CASE 1

J. Ferreira

Pathology Department, Hopital Maisonneuve-Rosemont, Montréal, Qc.

CLINICAL SUMMARY:

A 32 y.o. Senegalese woman, living in Canada since 2010, consulted on August 2014 for persistent de novo headaches. At the time she was 8 weeks pregnant. She had a spontaneous abortion 1 month later.

In October she presented atypical seizures with a negative clinical exam and para clinical investigation which included an MRI. She was referred to psychiatry for a possible conversion syndrome.

The 28th of November she was found in her home in cardiac arrest. She was resuscitated and transferred to the E.R. where they documented the presence of monocytes in her CSF. She was considered to have meningitis but passed away 2 days later.

MATERIAL SUBMITTED:

Scanned virtual slide

QUESTIONS: Diagnosis?

What is a possible associated disease/syndrome
CASE 2

Laura Davies, Lothar Resch

Department of Pathology and Laboratory Medicine, Division of Neuropathology, University of Calgary, Calgary Alberta

CLINICAL SUMMARY:

This 50-year-old woman had a history of multiple intracranial aneurysms. She been followed by the neurovascular clinic and had previously undergone multiple procedures for stenting and coiling. The most recent procedure was a successful pipeline stenting of a right paraclinoid internal carotid artery aneurysm on 1 October 2013. Postoperatively she was prescribed Plavix and aspirin.

On 20 October 2013 at 03:30hrs she had sudden worsening of a gradual onset right sided headache. She was transported to the emergency department at the Foothills Medical Center in Calgary. During transport she required intubation. Assessment in the emergency room revealed a Glasgow coma scale of 3 and a fixed and dilated left pupil. CT imaging revealed a right temporo-parieto-occipital hematoma measuring 6.6 x 5.6 cm. Neurosurgical intervention was deemed inappropriate because of a lack of neurological reflexes. The situation was discussed with her family and comfort measures were instituted. She died at 10:24hrs on 21 October 2013

MATERIAL SUBMITTED:

H&E stained section of posterior portion of subarachnoid haemorrhage and underlying brain parenchyma

QUESTION:

What do you think is the etiology of the haemorrhage?
CASE 3

M.M. Abdulkader¹, J.L. Smith², C.Y. Ho³, J.M. Bonnin¹

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²Department of Neurosurgery and ³Department of Radiology and Imaging Sciences,  
James Whitcomb Riley Hospital for Children,  
Indiana University School of Medicine, Indianapolis, Indiana USA

CLINICAL SUMMARY:

An 8-year-old girl had episodes of seizures with her eyes rolling upward, which were noticed by her  
teachers while in school. An EEG revealed mild diffuse slowing and two active independent foci of  
epileptogenic activity. Initially, she was treated with oxcarbazepine. Her previous medical history  
included mild developmental delay, ADHD, and learning disability. Comprehensive  
neuropsychological evaluation demonstrated diffuse severe impairment across multiple cognitive  
domains including intellectual ability, adaptive functioning, academic achievement, memory, attention,  
and language, as well as visuospatial and fine motor skills. Her father, an uncle, the paternal  
grandfather and two paternal first cousins were reported to have neurofibromatosis type 1.

Neurological and physical examinations were essentially unremarkable. She did not have any of the  
stigmata of neurofibromatosis. Neuroimaging studies revealed a 16 x 12mm right posterior parietal  
lesion with only minimal enhancement. It was best visualized in axial and coronal FLAIR images.  
There was no mass effect or midline shift. The process was suspected to represent either a low-grade  
glioma or cortical dysplasia. She underwent right parietal craniotomy using intraoperative  
electrocorticography and phase reversal mapping. Stealth stereotactic guidance was also used to  
localize the tumor.

MATERIAL SUBMITTED:

Digital image, H&E-stained section  
Representative MR images (A. Coronal FLAIR; B. Coronal STIR)

QUESTION:

Differential diagnosis
CASE 4

N. Sinha¹, J. J. S. Shankar², S. E. Croul³

¹,³Division of Anatomical Pathology, ²Department of Neuroradiology, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, Nova Scotia, Canada

CLINICAL SUMMARY:

A 65-year-old woman was admitted to the Halifax Infirmary hospital in September 2014 after being found confused by her husband. A day before admission, she had difficulty operating the TV remote. Her neurologic history dates to 1998 when she was admitted to hospital with transient aphasia and a CT scan showed deep and subcortical hypodensities suggestive of vasogenic edema, with an unclear etiology. Past medical history was also significant for pulmonary hypertension (on home oxygen), obesity, HTN, and DM type II. She has a 72 year old mother who suffers from dementia. Her two younger brothers and two sons are healthy.

