52nd Annual
American Association of Neuropathologists
Diagnostic Slide Session
Seattle, Washington
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Submitted by: Janna Neltner, Dianne Wilson, Peter T. Nelson, and Craig Horbinski
Department of Pathology
University of Kentucky Chandler Medical Center and Sanders Brown Center on Aging

Clinical History: The patient was a 56 year-old Caucasian female with a past medical history of hypertension, hypercholesterolemia, and insulin-independent diabetes mellitus, who presented with a five month history of diminished facial expression and voice softening. A modest cognitive deficit was also noted. Thus, a diagnosis of Parkinson Disease with accompanying dementia was given and Sinemet therapy was initiated. Her initial brain MRI at that time showed abnormal signal within the left basal ganglia and bilateral changes in the periventricular white matter. Despite the therapy, her neurologic status slowly declined. Two months after her initial workup, she was admitted for severe metabolic acidosis due to metformin toxicity; by this time she had increased memory loss and disorientation. Her gait had also worsened to the point where she needed a walker for ambulation.

Three months after the initial presentation, she was hospitalized again with worsening speech slurring and right-sided weakness. An MRI showed multiple areas of abnormal T2 hyperintensity in the bilateral cerebral hemispheres, midbrain, and pons. Additional foci of T1 hyperintensity were noted in the right caudate nucleus, as was a nonspecific area of enhancement in the posterior right frontal lobe. (Images, without enhancement, enclosed). A lumbar puncture showed only mildly elevated protein. The right frontal lobe was biopsied and showed vascular fibrinoid degeneration, intramural/perivascular lymphocytic infiltrate, occasional fibrin thrombi, and perivascular microhemorrhages most consistent with vasculitis (not shown). She was started on steroids and Cellcept, but continued to decline until her death one year after her initial symptoms began.
Key autopsy findings included extensive bilateral and symmetrical necrosis of the basal ganglia (see gross images A and B) and substantia nigra (gross image C).

**Material Submitted:**
1. [H&E stained](#) slide of left basal ganglia/thalamus
2. Serial MRI imaging
3. Postmortem gross photographs.

**Points for Discussion:**
1. Additional stains
2. Differential diagnosis
3. Review of literature
Submitted by: Drs. Mark Samols, Kari-Elise Codispoti, Barbara J. Crain
Johns Hopkins University School of Medicine
Dr. Marc K. Rosenblum
Memorial Sloan-Kettering Hospital

Clinical History: A 96-year-old Caucasian female was enrolled as a control patient in the Huntington disease research study because one of her sons was diagnosed with Huntington disease. She had a history of hypertension, chronic obstructive pulmonary disease, and coronary artery disease s/p coronary artery bypass graft surgery 11 years prior to death. Two years prior to death, she was hospitalized with a urinary tract infection, and during this admission, she was diagnosed with mild dementia of the Alzheimer type with mild memory deficits. She progressed slowly until six months prior to death, when she developed a sharp decline in cognitive function. Three months later, she was unable to recognize family members and was only able to have limited, basic conversations. She died while in hospice care. Permission was obtained for a brain only autopsy.

Autopsy Findings: The brain weighed 1100 gm and showed moderate global atrophy. Coronal sections showed old lacunar infarcts in the left frontal white matter and in the left putamen. There were no neuritic plaques (CERAD age-related plaque score 0). Moderate numbers of neurofibrillary tangles were seen in the hippocampus and entorhinal cortex, consistent with a Braak score of II/VI.

Material Submitted: H&E section

Points for Discussion: 1. Diagnosis
2. Clinical presentation
Submitted by: Cristiane M. Ida, M.D., Julie E. Hammack M.D., Jonathan M. Morris M.D. and Caterina Giannini, M.D. Ph.D
Mayo Clinic, Rochester, MN

Clinical History: A 37-year-old right-handed man with a past medical history of hypertension, depression, anxiety disorder, polysubstance abuse (mainly cannabis) and 1-year of mild short-term memory complaints, presented with progressive gait ataxia of 2-weeks duration. In the past month, he had noted a right neck mass the size of a golf ball and general malaise. On MRI, axial and coronal post-gad T1 weighted images demonstrated extensive hemispheric and focal cerebellar abnormalities with a perivascular pattern of enhancement.

