CANP 2023 Diagnostic Cases

Contents

Case #1

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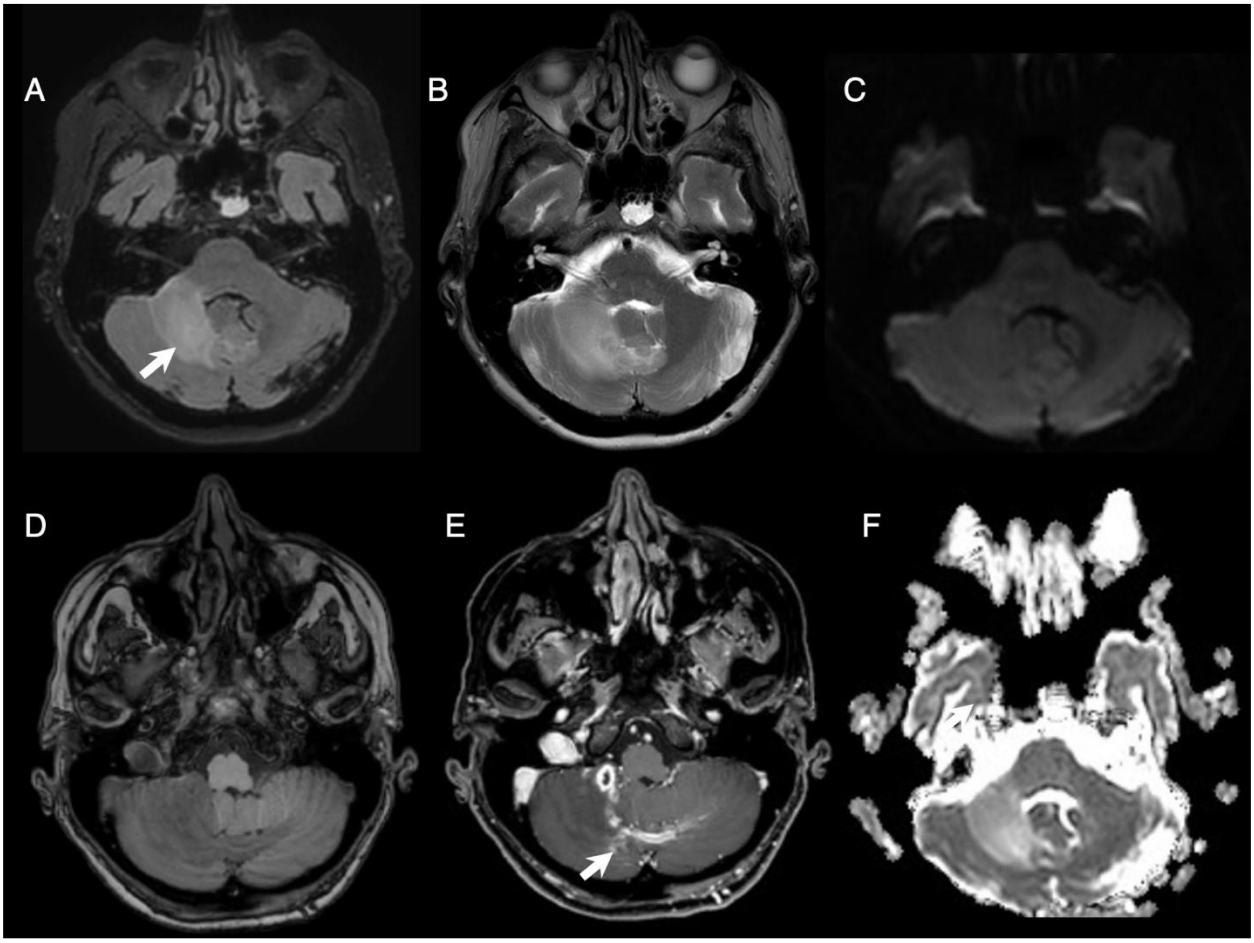
Clinical summary

A 74-year-old Caucasian woman was admitted for a 2-week history of a rapidly evolving cerebellar syndrome including ataxia, vertigo, nausea, vomiting and generalized fatigue. Her past medical history was significant for mild COPD and hypothyroidism. She had no history of recent travel. Besides horizontal nystagmus and slight right upper limb dysmetria, the physical and routine bloodwork were unremarkable. The initial lumbar puncture showed a slight pleocytosis, mildly elevated cerebrospinal fluid (CSF) proteins, and mildly reduced CSF glucose. The numerous cultures (bacteria, mycosis, tuberculosis), PCR (multiplex, tuberculosis, toxoplasmosis, JCV, echinococcus, Whipple), and other tests (cryptococcus antigen, adenosine deaminase activity, flow cytometry, and neoplastic cell) were negative on the (CSF). Initial imaging showed non-specific cystic lesions in the right cerebellar hemisphere and vermis. A thoracoabdominal-pelvic CT scan with contrast showed a non-specific 14 cm enlarged spleen and small parenchymal opacities in the right superior pulmonary lobe, probably secondary to a bronchiolar infection. A first brain biopsy was performed. The patient was treated on quadri-therapy for tuberculosis and dexamethasone. After an initial improvement two month later the patient presented with fatigue and control imaging revealed a mixed evolution of the lesions with an increase in the size of vermis enhancement foci and regression of bilateral cerebellar hemisphere enhancement foci. Unfortunately, the patient was readmitted one week later for newly appearing aphasia, dysphagia and right brachiofacial paresis. A cerebral MRI confirmed the appearance in a few days of multiple masses affecting all lobes as well as the brainstem. A second biopsy was performed.