On physical exam, her VS were: BP160/100 HR84 RR28 T37.3. Neurological exam showed increased right arm tone, bilateral flexor plantar responses, and a GCS of 11/15. CT scan demonstrated a left posterior parietal white matter hypodensity. Six days following admission, she experienced a noticeable change in her level of consciousness. A repeat CT of the head was performed. The patient died eleven days following admission. A brain only autopsy was performed.

MATERIAL SUBMITTED:

Scanned H&E slide from occipital lobe and a repeat CT Head.

QUESTIONS:

What is the Diagnosis?

What are the differential diagnoses of this case and how would you differentiate it?
CASE 5

P. Diamandis¹, D.G. Munoz², S.P. Symons³, N. Phan⁴, J. Perry⁵, M. Tsao⁶, J. Keith⁷

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²Department of Laboratory Medicine, Division of Pathology, St. Michael's Hospital, Toronto, Ontario
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⁶Department of Radiation Oncology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto
⁷Department of Anatomic Pathology, Sunnybrook Health Sciences Centre, Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto

CLINICAL HISTORY:

This 68 year old woman had a history of chronic back pain, which over the preceding month significantly worsened and was accompanied by progressive right leg weakness and numbness. Her past medical history was otherwise only significant for hypertension and hypercholesterolemia. Clinical work-up included MR imaging that revealed an intra-dural extra-medullary diffusely contrast enhancing nodule at T11 measuring 1.4 cm in greatest dimension. She subsequently underwent a T11/T12 laminectomy and resection of the nodule. Intra-operatively, the mass was seen intimately associated with the T11 spinal nerve root and not adherent to the dura, prompting a surgical impression of a schwannoma.

MATERIAL SUBMITTED:

Digital H&E stained slide of intra-dural nodule.

POINTS FOR DISCUSSION:

1. What is the histological differential diagnosis of this lesion?
2. What immunohistochemical stains and additional investigations could be used to resolve this differential diagnosis?
3. What is the appropriate management of this patient’s lesion?
CASE 6

Ana Nikolic, Launey Lowden, and Lothar Resch

Department of Pathology and Laboratory Medicine, ¹Division of Neuropathology, ²Department of General Pathology, University of Calgary, Calgary, Alberta

CLINICAL SUMMARY:

The patient was a 36-year-old woman who presented to hospital with a 5-week history of nausea, vomiting and dizziness. Her past history was significant for acute myelogenous leukemia diagnosed 15 months earlier. Treatment included idarubicin/AraC, FLAG-IDA protocol, consolidation with cytarabine, low-dose fractionated radiotherapy to the orbits (0.2 Gy, 20Gy boost) for retinal involvement, and allogeneic stem cell transplant 9 months before the current presentation. Post-transplant there was no residual disease, however one episode of blurred vision occurred 7 months prior and was thought to represent ocular graft-versus-host disease.

An MRI shortly after admission showed multiple FLAIR and T2-bright cortical abnormalities in the frontal and temporal lobes, with diffusion restriction. A repeat MRI two weeks later showed lesions in the frontal lobes, calcarine cortex, insula, and temporal operculum, without enhancement or diffusion restriction. An extensive infectious and paraneoplastic workup was performed on CSF, including PCR for HHV6 and JC virus, all of which were negative. CSF cytology and flow cytometry were unremarkable. Bone marrow biopsy was unremarkable.

Symptoms progressed over the next month to seizure-like episodes, intractable vomiting, headaches and visual disturbances. Peripheral blood flow cytometry was slightly abnormal but showed no neoplasm. A right frontal brain biopsy was performed approximately 6 weeks into the admission.