CT of the chest and abdomen demonstrated adenopathy in the right lower neck, mediastinum, and a 5-mm left pulmonary nodule. In the following 2 weeks, he became nonambulatory due to imbalance, and his memory and thinking were significantly impaired. Motor examination revealed: left upper extremity mild corticospinal weakness and apraxia; left upper & lower extremity slightly brisk deep tendon reflexes, with an equivocal left Babinski; tendency to fall to the left; and mild right upper extremity ataxia. No pain on percussion of the spine, rigidity, fever, chills or rash was noted. A spine MRI, performed due to the onset of urinary retention, showed conus medullaris and cauda equina enhancement. On CSF examination: protein 78 mg/dl; glucose 52 mg/dl; nucleated cell count 42 (87% lymphocytes, 13% monocytes); negative cytology and JC virus PCR. A right frontal stereotactic biopsy was obtained.

Material submitted: H&E section.

Points for discussion: 1. Diagnosis 2. Pathogenesis
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CASE 2011-4

Submitted by: Tracie N. Pham, M.D. (TNPham@ucla.mednet.edu), William H. Yong, M.D., Gary W. Mathern, M.D., and Harry V. Vinters, M.D. UCLA Medical Center.

Clinical History: The patient was a 13 year-old male with history of complex partial seizures since age 6 years. He was initially managed on Trileptal, with Keppra added in 2005 and was on Lamictal at the time of presentation. Past medical history includes diagnosis of neurofibromatosis 1 at age 18 months due to the presence of café-au-lait skin lesions and neurofibromas.

Imaging studies included a PET scan that showed a focus of hypometabolism in the right frontal lobe. MRI revealed a stable, cortical lesion in the right anterior frontal convexity with multifocal punctate enhancement, small cystic foci, and no perilesional edema. The lesion was hyperintense on the T2-weighted image.

Material submitted:

Two H\&E sections of cortical lesion

Points for discussion:

1. Diagnosis
2. Pathogenesis
CASE 2011-5

Submitted by: Sandra L. Cottingham, MD-PhD
Spectrum Health and
Helen DeVos Children’s Hospitals
Deptartment of Pathology
Grand Rapids, MI

Clinical History: An 11-year old male presented with new onset of seizures. Past medical history is significant for migraine headaches since age 5, increasing in frequency and severity over the past three weeks. In addition there was a history of hydrocephalus and Chiari 1 malformation diagnosed at 9 months of age. His last MRI performed at age 6 was noted to be “stable.”

MRI findings at presentation showed a right frontal cystic mass and Chiari 1 malformation.

Material submitted: H&E section of right frontal lobe mass (virtual slide)

Points for discussion:
1. Diagnosis(es)
2. Pathogenesis/relationship
Submitted by:
PEDRO DSC CIARLINI, YEZID GUTIERREZ
PIERLUIGI GAMBITTI, MARK L COHEN.
University Hospitals Case Medical Center
National Prion Disease Pathology Surveillance Center

Clinical History:
The deceased was a 54 year-old gentleman with a history of mental retardation, functioning at a level of a 5 year-old child. He presented with a history of staggering, difficulty moving legs and incontinence progressing to spastic quadriplegia in less than a week. The initial MRI revealed central and cortical atrophy, with no evidence of structural disease, stroke or trauma, but revealed significant cervical spinal stenosis at C5-6. Initial CSF studies were normal. He was then placed on high dose steroids and underwent a decompressive laminectomy, but failed to improve. He was then given IVIg for a possible stiff man syndrome. Repeat CSF revealed mild protein elevation (73 g/dl), but no pleocytosis. Repeat MRI showed several scattered bilateral 1-2 mm T2W/FLAIR bright foci scattered in the corona radiata, subcortical white matter and thalamus. He then developed mild headache and low grade fever, eventually became unresponsive and died two months after his initial presentation. A brain-only autopsy was performed and the brain was sent to the National Prion Disease Pathology Surveillance Center to rule out an atypical prion disease.