Submitted materials:

- Initial MRI
- Final MRI
- First brain biopsy
- Second brain biopsy

Initial brain MRI without and with contrast

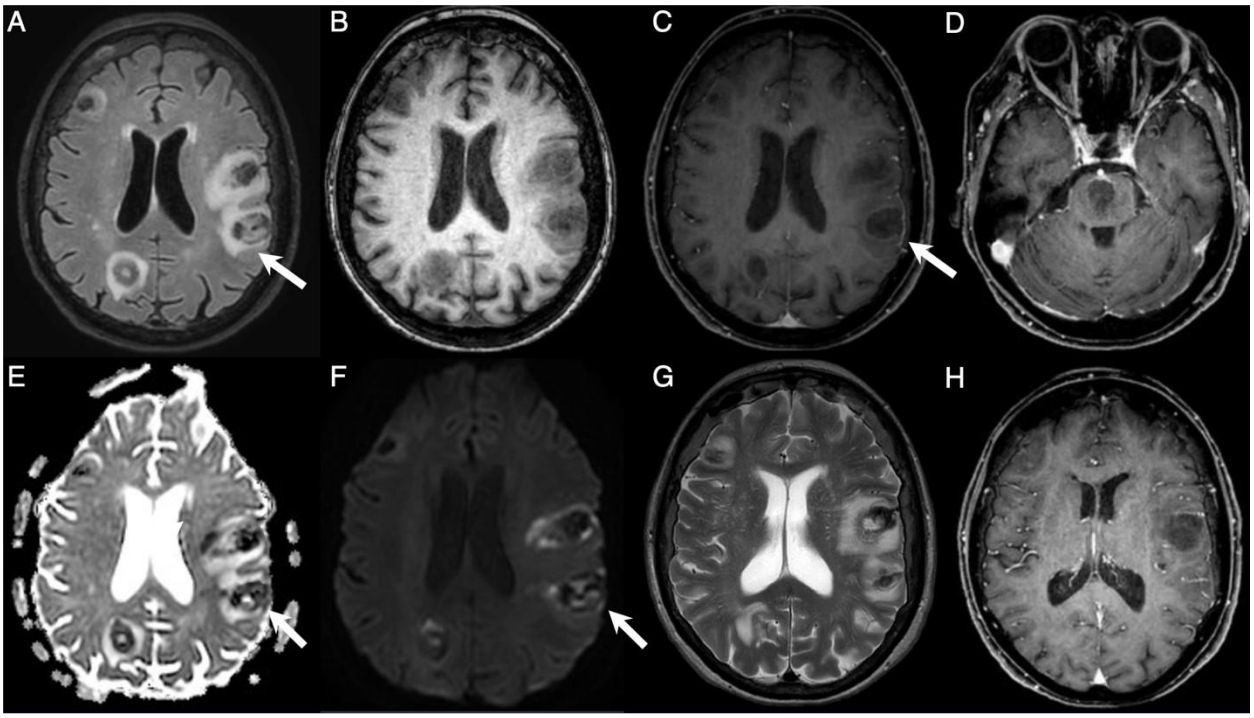


A) FLAIR and B) T2 without contrast: hyperintensity of the right cerebellar hemisphere and the vermis (arrow) compatible with edema.

C) Diffusion and F) ADC map: no evidence of restricted diffusion.

D) T1 without contrast and E) T1 with contrast: Clusters of cystic/necrotic enhancement with patchy enhancement (arrow) extending to the left cerebellum and signs of leptomeningeal involvement.

Final brain MRI without and with contrast



A) FLAIR and G) T2: Multiple new lesions with a lobar predominance (arrow) with surrounding hyperintense edema. Of note, the lesions were significantly hypointense on T2, compatible with associated hemosiderin/blood products.

B) T1 and C), D) and H) T1 fat saturated with contrast: faint peripheral enhancement (arrow) is noted.

D) ADC map, F) diffusion: areas of possible discontinuous restricted diffusion, especially at the periphery of certain lesions (arrow), though some of this signal could be artefactual related to the hemorrhagic components.

Discussion points:

- What is the diagnosis?

Case #2

Assem S. Alrumeh[1,2], Cynthia Hawkins[1,3], Gelareh Zadeh[4], Phedias Diamandis[1,2], Andrew F. Gao[1,2]

