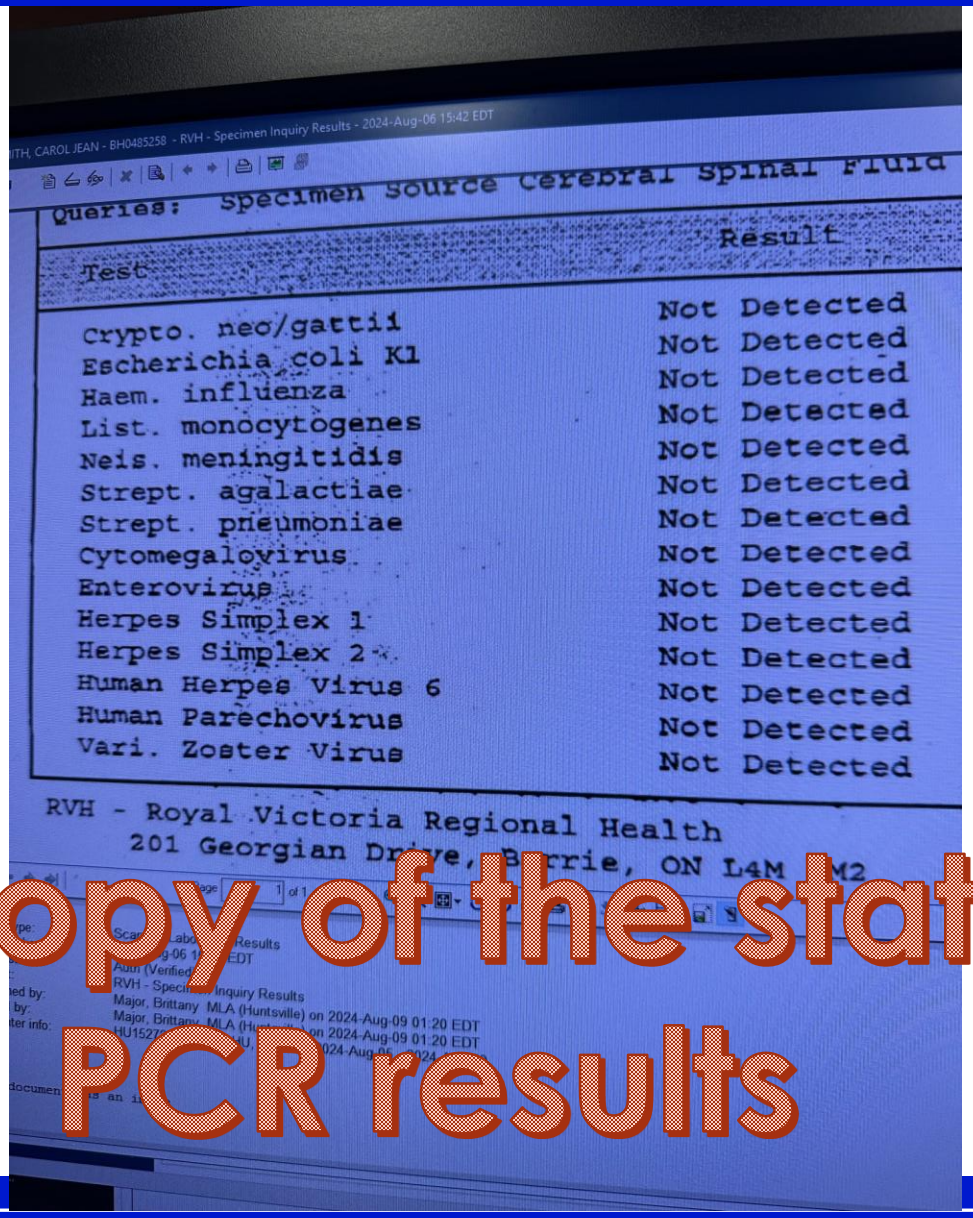


Interpretation of CSF Fluid

Bacterial meningitis	Viral meningitis	Fungal meningitis	Viral encephalitis
Increased WBC Especially neutrophils	Increased WBC Especially lymphocytes	Increased WBC but varies	Increased WBC Especially lymphocytes
Increased protein	Increased protein	Increased protein but varies	Increased protein
Decreased glucose	Normal or slightly low glucose	Normal glucose	Normal or slightly low glucose