Autopsy findings:
The brain weighed 1,318 grams post-fixation and had no external abnormalities. On section, numerous poorly defined, partially confluent areas of yellow-tan to red-tan discoloration were identified, involving predominantly the deep cerebral cortex and the superficial subcortical white matter. These areas occurred within all lobes of the cerebrum as well as in the cerebellar cortex. These same lesions were identified bilaterally in the thalami and surrounding the fourth ventricle.
Material submitted:
  Gross photograph of occipital lobe
  One H&E section of the brain

Points for discussion:
  1. Differential diagnosis.
  2. Pathogenesis
Clinical History: A 47 year old woman was diagnosed with HIV in 1993, and had not taken any therapy for the past 14 years. She is known to also have past medical history of shingles. She had been in a normal state of health until 4-5 weeks prior to presentation, when she developed slurred speech. She then presented to the emergency room with altered mental status, blurred vision, headaches and behavioral changes. Her CD4 count was 20 on admission. Upon further evaluation, she was found to have a large mediastinal mass and multiple brain lesions.

Her mediastinal mass was surgically resected first, and was consistent with adenomatous hyperplasia of the thyroid gland.

Subsequently, biopsies of her frontal lobe lesions were obtained. The viral cultures taken at the time of surgery were negative for CMV, HSV, Varicella, and Enterovirus. The bacterial and fungal cultures were also negative. A diagnostic study was performed.

Material submitted:  H&E section of cerebrum

Points for discussion: 1. Diagnosis
                        2. Pathogenesis
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CASE 2011-8

Submitted by: Jeremy Deisch, M.D., Dennis Burns, M.D., and Charles White III, M.D.
UT Southwestern Medical Center
Department of Neuropathology

Clinical History: The patient was a 21 year-old female with progressive neurologic deterioration. She initially presented at the age of 10 years with tremors and headaches. Her family history was remarkable for a paternal great grandfather with myasthenia gravis, a maternal great grandmother with tremors, (onset in the 7th decade), and a maternal grandfather with tremors (onset in the 6th decade). A maternal aunt was born with mental retardation. Notably, both parents reportedly had seizures in the past. At the age of 12 years, the patient developed dysarthric speech. A presumptive diagnosis of myasthenia gravis was excluded. A muscle biopsy performed in July 2004 revealed chronic neurogenic atrophy. The patient subsequently developed temperature instability, tongue fasciculations, worsening dysarthria, tremors, and cognitive decline. In July 2007 the patient underwent bilateral deep brain stimulator placement resulting in temporary improvement of her tremors. Her clinical condition worsened, progressing to disabling dyskinesia, severe dysphagia, and inability to walk or stand. Because of repeated complications and in agreement between the patient and her family, the gastric feeding tube was removed; death followed shortly thereafter.

Autopsy findings: The fixed brain weighed 1150 grams, not including the left frontal pole, which was removed at the referring institution prior to fixation. External examination of the brain demonstrated a normal gyral pattern. The cranial nerves and blood vessels showed no abnormalities. Coronal sections of the cerebrum demonstrate bifrontal tracks traversing the frontal neocortex, centrum semiovale, and basal ganglia, both terminating in the ipsilateral subthalamic nuclei. The cortical ribbon was uniform and of normal thickness. Cross sections of the brainstem and parasagittal sections of the cerebellum show tan discoloration of the substantia nigra, but are otherwise without significant gross abnormalities.

Material submitted: H&E section of cerebrum, unstained slide

Points for discussion: 1. Diagnosis, 2. Pathogenesis
Submitted by:
KATHY NEWELL, MD, BRIAN KELLEY, DO, ANIA POLLACK, MD
E. TESSA HEDLEY-WHYTE, MD, and EUGENIO TABOADA, MD
Departments of Pathology and Laboratory Medicine (KN) and
Neurosurgery (BK, AP), University of Kansas Medical Center,
Kansas City, Kansas; C.S. Kubik Laboratory for Neuropathology
(ETHW), Massachusetts General Hospital, Boston, MA; and
Department of Pathology (ET), Children’s Mercy Hospital Kansas
City, Missouri

Clinical History: A 15 year-old right-handed young man
presented with new onset of seizure activity, reported to be 30
seconds in duration consisting of generalized tonic clonic
movements of all extremities with drooling, no apparent
respirations, and no incontinence. Per report his eyes were open
without gaze deviation. Following the event, the patient
remained confused. There was no antecedent trauma. He had
just returned from an uneventful day at school. His mother
reported the history of a single seizure episode at one year of
age unassociated with fever. A workup at that time included
head CT and EEG, both of which were unrevealing. No other
significant medical or surgical history was reported. He was up
to date on vaccinations, had no allergies, and took no
medications. He has two siblings that were born without
clavicles.