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Clinical summary

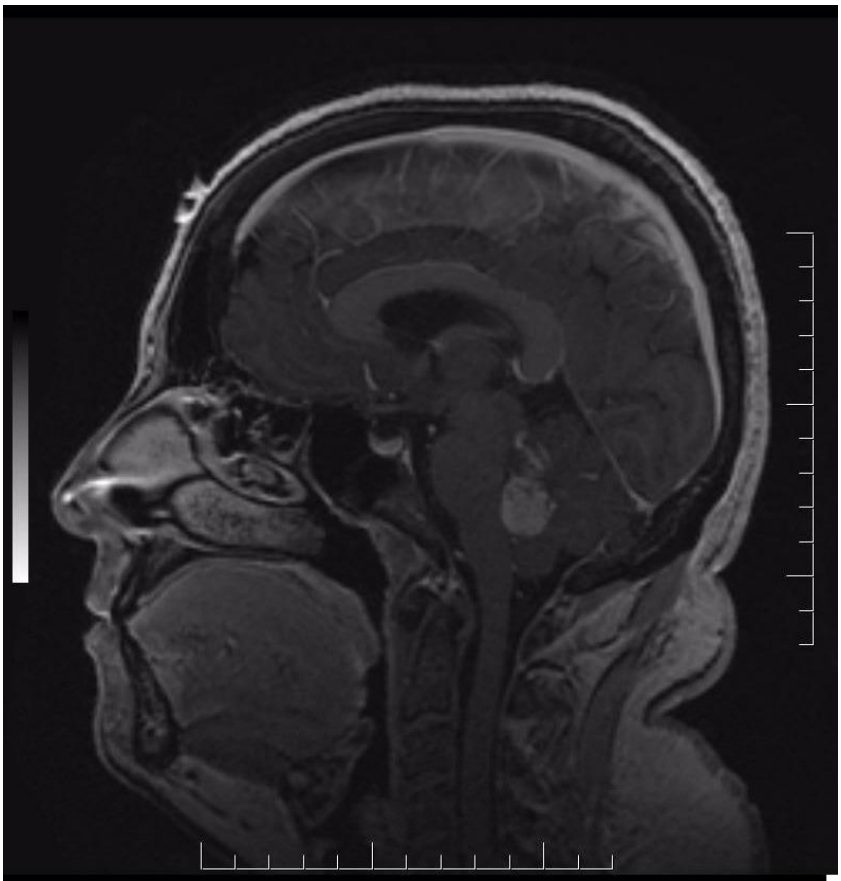
A 51-year-old woman presented with a 6-month history of persistent and progressive headache associated with dizziness and right tinnitus.

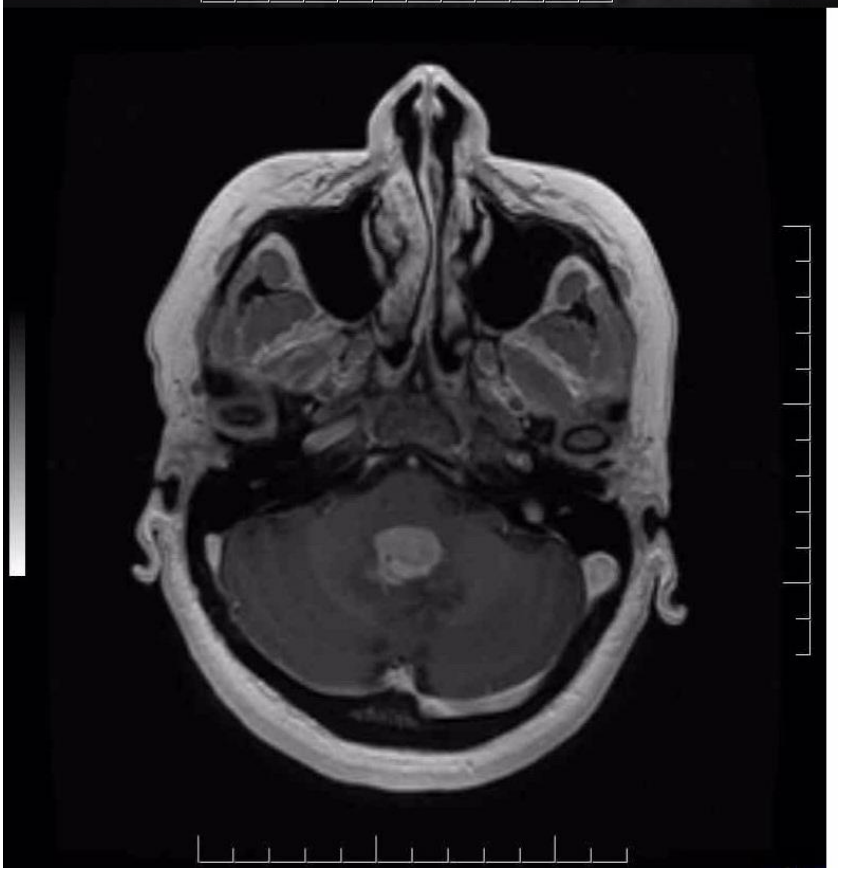
Neuroimaging revealed an enhancing tumor likely arising from the vermis with exophytic growth, filling much of the fourth ventricle. There was nodular enhancement along the superior cerebellar folia contiguous with the mass. Imaging of the spine was normal. Systemic imaging (CT chest, abdomen, and pelvis) was negative.

Following surgery, the patient was treated with 6 weeks of radiotherapy. Concomitant temozolomide was discontinued due to thrombocytopenia. Upon disease progression approximately 33 months after initial diagnosis, targeted therapy was trialed, but the patient ultimately succumbed to her disease 6 months later.

List of submitted materials:

- MRI sagittal view 1
- MRI axial view 2
- H&E slide





Discussion points

- Molecular differential diagnosis?
- Diagnostic workup?

