Dedicated to the memory of Dr. Bernd Scheithauer, a true giant in the field of surgical neuropathology, for his passion as an educator, colleague, and friend.

Diagnostic Slide Session

Chicago, Illinois
June 23rd, 2012
8:00 PM
CASE 2012-1

SUBMITTED BY:
Amanda O. Fisher-Hubbard¹, M.D., James J. Dowling², M.D., Ph.D., Paul E. McKeever¹, M.D., Ph.D., Sandra Camelo-Piragua¹, M.D.
Departments of Pathology¹ and Neurology², University of Michigan, Ann Arbor, MI

CLINICAL PRESENTATION:
L. C. is a 7 year-old Chinese boy with mild scoliosis who was evaluated in the neuromuscular clinic for fine and gross motor difficulties. He cannot run, jump, or throw a ball. He also has difficulty with stairs, buttons, and zippers. Regarding his developmental milestones, he began walking at 16 months. At 18 months, he had progressively more falls. Outside of his motor difficulties, there are no other concerns. He is cognitively normal. While in China, he had a brain MRI which was normal and an electromyogram that showed myopathic features. He has no family history of nerve or muscle abnormalities.

On physical examination, he was non-dysmorphic in appearance. Cardiac exam revealed a regular rate and rhythm and no murmurs. His cranial nerves were intact bilaterally. He had normal muscle bulk, though tone was mildly decreased. He had mild weakness, proximal greater than distal. He had Gowers' sign. Deep tendon reflexes were present but decreased throughout. Sensory examination was within normal limits. A biopsy of the right vastus lateralis muscle was obtained. Histopathologic examination revealed abnormalities. The tissue was then sent for genetic testing.

MATERIAL SUBMITTED:
Three Virtual sections of right vastus lateralis muscle
  One H&E-stained section
  One toluidine blue-stained section
  One Gomori trichrome-stained section

POINTS FOR DISCUSSION:
1. Discuss the differential diagnosis of congenital myopathies.
2. Review genetic alterations in various congenital myopathies.
CASE 2012-2

Submitted by:
Juan M Bilbao, Sandra Cohen, Al-Noor Dahmani, and Beverley Young.
Sunnybrook Hospital, University of Toronto

Clinical History:
This 76-year-old woman with remote history of hysterectomy and hydronephrosis secondary to ureteric stenosis was seen because of progressive weakness of 4 year's duration. There was no family history of neurological or neuromuscular diseases. Patient was on no medications. Four years previously she began to experience numbness in the sole of Rt foot progressing to the knee, and followed by weakness in both legs. She developed difficulties standing and climbing stairs requiring the use of a cane, and with swallowing solids that required treatment with bougies. There were no complaints of bowel or bladder dysfunction.

PE: wide gait, unable to walk on her heels, slurred speech, slight facial weakness. She cannot puff her cheeks and cannot whistle. Weakness: diffuse in neck flexors and extremities 4+, ankle dorsiflexors 4, and toe dorsi-flexors 1. Reflexes: 1+ in upper extremities but absent in lower extremities. Sensation: slight decrease of proprioception.

NC: length dependent, motor>sensory axonal polyneuropathy. EMG: no spontaneous activity, slight myopathic changes. CPK: 26
Clinical Dx: myopathy+distal polyneuropathy: metabolic + spinal stenosis
Muscle biopsy: Paraffin embedding, "Quench" freezing, plastic resin

Material Submitted:
Cryosections on same slide: H&E and Immunostain

Point for Discussion:
Diagnosis
CASE 2012-3

SUBMITTED BY: Joshua Menke, Mark Jentoft, Caterina Giannini, Mayo Clinic, Rochester, MN

CLINICAL HISTORY:
A 24 year-old gentleman with a history of polysubstance abuse was found unresponsive at a New Year’s party. He reportedly had taken several drugs, including liquid methadone, lorazepam, and cocaine. CPR was initiated and the patient was intubated and transported to the hospital where he was found to be acidotic with severe rhabdomyolysis. A head CT at the time of admission did not demonstrate any abnormality. The patient stabilized hemodynamically over the next 72 hours and was weaned from norepinephrine and dobutamine. He continued to be unresponsive and would only withdraw to pain. All reflexes remained intact. A MRI on day 4 showed significant and diffuse cerebral white matter changes with sparing of the brainstem and cerebellum. The patient was extubated on day 6 and was able to breathe unassisted with minimal oxygen support, but his mental status and neurological exam remained unchanged. His family elected to pursue comfort care measures with placement into a hospice facility where his nasogastric tube feedings were discontinued. He died 23 days after the initial incident.