CSF PCR

- Needs to be stat from ER
- If not it goes to public health and takes up to a week for results instead of 24 hours
- We talked to the lab and had it redirected
- Enterovirus, Herpes simplex, Varicella Zoster were negative
- WNv is not part of the test



Copy of the stat PCR results

How to test for West Nile virus

- Serology is recommended not CSF fluid, although either can be tested

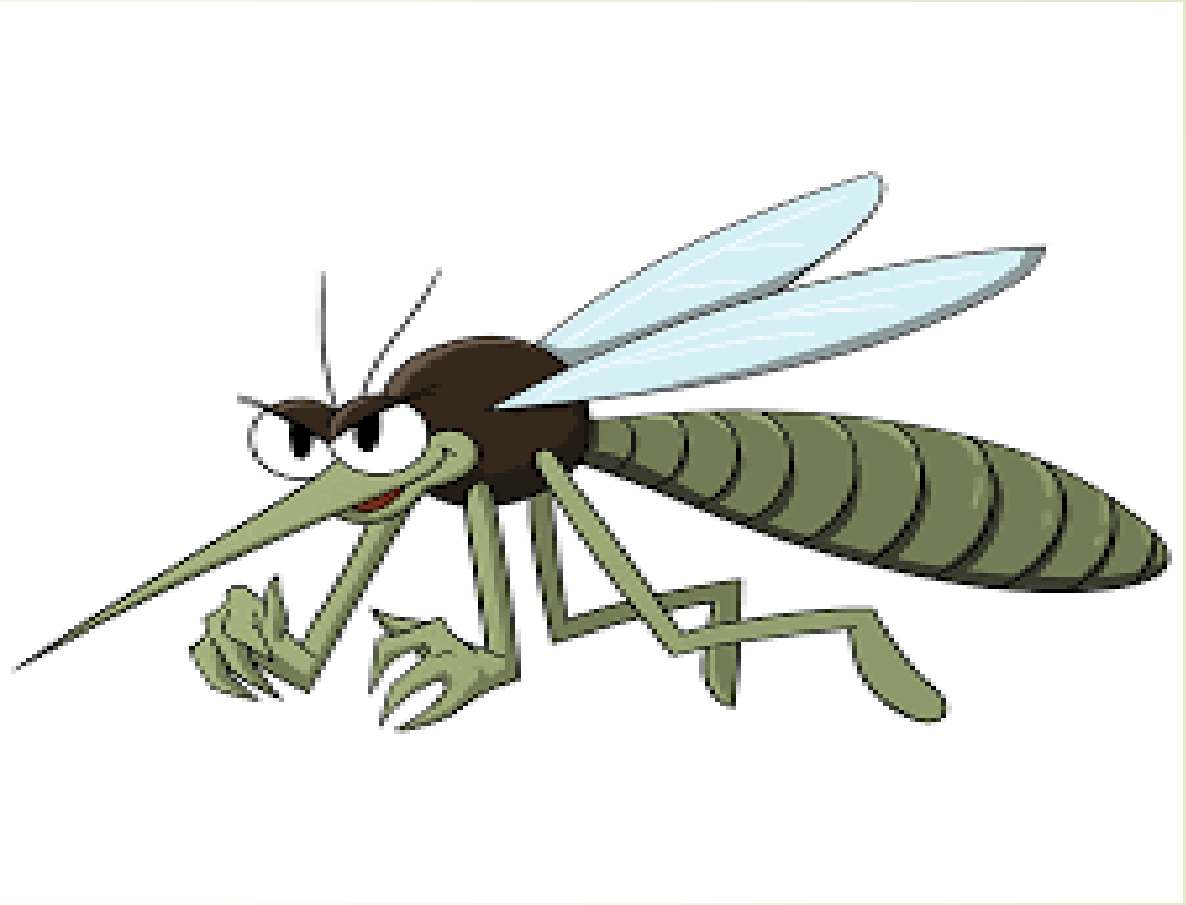
- His results:
  - IgG non- reactive
  - IgM reactive (detected 3-8 days after onset of illness)
  - IgM antibodies usually remain detectable 1-2 months following resolution of symptoms
  - West Nile PRNT (plaque reduction neutralization test): indeterminate
  - Interpretation: Possible recent or acute WNv infection