Case #3

Abigale D. Maclellan[1], Gwynedd E. Pickett[1,2], Alexander S. Easton[1,3]

[1]Faculty of Medicine, [2]Division of Neurosurgery, [3]Department of Pathology, Dalhousie University, Halifax, Nova Scotia, Canada

Clinical summary

This 63 year old Caucasian male developed symptoms of Covid in March 2020, associated with confusion regarding place and time. In fall 2020 he was diagnosed with Lyme disease associated with joint pains and hair loss, and treated with doxycycline. There were persistent symptoms of confusion and fatigue and in April 2021 he presented to hospital with presyncope, where a CT head scan was performed. This revealed a hypointense subcortical lesion in the right temporal lobe. MR brain was performed in May 2021 which showed a T2 hyperintense region with central enhancement. He was assessed by neurosurgery in July 2021. There was no history of seizures, headache, focal weakness or problems with speech. The patient was HIV positive, diagnosed in 1995, on antiretrovirals with an undetectable viral load. He had low blood pressure with episodes of presyncope. He had smoked for 40 years, but quit in 2016. He inherited a benign essential tremor from his father. CT angiography was arranged, which demonstrated a serpiginous cluster of vessels fed by a prominent artery and draining vein. A stereotactic biopsy was performed, whose neuropathology was inconclusive. Unfortunately, the patient developed a generalized seizure after the biopsy, and has required long term anticonvulsants. He underwent a complete surgical resection in August 2021.

Material submitted

- Scanned single H&E stained slide (Aperio format)

Discussion points

- What proportion of infants with these tumors have intracranial involvement?
- What proportion of these intracranial tumors are intra-axial?
- What tumors are in the differential diagnosis?

Case #4

Karina Chornenka Martin[1], Peter W. Schutz[1]

1- Department of Pathology & Laboratory Medicine, University of British Columbia, Vancouver, British Columbia, Canada

Clinical Summary

A 33-year-old female with past medical history of hypothyroidism presents with a 3-year history of insidious onset weakness in the ankles with recurrent falls. Later in the course she develops additional weakness in her hands. She begins requiring bilateral ankle-foot orthoses, experiencing difficulty with ambulating long distances, and performing any kind of dextrous movements with her hands. She does not report sensory changes. There is no family history of neuromuscular or inflammatory diseases. On physical examination, there is asymmetric muscle wasting involving the intrinsic hand and foot muscles and forearm musculature. She demonstrates bilateral steppage gait and cannot heel walk but is able to walk on her toes. She can perform a low squat with some difficulty. Her hands show weakness of finger abduction and flexion. Reflexes are intact. There are no fasciculations or spasticity. Electromyography demonstrates a combination of myopathic and neurogenic features. MRI of the cervical and lumbar spine is normal. Laboratory investigations reveal a CK of 493, a medium positive result for anti-Ro52 antibodies, weak positive anti-PM/Scl 75, normal CRP, negative ANA and rheumatoid factor, negative serum electrophoresis, and non-reactive serology for Lyme, hepatitis B, C, HIV, and syphilis. All anti-ganglioside antibodies are negative. The patient is treated with monthly IVIG with no improvement in symptoms. A muscle biopsy is pursued for further evaluation.

Materials submitted

- H&E, frozen section
- Modified Gomori trichrome, frozen section
- TDP-43 immunohistochemistry, paraffin section

Discussion points:

- What is the histopathologic differential diagnosis and what is the most likely clinicopathologic diagnosis?
- What further stain can be pursued on the muscle biopsy to support the diagnosis?

Case #5

Claire I. Coire[1], David G. Munoz[2], Mihaly Kis[3]

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[3] Trillium Health Partners, Mississauga Hospital and Division of Neurosurgery, University of Toronto, Toronto, ON Canada

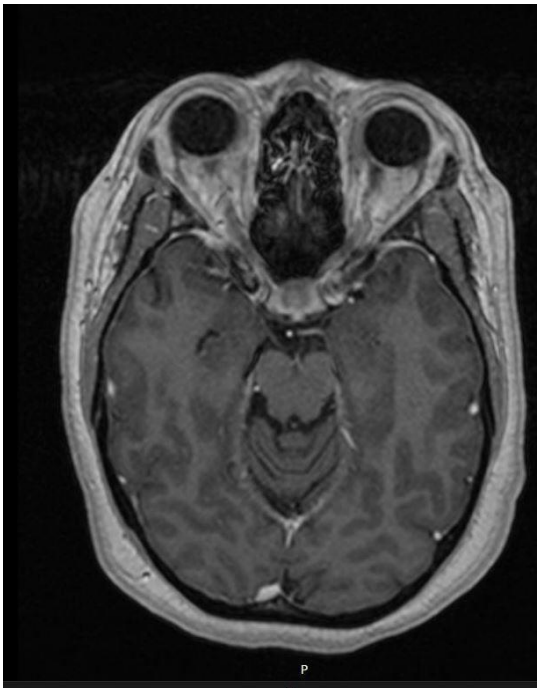
Clinical Summary

A 44-year-old female referred to a neurosurgeon for management of a sellar and suprasellar mass causing mass effect on the optic chiasma. The patient reported frequent bitemporal headaches and some visual blurring. She did not appear acromegalic. She did not report change in her facial features, or increase in the size of her hands and feet. She endorsed excessive sweating and numerous skin tags. Her weight had been relatively stable. Endocrine evaluation had been normal other than slightly elevated IGF-1 levels.