MATERIALS SUBMITTED:

One H&E stained section

QUESTION: What is the differential? What is the most likely diagnosis?
CASE 7

Y.A. Alwelaie\textsuperscript{1,2}, J.A. Maguire\textsuperscript{1,2}, K. Dorovini-Zis\textsuperscript{1,2}, F. Vice\textsuperscript{2,4}, M.C. Boyd\textsuperscript{1,2}, M.R. McKenzie\textsuperscript{2,3}, M.Z. Matishak\textsuperscript{2,4}, J. Shewchuk\textsuperscript{1,2}, G. Sidhu\textsuperscript{2,4}, G.R.W. Moore\textsuperscript{1,2}

\textsuperscript{1}Vancouver General Hospital, \textsuperscript{2}University of British Columbia, \textsuperscript{3}British Columbia Cancer Agency, \textsuperscript{4}Royal Columbian Hospital

CLINICAL SUMMARY:

At the age of 29, this previously healthy man presented to hospital in May 2004 with a one-month history of increasing leg pain and 10-day history of weakness, bowel and bladder difficulties, and perianal saddle anesthesia.

Spine MRI showed a 4.8 cm, well-circumscribed, markedly enhancing ovoid lesion filling the spinal canal at the L5-S1 vertebral level. Subsequently, the patient underwent an uneventful gross total removal of his intradural tumor. This was followed by radiotherapy.

In April 2006, MRI showed two recurrent nodules in the lumbar spinal cord and he was given further radiation to those lesions.

In 2008, MRI documented evidence of progressing recurrent tumor in the distal cauda equina, in addition to more stable lesions rostrally. Consequently, debulking was carried out and residual tumor was left behind to preserve nerves supplying bowel and bladder.

Imaging in 2010 showed multiple metastatic nodules in the thoracic and cervical spinal cord, the largest of which was an 8 mm nodule compressing the spinal cord at the level of T8.

In April 2015, he presented with a cerebral hemorrhage and was found to have a left sylvian fissure metastasis that had bled and this was resected. Pre- and post-operative imaging also showed several other cerebral lesions consistent with leptomeningeal metastases.

MATERIALS SUBMITTED:

H&E section of the 2004 resection of the cauda equina tumor.

QUESTIONS:

1. Diagnosis?

2. Discrepancies between the diagnosis and biological behaviour?
CASE 8

Claire I. Coiré1, David G. Munoz2, Loch Macdonald2 and James Perry3

1Divisions of Pathology and 2Neurosurgery, Saint Michael’s Hospital, Toronto and 3Department of Medicine, Division of Neurology, Sunnybrook Health Science Centre, University of Toronto, Departments of Laboratory Medicine and Pathobiology, 2Surgery and 3Medicine.

CLINICAL SUMMARY:

This 20-year-old male, survivor of high risk childhood leukemia 11 years earlier (treatment had included cranial radiation with 18 Gy in 12 fractions and intrathecal methotrexate) had presented with a one week history of intermittent headaches, nausea and vomiting. Imaging had shown a right fronto-parietal tumour, which had been resected. A diagnosis of glioblastoma with PNET-like areas had been rendered. Post-surgical treatment had included radiotherapy with 60 Gy in 30 fractions and concurrent Temozolomide. Five weeks after the last radiotherapy session, the MRI was reported as stable. However, 14 weeks after the last radiotherapy session, another follow up MRI showed interval worsening manifested by progression in the irregular enhancement around the surgical cavity and expansion in the extent of non-enhancing T2 hyperintense FLAIR signal around the surgical cavity. He was asymptomatic. He was offered surgical excision. A 2 cm fragment of yellow/tan soft tissue was received for microscopic examination. A representative section has been circulated.

MATERIAL SUBMITTED:

Glass slide of “recurrent tumour” - stained with H&E and digital image
Representative MRI images from 2014 (original mass) and 2015 (recurrent mass)
Representative digital image of the original tumour.

QUESTION: Diagnosis
CASE 9

S. Jozaghi¹, S. Labonte¹, P. Gould²

¹Department of Anatomical pathology, Hotel Dieu de Quebec; Laval University, Quebec city, Quebec
²Department of Anatomical pathology, Division of Neuropathology, Hôpital de l'Enfant-Jésus; Laval University, Quebec City, Quebec

CLINICAL SUMMARY:

A 68 year old female patient presented with a progressive right sided visual loss during 6 months following a two year history of persistent diplopia due to oculomotor nerve palsy, and hypoesthesia of the first branch of the fifth cranial nerve. She also suffered from occasional right hemi-frontal and periorbital headaches. A previous magnetic resonance imaging (two year before the incidents) was normal.