First Lab-Confirmed West Nile virus Case in SMDHU

WEST NILE VIRUS

- By the end of summer there were 12 WNv cases in Ontario in 2024
- Clinical presentations: asymptomatic, non neurological and neurological
- 20% of people develop the less severe symptom complex known as WNv non neurological syndrome

Transmission



Incubation period is 2– 14 days

WNv non neurological syndrome symptoms

- Flu like illness with fever headache
- Occasionally skin rash (20-50%)
- Occasionally swollen lymph nodes
- Other symptoms may include nausea, vomiting, eye pain or photophobia

WNv Neurological symptoms

- Encephalitis (more common in elderly patients)
- Meningitis (more common in children)
- Flaccid paralysis
- Conditions similar to Parkinson's syndrome
- Fewer than 1% of patients will develop neurological symptoms

Symptoms of West Nile Encephalitis

- Varies from mild confusion to severe encephalopathy, coma and death
- Extrapyramidal symptoms are common
  - Coarse tremor, myoclonus especially in upper extremities
  - Rigidity, postural instability and bradykinesia
  - Cognitive difficulties
- Acute flaccid paralysis results from an anterior horn cell process like polio
  - 1/ 3 recover strength, 1/3 modestly improve and 1/3 don't recover
  - Recovery occurs in the first 6-8 months of the illness
- Many other presentations like brachial plexopathy or demyelinating neuropathy or symptoms like GBS
- Less commonly presentation is cranial nerve palsies

UPDATE ON THE PATIENT

- ACCORDING TO MY CHART REVIEW, IT IS NOW 6 MONTHS LATER AND THERE HAS NOT BEEN SIGNIFICANT IMPROVEMENT

IT'S TIME FOR WARM UP TRIVIA

HOPE YOU ARE READY FOR WEDNESDAY FEBRUARY 26…GAME ON!

HOW WELL DO YOU REALLY KNOW YOUR STUDENT???

Which medical student was almost investigated for narcolepsy?