The preoperative MRI imaging of the sella had shown an expansile bilobed enhancing mass centered in the sella and suprasellar cistern that measured 12 x 12 x 10 mm.

Material submitted

- One H&E stained virtual slide



Discussion points

- Diagnosis
- What further immunostain(s) should be done in this case?
- What is the histogenesis of these lesions?

Case #6

Karam Han [1], Harry V. Vinters [2,3], Shino D. Magaki [2]

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[3] Department of Neurology, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California, USA

Clinical summary

61-year-old man who initially presented with word-finding difficulty and motor speech deficit, five years prior to his death. He also reported difficulties recalling information but denied personality changes, aggressive behaviors, or getting lost. Over the years, he became completely dependent in activities of daily living, with minimal verbal output. A family history of dementia on the paternal side is noted.

Submitted materials:

- 2 HE sections of frontal lobe, hippocampus
- 2 Tau (AT8) sections of frontal lobe, hippocampus
- Images (3R and 4R tau isoforms, Abeta section of frontal lobe)

Discussion points

- Differential diagnosis?
- Additional workup?
- Pathogenesis?

Case #7

Arnulf H. Koeppen

Research Service, VA Medical Center, Albany, NY12208

Clinical summary

A forensic pathologist forwarded the brain of a 56-year-old man who ran a rural tavern in upstate New York. The neuropathological interest arose from the patient's cognitive problem: He failed to record the sales of drinks at his bar. The forensic pathologist did not supply the forensic reason or the cause of death.

Submitted materials:

- 1 HE section.

Discussion points

- Learn about a new etiology of dementia.

Case #8

Christopher Newell [1], Katayoon Jafari [1], Kristopher D. Langdon [1], Denise Ng [1]

[1] Department of Pathology and Laboratory Medicine, University of Calgary, Calgary, AB, Canada

Clinical Summary

A 26-year-old male presented in January 2020 with a 5-day history of nausea, vomiting, and photophobia, who was found to have cranial lesions demonstrating contrast enhancement. Thirty-one months later (August 2022), he presented with a viral illness and anemia, and was found to have innumerable enhancing bony lesions throughout the entire visible axial and appendicular skeleton. Past medical history is significant for a remote resection of a pilocytic astrocytoma of the thoracic spine in Brazil (age 12), and a T2-T12 fusion for scoliosis in Brazil (age 14). A bone marrow biopsy was performed.

Submitted materials:

- One hematoxylin and eosin (H&E) stained slide.

Discussion points:

- What are the major histological findings?
- What is the differential diagnosis?
- What further investigations are warranted?

Case #9

Shane Eaton[1], Liesly Lee[2], Zachary Feilchenfeld[3], Chris Heyn[4], Cynthia Hawkins[1,5], Julia L. Keith[1,6]

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[2] Department of Medicine, Division of Neurology, Sunnybrook Health Sciences Centre and University of Toronto, Toronto, ON, Canada

[3] Department of Medicine, Division of Internal Medicine, Sunnybrook Health Sciences Centre and University of Toronto, Toronto, ON, Canada

[4]Department of Diagnostic Imaging, Sunnybrook Health Sciences Centre, Department of Medical Imaging, University of Toronto, Toronto, ON, Canada

[5] Department of Paediatric Laboratory Medicine, Hospital for Sick Children, Toronto, ON, Canada

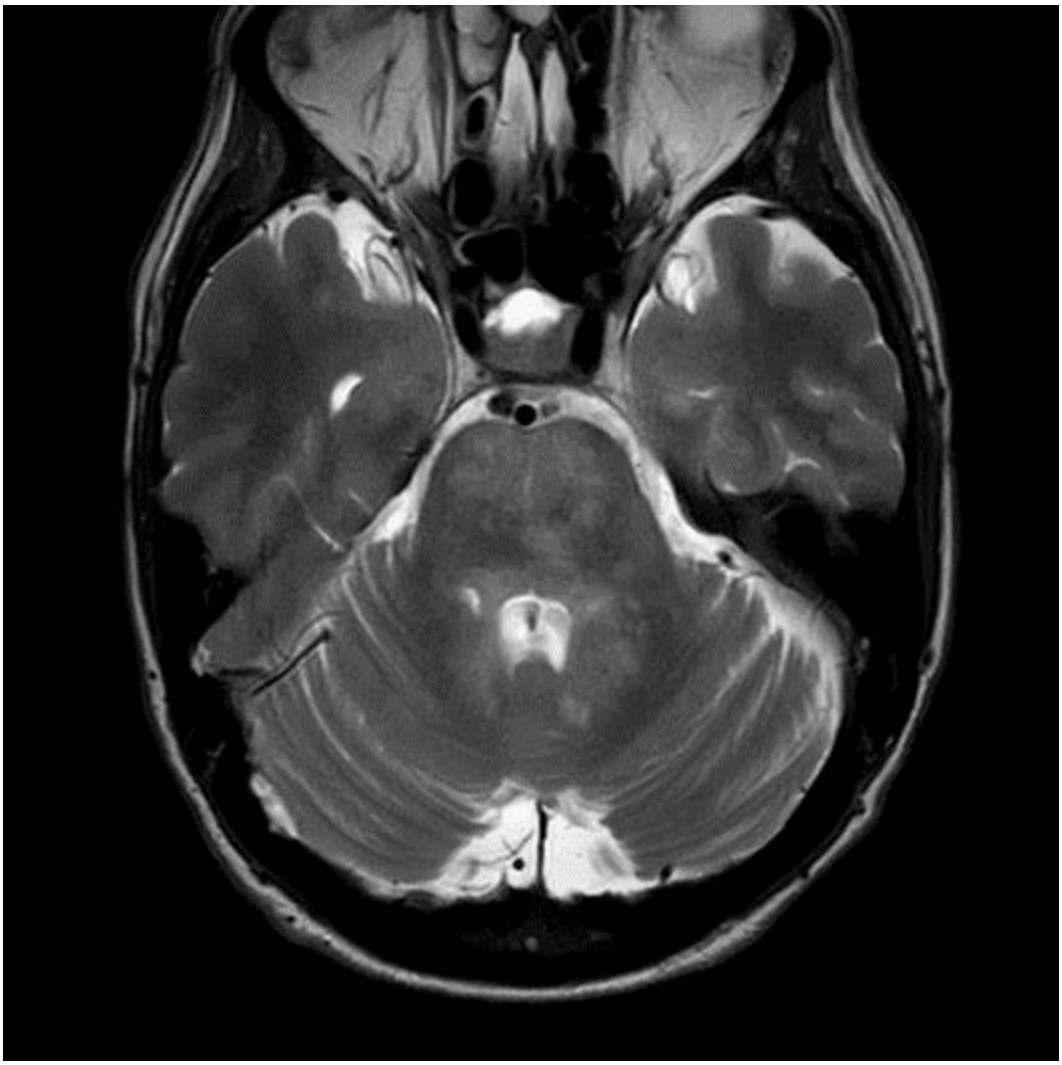
[6] Laboratory medicine and Molecular Diagnostics, Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Clinical summary