MATERIAL SUBMITTED: H&E section of gray and white matter at the splenium of the corpus callosum.

POINTS FOR DISCUSSION:
1. Diagnosis
2. Pathogenesis
CASE 2012-4

SUBMITTED BY: Raymond A. Sobel, MD Department of Pathology / Stanford University School of Medicine / Laboratory Service (113) / Veterans Affairs Health Care System / 3801 Miranda Avenue / Palo Alto, California 94304

CLINICAL HISTORY:
This 60 yo M presented in August, 2010 with jaundice. The diagnosis of cholangiocarcinoma causing biliary obstruction was made by liver FNA. Based on CT scan at presentation, the tumor was known to be metastatic to liver, lungs and iliac/sacrum. His past medical history included hyperlipidemia, hypertension, and gastroesophageal reflux. He was admitted for jaundice and renal failure. He had endoscopic retrograde cholangiopancreatography (ERCP) and a stent was placed, but it was not effective. Shortly thereafter, he developed acute renal failure and was placed in hospice. Two days before death he was confused. He died on 10/05/2010 following two grand mal seizures. There was no other neurological history and no neuroimaging.

General Autopsy: Intrahepatic cholangiocarcinoma, metastatic to the lungs. A common bile duct metal stent was intact and patent; there was splenic and pulmonary congestion, pancreatitis, jaundice, acute and chronic peritonitis, atherosclerosis and an incidental colonic ganglioneuroma

Neuropathology: The scalp, skull, dura and brain were bile-stained. The fresh brain weighed 1400 g; the fixed brain weighed 1520 g. There was severe cerebral atherosclerosis. The leptomeninges were clear; there was no focal softening; there was a small fresh subarachnoid hemorrhage over the right parieto-temporal region. The cortical ribbon was grossly intact. There were scattered prominent vessels or petechiae, some with tan discoloration, in the cerebral white matter. Deep gray nuclei and hippocampi were unremarkable. The basis pontis and bilateral middle cerebellar peduncles had multiple round hemorrhagic areas measuring up to 0.3 cm in maximum dimension in a mostly symmetric distribution.
Material Submitted:
Images (Gross, LFB, B-APP), 1 H&E and 1 unstained slide of basis pontis

Points for Discussion:
1. Diagnosis
2. Pathogenesis
CASE 2012-5

SUBMITTED BY: Mohamed El-Hag, Duncan Stearns, Michael Coffey, & Mark Cohen
University Hospitals Case Medical Center
Cleveland, Ohio

CLINICAL HISTORY:
This 3-month-old female was seen in the emergency department after her mother noticed a “bump on the right side of her head”. The patient was feeding well and meeting her developmental milestones. She was up to date with her vaccinations, had no prior hospitalizations, was on no medications, and had demonstrated no abnormalities on prenatal ultrasounds.

Physical examination revealed a 3 x 3 cm raised soft swelling over the right parietal region. The head circumference enlarged (44 cm; >95%ile). No focal neurological deficits were appreciated.
Axial T2 weighted images revealed a large mixed signal cystic and solid right hemispheric lesion with a hypointense, peripheral plaque-like solid component. There was significant associated mass effect and hydrocephalus. Post gadolinium T1 weighted images demonstrated heterogeneous enhancement of the solid component as well as enhancement of the cyst walls.

Her tumor was resected in staged surgeries due to excessive hemorrhage during the first procedure. Operative findings included large feeding vessels and areas of thinned/eroded skull overlying the tumor. Ventricular CSF cytology from this procedure showed no malignant cells. Subsequent spine MRI showed no evidence of metastatic disease.