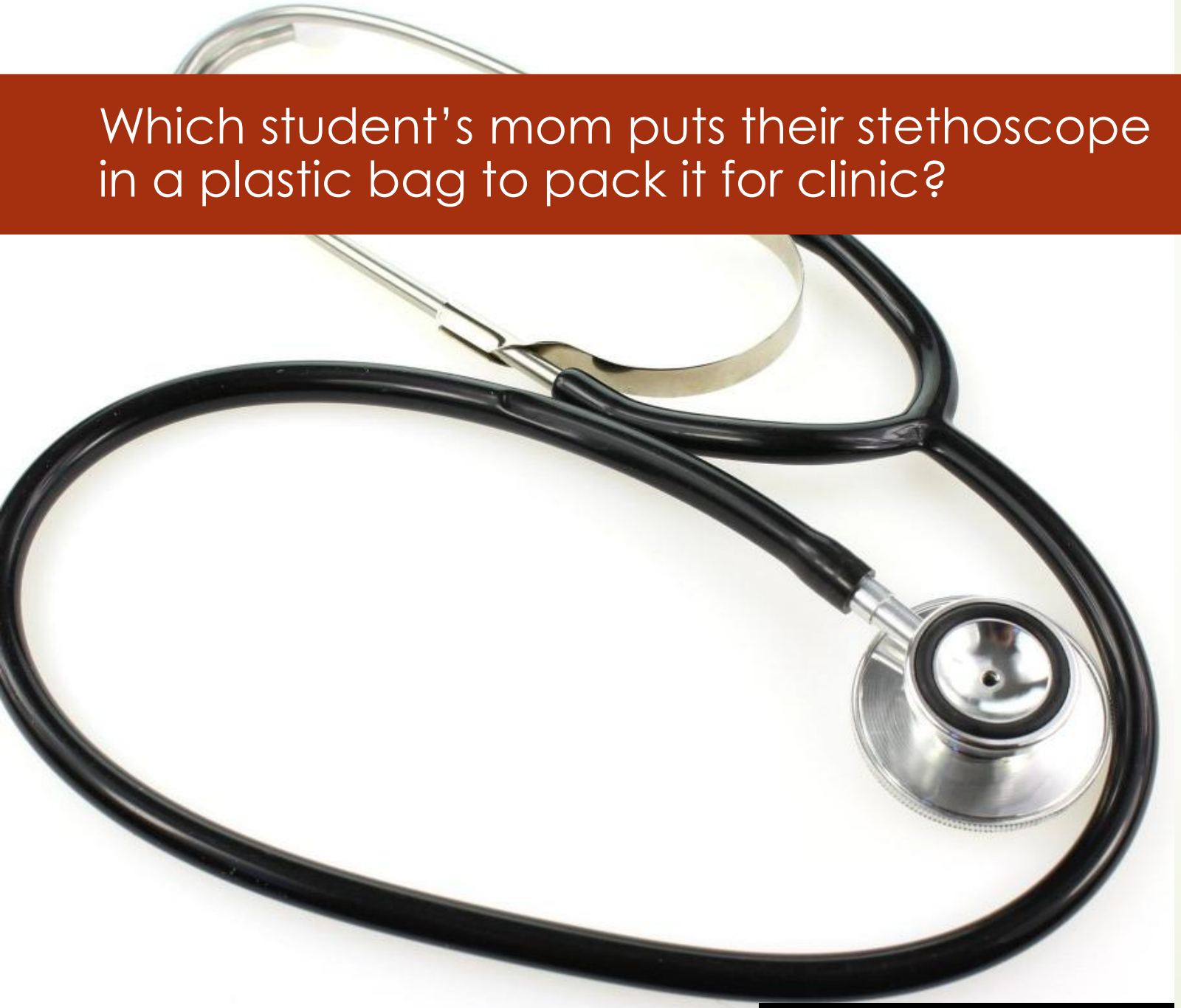
Which medical student prefers to do charades of their patients symptoms when presenting to their preceptor?