This 71 year old woman with a past medical history of coronary artery disease presented with a variety of neurologic symptoms. These included a two year history of slowly progressive slurred speech and left hand clumsiness. Over the few months prior to presenting to hospital she also developed weakness and gait difficulties with multiple falls followed by diplopia and weight loss. MRIs of the brain demonstrated progressive, ill-defined T2/T2 FLAIR hyperintensity within the midbrain, hippocampi, pons, brachium pontis and cerebellar white matter. On post-gadolinium sequences there were punctate foci of enhancement within the midbrain tegmentum. The differential diagnosis for the imaging findings included rhombo-cerebellar-limbic encephalitis. Extensive workup was negative, including CSF and serology for paraneoplastic and autoimmune encephalitis associated antibodies. Systemic imaging showed sclerotic bony lesions in the right ilium, femur and the T12 vertebral body originally thought to represent widespread metastases from an unknown primary. Biopsies of her T12 vertebral body had been reported at a community hospital as negative for carcinoma and multiple myeloma. Her symptoms did not improve on steroids or a course of IVIG. Given the complexities of her clinical presentation and lack of an established unifying diagnosis a pathology review of the bone biopsies was requested.

Materials submitted:

- Axial T2 weighted MRI image
- H&E stained slide of the T12 vertebral body core biopsy



Discussion points:

Diagnosis, and how would you confirm this?

Case #10

Romain Cayrol[1], Abdelhakim Khellaf[1], André Lamettti[2, 3], Marie-Christine Guiot[2, 3, 4], Jason Karamchandani[2, 3, 4], José Ferreira[5]

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[4]Department Neurology and Neurosurgery, Faculty of Medicine, McGill University, Montreal, Quebec, Canada

[5]Division of Pathology, Department of Clinical Laboratory Medicine, Hoptial Maisonneuve-Rosemont, Montreal, Quebec, Canada and Department of Pathology and Cell Biology, Faculty of Medicine, Université de Montréal, Montreal, Quebec, Canada

Clinical summary

The patient is a 54 year old male who presents with a 2.5 cm metabolic lung nodule. His past medical history is significant for a dural tumor resected in another center (2019). The lung nodule was resected and in the context of the prior medical history the neuropathology service was consulted.

Material submitted:

- Lung nodule

Discussion points:

- What is the differential diagnosis on histology?
- What additional studies are indicated?

Case #11

Benjamin Ellezam[1], Nathalie Langlais[2]

[1]Division of Pathology, CHU Sainte-Justine, Montréal, QC, Canada

[2]Division of Rheumatology, CHR de Lanaudière, St-Charles-Borromée, QC, Canada

Clinical summary

A 48-year-old male with a history of Raynaud phenomenon and rheumatoid arthritis stable with hydroxychloroquine presented after 2 months of slowly progressive proximal weakness and myalgia. Lab results included elevated creatine kinase (10x normal), positive anti-nuclear antibodies (1/2560, granular pattern) and normal levels of rheumatoid arthritis activity serologic markers. Thoracic scan was normal except for a prominent esophagus. Electromyography or muscle MRI were not performed. Quadriceps muscle biopsy was obtained.

Submitted material:

- 1 H&E (+ saffron), immunohistochemistry for MHC class 1, MHC class 2 and C5b-9 (MAC).

Discussion points:

- What is the differential diagnosis on H&E?
- What is the differential diagnosis with the submitted immunohistochemistry?
- What further studies are needed to resolve the differential diagnosis?