On presentation, the patient was afebrile with a pulse of 114
beats/minute, blood pressure of 164/60, and a respiratory rate of
20/minute with a saturating hemoglobin at 97% on room air. He
reported no headache, vision changes, or nausea/vomiting. He
was alert but confused, requiring frequent redirection. He was
oriented to person, place, and year. His pupils were equal,
round, and reactive to light. All twelve cranial nerves were
independently tested and found to be intact. Strength and
sensory examinations and reflexes were unremarkable. No
current seizure activity was appreciated. A complete metabolic
profile and CBC were unremarkable.
A noncontrast CT and subsequent MRI of the head with/without contrast showed a well-defined 1.1 x 1.6 cm mass in the left parietal lobe just posterior to the Sylvian fissure. There was surrounding edema and minimal enhancement with no midline shift appreciated. The cortical sulci, basilar cisterns, and ventricles were within normal limits. There were normal signal flow-voids in the circle of Willis and major dural venous sinuses. No signal abnormalities on diffusion weighted imaging were noted. MR spectroscopy did not suggest an astrocytic lesion. He was loaded on Dilantin and started on Decadron. After review of these findings, the patient underwent an image guided temporoparietal craniotomy with resection of the lesion.

Material submitted:
1. Virtual slides of the left temporoparietal lesion:
   - H&E stained section
   - Ki-67 immunohistochemically stained section
2. Digital MRI brain images, T1 and T2 (jpg files)

Points for discussion:
1. Diagnosis
2. Pathogenesis
3. Epidemiology
4. Treatment
Submitted by: Mark E. Jentoft, Dr. Nancy Kois, Bernd W Scheithauer

1Mayo Clinic, Rochester, MN.
2St. Alphonsus Regional Medical Center, Boise, ID.

Clinical History: The patient is an 11 year old Caucasian male who presented to the emergency department with a 2 month history of progressive headaches and 2 week history of confusion, nausea, and vomiting who was thought by his parents to have severe “flu”. Physical examination at that time demonstrated bilateral papilledema. A CT scan showed a right frontotemporal mass causing a 1.1 cm right-to-left shift. Given the clinical finding of increased intracranial pressure, the patient received mannitol and steroids and was scheduled for surgery. Subsequently an MRI was performed which demonstrated a large (9.6 x 7.4 x 5.9 cm) mostly homogenously enhancing extra-axial mass in the right sylvian fissure extending almost to the midline of the brain and causing edema in the right temporal, frontal, and parietal lobes. At frontotemporoparietal craniotomy the tumor involved the frontal pole, anterior temporal fossa, and sphenoid wing region. It was described as firm and fibrous, only the basal portion being dura attached. The gross impression was a meningioma of the sphenoid wing.

Material submitted: H&E-stained section

Points for discussion:
1. Diagnosis
2. Pathogenesis
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CASE 2011-11

Submitted by: DR. B. LACH
Department of Pathology & Molecular Medicine
Hamilton Health Sciences, Hamilton General Site

Clinical History: This 76-year old lady with a five year history of multiple myeloma had a lytic lesion in the parietal bone, first time detected in July 2003. The lytic lesion involved “the right frontal calvarium” and measured approximately 4.3 x 6.3 cm; it was considered a metastatic carcinoma or a sarcoma. Radiologic follow-up four months later revealed parasagittal, intracranial and subcutaneous extension of the lesion along the right frontal convexity, associated with dural thickening. This tumour was resected and diagnosed as meningioma II/III, with extensive invasion of bone and subcutaneous tissue. She did not have radiotherapy or chemotherapy.

Follow-up in 2004 revealed no evidence of meningioma or other lesions in the brain or cranium.

Three years later she was admitted to the hospital due to cognitive decline and behavioral changes. Radiological study in March 2007 revealed a recurrent enhancing extra-axial parasagittal frontal tumour measuring approximately 7.0 x 6.0 x 4.0 cm, located mostly in the midline of the vertex. The surrounded brain showed vasogenic edema. The tumour was resected and subsequent MRI’s showed no evidence of residual lesion.

Material Submitted:
Sections of the tumour from the second surgery.

Point for Discussion:
Histological nature of the spindle cell component in the tumour