Which med student worked at

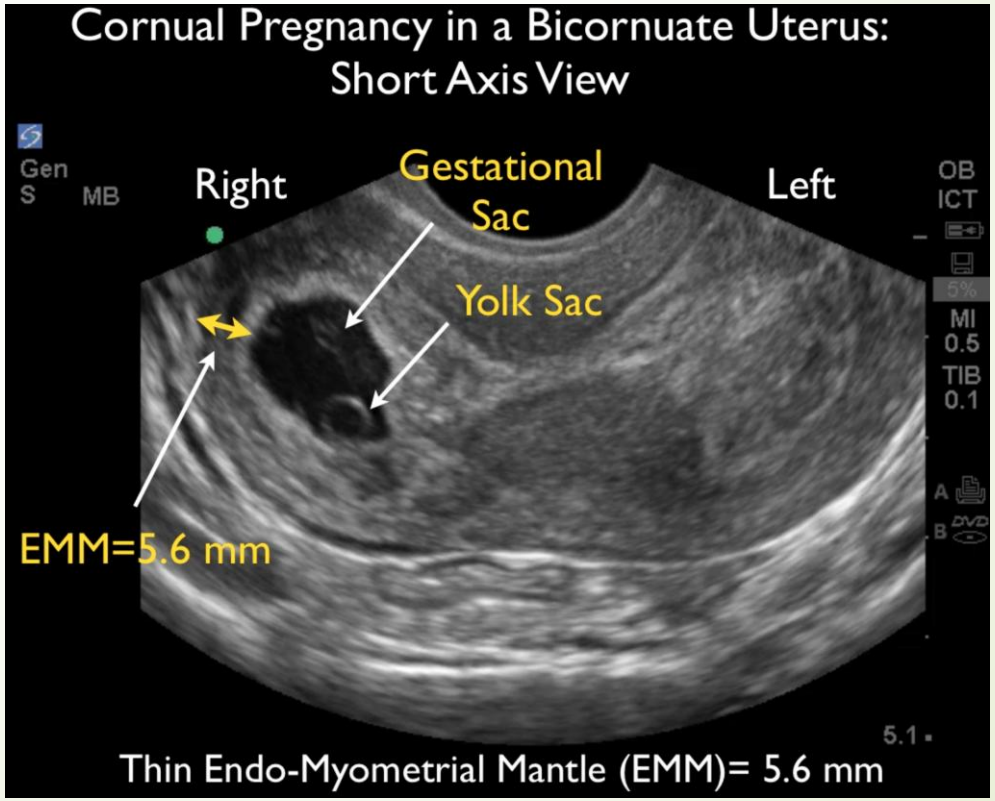
Which preceptor took his spouse to Hooters for their First Anniversary?