Case #12

Gabrielle A. Yeaney

Division of Neuropathology, Pathology and Lab Medicine Institute, Cleveland Clinic, Cleveland, OH

Clinical summary

A 58-year-old man with history of a lung mass now has a right cerebellar tumor on imaging. The mass is resected and submitted for review.

Submitted material:

- 2 H&E slides

Discussion points:

- What is your differential diagnosis?
- What stains would you order?

Case #13

John P. Rossiter, Minqi Xu, Sandip SenGupta

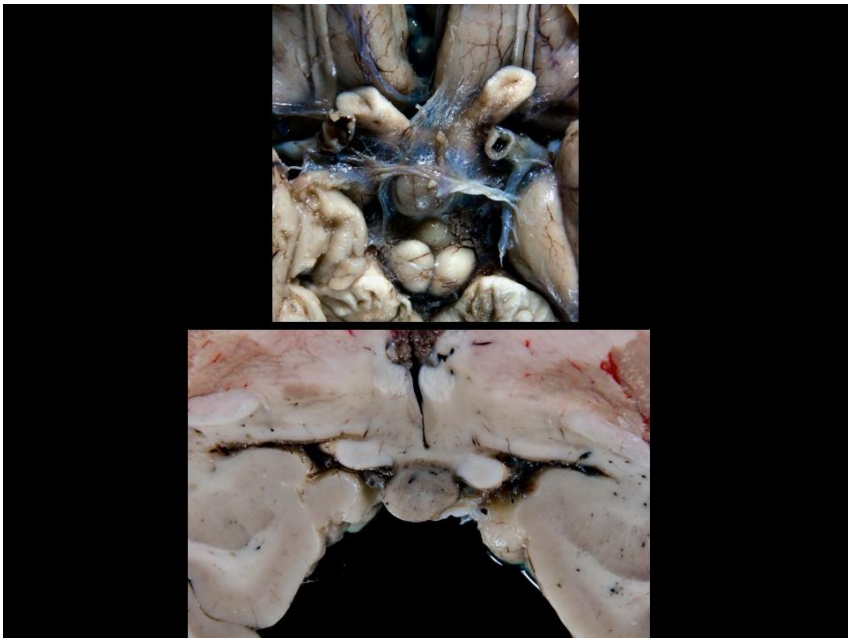
Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON, Canada.

Clinical Summary

A 29 year old man died suddenly and unexpectedly. Following detailed postmortem examination the cause of death was determined to be 'atherosclerotic, hypertensive, and obesity-associated heart disease'. Autopsy findings included: body mass index 45 (166cm, 124 kg); pre-pubertal male sex characteristics, cardiomegaly (680 g) with concentric left ventricular hypertrophy and severe coronary atherosclerosis, hepatomegaly/steatohepatitis, and an abnormally small pituitary gland. Additional information was obtained and indicated the decedent had pituitary failure found in infancy, hypothyroidism and hypertension, and had been using topical and injectable testosterone for years. Laboratory testing had shown long term decreased levels of LH, FSH and testosterone.

Materials Submitted

- Macroscopic image 1: interpeduncular fossa region, following removal of brainstem at autopsy and 48 hours of formalin fixation.
- Macroscopic image 2: coronal section through basal forebrain region.
- HPS Slide 1: Pituitary gland, sagittal.
- HPS Slide 2: Basal forebrain region at level of Macro image 2.



Discussion points

- Differential diagnosis based on macroscopic images?
- Diagnosis based on integration of history and morphological findings?

Case #14

Jacob A. Houpt [1], Tommaso Romagnoli [1], Christopher Howlett [1], Shayna Zelcer [2], Lee-Cyn Ang[1]

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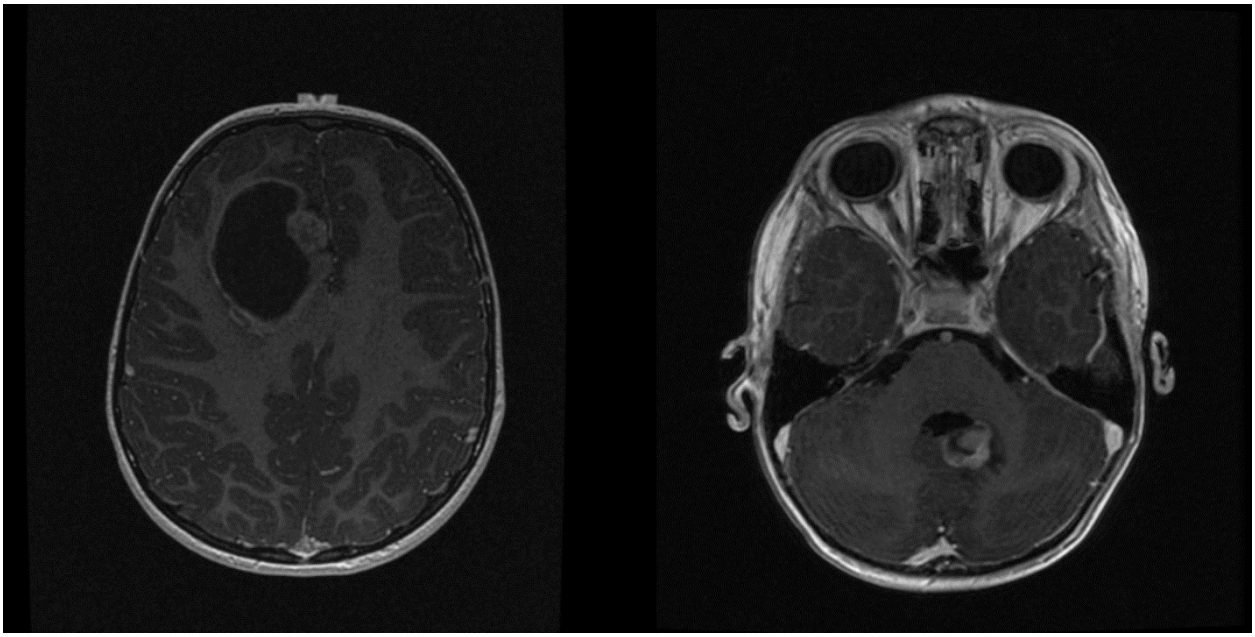
[2] Division of Haematology/Oncology, Western University, London, ON, Canada