A new magnetic resonance imaging revealed an expansive extra-axial lesion of 28 x 23 x 23 millimetres centered on the sphenoid wing with invasion of the orbital apex and optic nerve compression. Radiologic findings were suggestive of a right spheno-orbital meningioma. She was referred with this preoperative diagnosis to a neurosurgeon in our center and 95% of her tumor was resected. The patient has had an improvement in her visual acuity since the surgery but the diplopia still persists.

MATERIAL SUBMITTED: Virtual slide - stained with H&E.

QUESTIONS: Diagnosis?
Clinical course?
CASE 10

Reena Baweja, Boleslaw Lach, Kesava Reddy

Department of Pathology and Molecular Medicine, and Neurosurgery, McMaster University, Hamilton Ontario

CLINICAL SUMMARY:

A 50 year old right hand dominant man presented with speech impairment and a Bell’s palsy which recovered by the time of hospital admission. His background history was significant for obstructive sleep apnea, dyslipidemia, type 2 diabetes mellitus (treated with both insulin and metformin) and bilateral shoulder surgery. His neurological examination revealed right sided visual acuity of 20/100 and intact visual fields. He did not appear to be acromegalic or cushingoid. MRI showed 2.8 cm sellar/suprasellar mass for which he underwent endoscopic transsphenoidal resection on June 3 2015. Surgery was uneventful. Postoperative MRI revealed significant decrease in the volume of the tumor with no compression of the optic chiasm.

Immunohistochemistry:

Positive: S-100, Vimentin
Negative: Neurofilaments, Synaptophysin, Chromogranin, Cytokeratins (all), EMA, GFAP, P53, Pituitary hormones (GH, FSH, LH, ACTH, PL), CD 34, CD 56, E-cadherin, HMB45, melanoma cocktail Abs, SMA, HHF-35 as well as ER- and PR-receptors.

MATERIAL SUBMITTED: Three radiology images and one slide for scanning

QUESTIONS: Diagnosis?
CLINICAL SUMMARY:

An otherwise healthy 9-month old girl presented with a history of swelling in the lumbosacral region since birth. On examination, the swelling was mobile and soft in consistency. No neurological abnormalities were identified. MR imaging of spine revealed an L4 myelomeningocele and spinal cord tethering to S1. In addition, a syrinx noted at L1- L2. The patient underwent de-tethering of the cord and repair of myelomeningocele.

MATERIALS SUBMITTED:
1. One representative H&E stained section
2. MRI image

QUESTIONS: Diagnosis? Prognosis?
A 12 week-old baby was admitted because of feeding difficulties and slow growth. He was born at 38 weeks gestation. Pregnancy was complicated by oligohydramnios and hypertension. Initial development was unremarkable and he had his first set of vaccinations at 10 weeks. Shortly thereafter there were significant changes; he was either lethargic or screaming, had intermittent tachypnea, irritability, and episodes of “tensing up and arching his back” during feedings. The occurrence of aspiration was confirmed by a video fluoroscopic feeding study and a nasogastric tube was placed. An echocardiogram indicated a small patent foramen ovale, mild hypovolemic left ventricle, and borderline left ventricular hypertrophy. MRI revealed diffuse supratentorial white matter T1-hypointensity and T2-hyperintensity. Large areas of FLAIR suppression were noted. Cystic foci were observed in the periventricular region, particularly in the left frontal white matter, associated with areas of mild T1-shortening and susceptibility artifacts likely representing punctate hemorrhages. The thalami were also involved while the cerebellar white matter appeared to be spared. There were no lesions in the brainstem. In view of the grim prognosis and worsening respiratory insufficiency, all life support was withdrawn.

MATERIAL SUBMITTED:

Digital image, medial temporal lobe, H&E. 
Gross image, frontal lobe (A) and frontal lobe section, H&E (B) 
Representative MR images (A. Axial FLAIR; B. Coronal T2 TSE; C. Coronal T1 SE+C)
CASE 13

V. Hirsch-Reinshagen¹, J. Hukin² and C. Dunham¹

Departments of ¹Pathology and ²Pediatrics, British Columbia’s Children’s Hospital.