Which student holds each orange slice up to the light to make sure it doesn't have seeds because they choked on one as a child

Which student's mom puts their stethoscope in a plastic bag to pack it for clinic?



Which student hid in the shower of the change room to review ultrasound videos while on Anesthesia rotation?



CASE 2- A 70-80 YEAR OLD FEMALE

- She presented with a month of increased confusion, bizarre behaviour associated with 2 weeks of nausea, vomiting, hallucinations, Left hemiparesis and some hemineglect
- She has a diagnosis of myasthenia gravis and was on a taper of prednisone supervised by her neurologist in Toronto
- She had a negative CT of her head and C spine and CTA on admission
- Her first MRI of her brain was reported as normal but a repeat scan documented probable encephalitis of her right parietal lobe
- her admission Lumbar puncture was negative
- her admission laboratory investigations were unremarkable

Early Treatment during this Admission

- Ceftriazone for a UTI
- IVIG and prednisone for possible myasthenia crisis
- Thiamine for report of at least 2 alcoholic beverages per day

CLINICAL COMPLICATIONS DURING THIS ADMISSION

SHE HAD SEIZURE LIKE ACTIVITY

TREATED WITH KEPPRA AT THE SUGGESTION OF NEUROLOGY

CLINICAL OUTCOME

She slowly improved with physiotherapy and occupational therapy

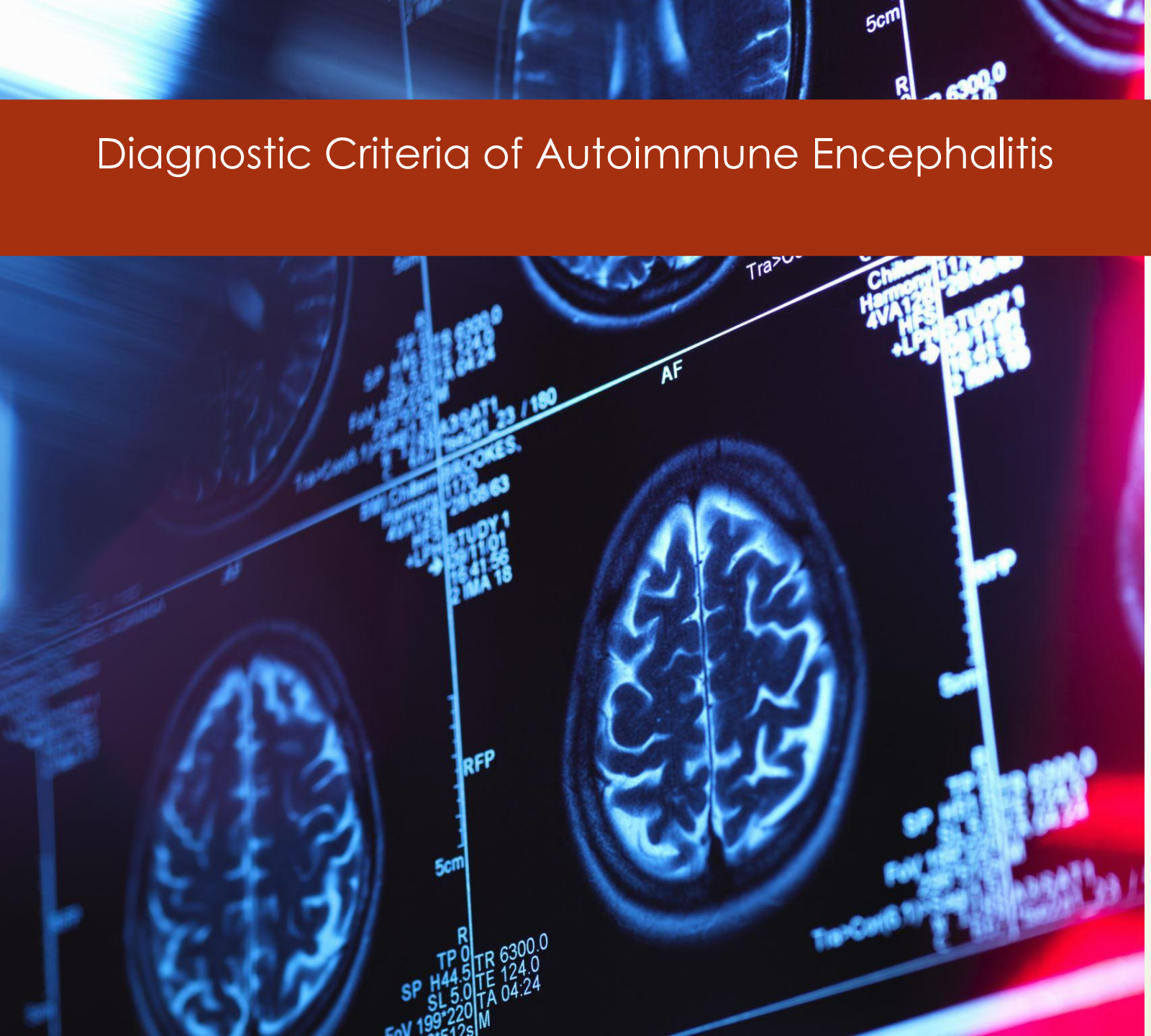
She was transferred to her home hospital while waiting for rehab