**Material Submitted:**
- Axial T2 & T1 images
- One H&E and one unstained section

**Point for Discussion:**
Expected biologic behavior
CASE 2012-6

SUBMITTED BY: Misti Coronel, MD\textsuperscript{1}, Lawrence Kenyon, MD, PhD.\textsuperscript{1} David W. Andrews, MD\textsuperscript{2}
1. Department of Pathology, Thomas Jefferson University Hospital Philadelphia, PA 19107
2. Department of Neurological Surgery, Thomas Jefferson University Hospital Philadelphia, PA 19107

CLINICAL HISTORY:
In 2002, a 24 year-old Saudi Arabian female underwent excision of a left frontal lesion that was diagnosed as pilocytic astrocytoma. Slides of this resection were not available for review. She subsequently underwent radiation therapy. Tumor recurred and was resected in 2005. A second recurrence in 2009 was resected. At this time the patient underwent chemotherapy, but her symptoms did not resolve. A fourth resection was performed in 2010 and the patient underwent a second course of radiation therapy. Now 34 years old, progression of disease led the patient to seek further treatment options at Thomas Jefferson University Hospital in Philadelphia.

Imaging showed the previous left frontoparietal craniotomy site as well as an adjacent large mass in the fronto-temporal operculum extending into the deep frontal lobe. There was an associated 7 mm midline shift. There was extensive patchy enhancement that was felt to represent tumor versus post-radiation changes. A partial resection of tumor was performed. Intra-operatively, there was a clear surgical plane.

Material submitted: H&E sections of tumor.

Points for discussion:
1. Diagnosis
2. Evolution of lesion
Clinical History:
KB was a 22-year-old African American male inmate with no significant past medical history who was admitted with a 2 month history of gradually progressive left-sided weakness, dizziness, headaches, and vomiting. MRI revealed 10 cm enhancing lesion situated in the right frontotemporal region with extension into the corpus callosum, suspicious for high grade glioma. A stereotactic biopsy was performed, and the patient was given the appropriate treatment based upon the pathology finding in this tissue sample. However, postoperatively his symptoms continued to progress. Subsequent neuroimaging studies revealed increased mass effect with development of midline shift, hydrocephalus related to extension of the process into the lateral ventricles (necessitating ventriculostomy placement), and acute infarction of the right cerebellum with edema causing mass effect on the brainstem. Notable, an extensive laboratory workup confirmed that he was HIV negative and not immunocompromised. However, imaging of the patient's chest revealed a right upper lobe lesion, urine culture grew out Klebsiella pneumoniae, and cytopathology performed on a bronchoalveolar lavage specimen indicated Herpes viral cytopathic effect (viral culture negative). A "do no resuscitate" order was issued by the family. The patient was pronounced dead shortly thereafter, and permission for a complete autopsy was obtained.
Autopsy findings:
The unfixed brain weighed 1305 grams. The cerebral hemispheres were grossly edematous. The cranial nerves and arteries at the base of the brain were enmeshed within dense clotted material that covered the ventral aspect of the brainstem and adjacent cerebellum. The right cerebellar hemisphere was infarcted. A large necrotic hemorrhagic lesion was identified in the right frontotemporal region, with hemorrhage present within the right lateral, 3rd, and 4th ventricles. Diffuse parenchymal softening was present within bilateral frontotemporal white matter and basal ganglia with blurring of the grey-white junctions. The right occipital lobe contained a firm, tan-yellow lesion (up to 3cm in maximal dimension). Brainstem structures, especially the basis pedunculi, basis pontis, and pyramids, were softened and distorted.