CLINICAL SUMMARY:

A two year-old, developmentally normal female presented with a two-week history of progressive ataxic gait, left leg weakness, facial asymmetry, right esotropia and a tendency to fall to the left when sitting. Neurologic evaluation revealed right 6th nerve palsy, nystagmus, central weakness of the left 7th cranial nerve, absent gag reflex and mild weakness of left upper and lower extremities with increased deep tendon reflexes and positive Babinski on the left. Gait was unsteady and broad based. Finger to nose testing was abnormal on the left. Past medical history was non-contributory.

Initial MRI revealed a relatively well circumscribed 3.0 x 3.2 x 3.2 cm lesion centered in the right pons with involvement of the right cerebral peduncle. The tumor was T2 hyperintense, T1 hypointense and did not exhibit contrast enhancement, calcification or restricted diffusion. Biopsies were not taken and the patient was treated for a ‘diffuse intrinsic pontine glioma’ with radiotherapy, concurrent adjuvant chemotherapy and steroids. Slight initial symptomatic improvement was followed by deterioration of her neurological status over 6 months time.

Repeat imaging at 3 months after treatment revealed mild enlargement of the pontine lesion with new foci of contrast enhancement and restricted diffusion. Further imaging 6 months after treatment revealed new and widespread dissemination of disease exhibiting restricted diffusion but no enhancement. CSF cytology confirmed the presence of malignant cells of unclear lineage. The patient passed away shortly thereafter. A brain-only autopsy was performed.

MATERIAL SUBMITTED:

Representative MR images.
One scanned H&E stained section of the right pontine tumor.
Representative H&E stained glass slides of the medulla.

QUESTIONS:

1. Diagnosis?

2. Are there any ancillary studies that could be done to confirm your diagnosis?
CASE 14

B. Ellezam¹ and M. Vanasse²

Departments of ¹Pathology and ²Neurology, CHU Sainte-Justine, Université de Montréal, Montréal, QC

CLINICAL SUMMARY:

This 17 year old boy presented to the emergency room for chest pain and left upper limb paresthesia. Since cardiac workup was entirely normal and given the family history of weakness he was referred to neurology.

On questioning, the patient admits to mild weakness and below average performance in sports since childhood and describes fluctuating difficulty in walking or running as well as occasional myalgia walking up the stairs. Developmental history reveals walking at 18 months and suspected language delay. His mother, sister, and maternal grandfather all suffer from mild weakness and muscle atrophy, none of them having a formal diagnosis.

On exam, strengths in limb girdles are 4/5 proximally and 5/5 distally. Ankle contractures are noted. Facies is not myopathic. Creatine kinase elevations vary between 2000 and 3000. Lactic acid and acylcarnitine profile are normal.

The patient did not come for his EMG. Muscle biopsy was obtained during surgery for inguinal hernia.

MATERIALS SUBMITTED: One NADH-TR stained section (virtual slide) from muscle biopsy.

QUESTION: Diagnosis?

Which gene(s) should be sequenced?

LEARNING OBJECTIVES:

This presentation will enable the learner to:

1. To describe the differential diagnosis of blue inclusions on NADH-TR.

2. To examine the pathology, clinical features and genetics of this autosomal dominant myopathy.
CASE 15

Boleslaw Lach and Mark Tarnopolsky

Department of Pathology and Molecular Medicine, Department of Medicine and Pediatrics, McMaster University, Hamilton, Ontario

CLINICAL SUMMARY:

This previously very healthy and physically fit 30-year-old gentleman presented for the first time to his general practitioner’s office due to insidious onset of general weakness. He had markedly elevated CPK (“levels in thousands”). However, these changes were not associated with rise in white blood count, CRP or ESR. He had transient increase anti-nuclear antibody level (1:80) three years before this doctor appointment.

On examination he showed papulæ across the metacarpal-phalangeal joints, as well as the dorsal finger joints. There was also a raised erythematous rash on the right thoracic region, anteriorly and across the back. Neurological examination revealed no abnormalities. He had Raynaud’s phenomenon for an undetermined time in the past.

MATERIALS SUBMITTED: One H&E stained slide (virtual slide).

QUESTION: Diagnosis?