Autoimmune encephalitis is an inflammatory condition of the brain

Antibodies against neuronal cell surface synaptic proteins

Antibodes against intracellular neuronal proteins

Diagnostic Criteria of Autoimmune Encephalitis



- Subacute onset (<3 months) of memory deficits, altered mental status or psychiatric symptoms
- At least one of
  - New focal CNS findings
  - Seizures not explained by previous known seizure disorder
  - CSF pleocytosis (>5 WBC/mm3)
- Reasonable exclusion of alternative causes

Differential Diagnosis of Autoimmune encephalitis

Differential diagnosis of autoimmune (including paraneoplastic) encephalitis

Disorder	Clinical clues and diagnostic testing
Infectious etiologies	
Viral encephalitis (eg, HSV, HHV6, VZV, EBV, CMV, HIV, enterovirus, arbovirus)	CSF testing: Cultures, AFB smear, HSV1/2 PCR, HHV6 PCR, VZV PCR, EBV PCR, CMV PCR, HIV RNA, VDRL, Lyme antibodies, arbovirus panel, enterovirus PCR, T. whipplei PCR, 14-3-3, tau
Bacterial encephalitis (eg, Listeria, Bartonella, Mycoplasma, Rickettsia)	Serum testing: HIV, Lyme serologies
Spirochetal encephalitis (eg, syphilis, Lyme, leptospirosis)	Travel and exposure history
Fungal infection (eg, cryptococcus, coccidiomycosis, histoplasmosis)	
Tuberculosis	
Creutzfeldt-Jakob disease	
Whipple disease	
Toxic-metabolic	
Drug ingestion (eg, alcohol, ketamine, phencyclidine, organophosphates)	Serum and urine toxicology screens
Carbon monoxide	Carboxyhemoglobin, MRI (eg, diffusion restriction in basal ganglia, white matter)
Wernicke encephalopathy	Alcohol misuse or malnutrition, oculomotor dysfunction, MRI (periaqueductal gray, mamillary bodies, medial thalami)
Brain fog due to chemotherapy, polypharmacy, or post-COVID	History of exposure, temporal relation to the event
Immune effector cell-associated neurotoxicity syndrome	Causative medication (eg, CAR-T cell therapy), concomitant cytokine release syndrome (often but not always)
Neuroleptic malignant syndrome	Causative medications (eg, neuroleptics, antiemetics, concomitant lithium), dopaminergic withdrawal, elevated creatine kinase
Vascular disorders	
Reversible posterior leukoencephalopathy syndrome	Headaches, hypertension, causative medications (eg, immunosuppression, angiogenesis inhibitors), MRI (posterior predominant or brainstem T2 hyperintensities)
Primary or secondary angiitis of the central nervous system	Strokes involving multiple vessels, abnormal vascular imaging, ANCA, cryoglobulins, aPL antibodies, brain biopsy
Behçet disease	Painful mucocutaneous ulcers, uveitis, positive pathergy test
Susac syndrome (autoimmune vasculopathy)	Hearing loss, branch retinal artery occlusions on fluorescein angiography, MRI (corpus callosum and periventricular white matter abnormalities)
Neoplastic disorders	
Leptomeningeal metastases	MRI (leptomeningeal enhancement, communicating hydrocephalus), CSF cytology
Diffuse glioma	MRI (expansile, T2 hyperintense lesion), normal CSF
Primary or secondary central nervous system lymphoma	MRI (parenchymal or leptomeningeal enhancement); CSF cytology, flow cytometry, and IgH gene rearrangement
Demyelinating or inflammatory disorders	
Multiple sclerosis	CSF oligoclonal bands (nonspecific), lesions separated in time and space
Neuromyelitis optica spectrum disorder	AQP4-IgG antibodies
Myelin oligodendrocyte glycoprotein antibody-associated disease	MOG-IgG antibodies
Acute disseminated encephalomyelitis (ADEM)	Preceding infection or vaccination; MRI with diffuse, multifocal, poorly demarcated lesions predominantly involving white matter; no new clinical or MRI findings after three months
Rasmussen encephalitis	Unilateral seizures and progressive neurologic deficits
Neurosarcoidosis	Hilar adenopathy or pulmonary parenchymal changes, elevated ACE level (nonspecific)
Neurodegenerative dementias	
Alzheimer disease dementia	MRI (often normal early in the course, may show focal atrophy); regional abnormalities on brain PET/SPECT, family history (for frontotemporal dementia)
Frontotemporal dementia	
Dementia with Lewy bodies	
Vascular cognitive impairment	
Psychiatric disease	
Schizophrenia and other psychotic disorders	Toxicology screens
Bipolar disorder	Family history
Functional neurological symptom disorder (conversion disorder)	Negative imaging and CSF
Substance abuse	
Inherited and metabolic disorders	
Mitochondrial cytopathies	Serum or CSF lactate elevation, lactate peak on MR spectroscopy

HSV: herpes simplex virus; HHV6: human herpes virus 6; VZV: varicella zoster virus; EBV: Epstein Barr virus; CMV: cytomegalovirus; HIV: human immunodeficiency virus; CSF: cerebrospinal fluid; AFB: acid fast bacilli; PCR: polymerase chain reaction; RNA: ribonucleic acid; VDRL: Venereal Disease Research Laboratory; MRI: magnetic resonance imaging; CAR-T: chimeric antigen receptor-T; ANCA: antineutrophil cytoplasmic antibodies; aPL: antiphospholipid; IgH: immunoglobulin heavy chain; AQP4: aquaporin-4; IgG: immunoglobulin G; MOG: myelin oligodendrocyte glycoprotein; ACE: angiotensin converting enzyme; PET: positron emission tomography; SPECT: single photon emission computed tomography.

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COMPREHENSIVE AUTOIMMUNE ENCEPHALITIS PANAL

- Anti – AQP4,S
- Anti- MOG, S
- Anti – AMPAr1
- Anti- CASPR2
- Anti- DPPX CBA
- Anti – GABARB1
- Anti – LGI1
- Anti – NMDAR
- Anti - Amphiphysin
- Anti CV2
- Anti GAD65
- Anti Hu immunoblot
- Anti- MA2
- Anti -Recoverin
- Anti –Ri Immunoblot
- Anti -Titin
- Anti- Tr (DNER)
- Anti- Yo Immunoblot

All tests were negative

QUESTIONS?