Material submitted:
Post contrast images of brain
Cross photo of frontotemporal lesion at autopsy
1 H&E stained microscopic section from frontotemporal lesion

Points for discussion:
1. Diagnosis.
2. Differential diagnosis based on clinical history, imaging, gross, and microscopic findings.
3. Additional studies that would be useful in diagnosing this lesion.
CLINICAL HISTORY:
The patient is a 42 year old woman who presented with left transverse sinus occlusion. She was treated with warfarin and followed by neurology. MRI showed prominent dural thickening and nodularity involving the majority of both cerebral hemispheres including the falx and tentorium. Repeat MRI a few months later showed worsened dural thickening. She was referred to neurosurgery and a biopsy was performed in the region of the left temporal lobe at Sunnybrook Health Sciences in Toronto.

MATERIAL SUBMITTED:
1. Brain MRI (digital image)
2. Virtual H&E stained section of meningeal biopsy

POINTS FOR DISCUSSION:
1. Differential Diagnosis
2. Ancillary studies
3. Diagnosis and diagnostic criteria
CASE 2012-9

SUBMITTED BY: David J. Pisapia, M.D. and John F. Crary, M.D.-Ph.D.
Division of Neuropathology/PH15-124
Department of Pathology & Cell Biology
College of Physicians & Surgeons, Columbia University
Medical Center 630 W 168th Street, New York, NY 10032

CLINICAL HISTORY:
The patient was a 67-year-old woman with a history of chronic lymphocytic leukemia (CLL) diagnosed one year prior to admission. For her CLL, she was treated with bendamustine three months prior to admission and later with cyclophosphamide, vincristine, and prednisone several weeks prior to admission. Several days prior to admission, she presented to the emergency room with chest pain and was found to have sinus tachycardia. She was treated with digoxin and discharged. Over the next 24-48 hr, she developed dizziness and generalized weakness. She was unable to walk without assistance and complained of bilateral lower extremity sensory loss that was worse on the right. She returned to the emergency room and was admitted to the stroke service. Her neurological status rapidly declined. Radiological and laboratory studies are outlined below. She was transferred to the neurological intensive care unit with bilateral lower extremity flaccid paraplegia four days following admission and became comatose within days thereafter. A brain biopsy of the right frontal cortex was performed. Despite aggressive treatment including steroids, attempted plasma exchange, and IVIg, she died eight days following admission.
**SELECTED LABORATORY STUDIES:**
Peripheral WBC count: 25.5 x 10^9/L
CSF: 4 WBCs
CSF cytology: negative
CSF flow: Hemo-contaminated. Monotypic B-cell population consistent with known CLL.

**MATERIALS SUBMITTED:**
1. MRI studies shown above
2. Virtual slide of an H&E stained section from the right frontal lobe biopsy

**POINTS FOR DISCUSSION:**
1. Diagnosis & differential diagnosis
2. Pathogenesis

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**Figure 1.** T2-fluid attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI). Hyperintensities originated in the cerebral cortex (A) that progressed to the subcortical white matter and corpus callosum (B, C). Punctate signal on diffusion-weighted imaging (DWI) progressed to diffuse DWI signal throughout the white matter; no contrast enhancement was seen at any point (not shown).
CASE 2012-10

SUBMITTED BY:
Brent A. Orr M.D., Ph.D., Gary L. Gallia M.D., Ph.D., and Fausto J. Rodriguez M.D.
Johns Hopkins Hospital
Sheikh Zayed Tower, Room M2101
1800 Orleans Street
Baltimore, MD 21231

CLINICAL HISTORY:
The patient is a 38 year-old Caucasian female with a clinical history of chronic headaches and hemochromatosis. The patient presented in 2007 with grand mal seizure. An MRI revealed a T2 intense and T1 hypointense lesion with irregular peripheral enhancement measuring 2.7 X 2.0 X 2.2 cm centered in the right parietal lobe. A biopsy and subsequent resection was performed and interpreted as showing inflammatory changes. Despite surgical intervention, the patient’s seizures persisted. The patient was followed with serial MRI, noting no change until July of 2011 at which time the lesion was found to show increases in heterogeneous enhancement and extension to the ependyma of the lateral ventricle. She presented for additional evaluation and management.
MATERIAL SUBMITTED:
1. Virtual H&E section of right parietal lobe mass
2. Representative MRI images

POINTS FOR DISCUSSION:
1. Diagnosis
2. Pathogenesis