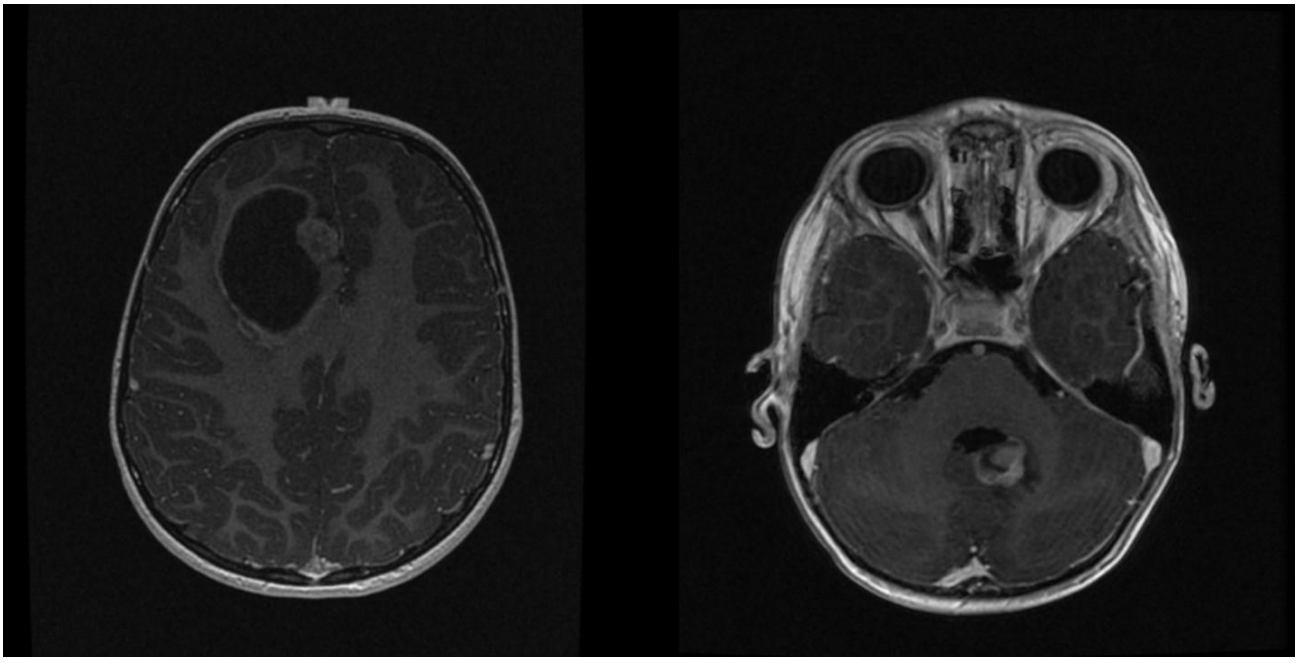
Clinical Summary

A 4-year-old left-hand dominant boy with a two-week history of morning headaches and vomiting, constipation, and lethargy. A CT scan of the head revealed a right frontal cystic lesion with a peripherally enhancing nodule, for which he was treated with two resections (the second after local recurrence), chemotherapy, and consolidative radiotherapy. Four months from initial diagnosis, he developed dizziness, unsteadiness, and right leg numbness and weakness, with imaging demonstrating a second cystic/solid lesion in the deep left cerebellum. This new lesion was also treated with surgical resection, and prompted a second course of radiotherapy.
Shortly after this third surgery, the patient began experiencing episodes of repetitive protrusions of the tongue and jerking movements of the eyes. He also had right facial rigidity and tight flexion of the left arm. His admitting neurologist attributed this presentation to dystonia rather than seizure activity.
Following travel for focal proton radiotherapy, the patient returned to hospital with a 48-hour history of severe abdominal pain, constipation, and distention. He unfortunately passed away 3 days after admission.

Materials Submitted

- MR images of the original lesion and the cerebellar lesion
- H&E slides corresponding to these resections
- autopsy H&E+LFB slides of the brainstem.





Discussion points:

- What is the differential diagnosis for the original tumour, and what special stains, IHCs, or ancillary testing would be most informative?
- What are possible causes of the patient's neurological findings after his 3rd surgery, and what autopsy findings could explain them?
- What is the likely cause of the abdominal symptoms?