59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018.

CASE 2018-1

Submitted by:
Diana Thomas, MD, PhD and Julia Kofler, MD
UPMC Department of Pathology
200 Lothrop Street, Scaife Hall S701
Pittsburgh, PA 15261

Clinical History:
The patient was a 61 year old woman who started to experience syncopal episodes at about age 49. As part of her work-up she had a CT scan of the brain which revealed abnormalities in the white matter. She subsequently developed gait abnormalities but remained cognitively intact with preserved memory. In her late 50s, she lost the ability to walk and developed urinary incontinence. In the last few months before death, she experienced progressive lapses in her short-term memory.

Her family history was notable for a similar disease process in her father, two of her three siblings and in one cousin.

Material submitted:
Gross image, 1 H&E slide, 1 Luxol fast blue/PAS stain

Points for discussion:

1. Diagnosis and differential diagnosis
2. Ancillary studies

59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018.

CASE 2018-2

Submitted by:

Julieann Lee[1], Sean Ferris[1], David Solomon[1], Dimitri Trembath[2], Arie Perry[1]

1. Neuropathology, University of California, San Francisco, CA.
2. Neuropathology, The University of North Carolina at Chapel Hill, Chapel Hill, NC.

Clinical History: The patient is a 25-year-old man who presented with left hand numbness and headaches. He was found to have a 4.7 cm heterogeneously enhancing intra-axial mass in the left cerebellar hemisphere, with mass effect on the fourth ventricle. A biopsy was performed.

Material submitted:
H&E slide from biopsy of cerebellar mass

Points for discussion:
1. Differential diagnosis
2. Immunohistochemical and molecular evaluation

59th ANNUAL DIAGNOSTIC SLIDE SESSSION 2018.

CASE 2018-3

Submitted By:
Karra A. Jones, MD, PhD and Steven A. Moore, MD, PhD
The University of Iowa, Department of Pathology, Iowa City, IA 52242

Clinical History:
2 year old male with mild global developmental delay, frequent falls, and oropharyngeal dysphagia. Neurologic exam revealed a positive Gowers' sign and abnormal gait consistent with a compensated Trendelenburg. His family history was positive for a maternal uncle with unknown neuromuscular disease requiring the use of a wheelchair since age 12. The serum CK was elevated in the range of 1300-1400 U/L.

Genetic testing prior to muscle biopsy included a non-diagnostic microarray, normal *DMD* del/dup testing and complete sequencing, normal GAA enzymatic assay, and negative congenital hypotonia next generation sequencing panel.

Material Submitted:
H&E stained cryosection of muscle

Points for Discussion:
1. Differential diagnosis
2. Approach to diagnostic testing

59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018.

CASE 2018-4a

Submitted by:

Anne Shepler, MD and Julia Kofler, MD
University of Pittsburgh Medical Center Presbyterian Hospital
Division of Neuropathology
200 Lothrop Street, Room S701 Scaife Hall
Pittsburgh, PA 15213

Clinical History:

The patient was a 37-year-old lawyer with no family history of dementia, who at age 33 began to have performance issues at work with inattentiveness to detail and a lack of concern for deadlines. He became progressively abulic and socially withdrawn with a loss of interest in his hobbies and personal appearance. By age 34, he began to choke frequently on food and was noted by his wife to have developed a nasal voice and bilateral ptosis. While he could remember his two young children's names, he was unable to care for them. He also developed reduplicative paramnesia wherein he insisted that there were two "2B" apartments in his apartment building where another woman (with his wife's name) lived with two children. While he did not get agitated if corrected, he returned to this delusion repeatedly.

On neurological examination, he showed no lateralizing sensory or motor signs and muscle strength was normal. No fasciculations were present. His reflexes were brisk and symmetric with no sustained clonus or Babinski sign. He was fluent with intact comprehension, repetition, naming, reading, and writing. He often answered questions too quickly with impulsive errors as he would not wait of the conclusion of the question; he was undisturbed when he made a wrong answer. Other than ptosis and a mild weakness of the orbicularis oculi, the cranial nerve examination was unremarkable. Initial MRI and CT scans were normal. A PET scan revealed bilateral frontal diminution of glucose utilization, worse on the right than the left, with extension to the right caudate. An EMG was negative.

Autopsy findings:

The brain weight was 1160 grams (fresh). Neuropathologic examination was notable for moderate atrophy of the frontal lobe and caudate and mild atrophy of the temporal and parietal lobes.

Material submitted:

One H&E slide of frontal cortex

Points for discussion:

1. Differential diagnosis
2. Useful immunohistochemical stains

59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018.

CASE 2018-4b

Submitted by:

Aivi T. Nguyen and Edward B. Lee

Hospital of the University of Pennsylvania
3400 Spruce Street
Philadelphia, PA 19104

Clinical History:

The decedent was a 72-year-old right handed female who presented for evaluation of incoordination and frequent falls. She complained of multiple episodes of imbalance and demonstrated increasing forgetfulness, anosmia, and micrographia. She was evaluated by multiple neurologists and eventually treated with carbidopa/levodopa with no improvement. Physical exam was remarkable for masked facies, impaired extraocular movements with jerky saccades, axial rigidity, moderate bradykinesia, and a narrow-based gait with short strides, absent arm swing, and no postural control. Over the course of five years she developed severe cognitive defects, including word finding difficulties and memory decline, and was eventually transferred to hospice where she died.

Autopsy findings:
The brain was examined 14 hours post-mortem and weighed 1147 grams. Gross findings included diffuse cerebral atrophy, severely atrophic hippocampus and amygdala, ex-vacuo hydrocephalus, and substantia nigra depigmentation.

Material submitted:
1 H&E section of the hippocampus

Points for discussion:

1. Differential diagnoses
2. Useful immunohistochemical/additional stains
3. Revised differential diagnoses after additional stains and biochemical work-up

59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018.

CASE 2018-5

Submitted by: E. Kelly S. Mrachek, M.D.
M. Beatriz S. Lopes, M.D., Ph.D.
University of Virginia Health System
Department of Pathology, Division of Neuropathology
Box 800214
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Clinical History:
The patient is a 6-year-old male who presented with a two week history of headaches with recent nausea and vomiting. His PCP diagnosed strep throat, and treatment with antibiotics failed. While getting additional labs drawn, the patient had acute onset of left sided facial drooping, and was brought to the ER. MRI of the brain with and without contrast showed a 5.2 cm avidly enhancing, extra-axial mass in the left cerebellopontine angle with extension into the internal auditory canal. A left retrosigmoid craniotomy and gross total resection were performed at the University of Virginia.

Material submitted:
MRI image of brain demonstrating a left CPA mass, and an H&E section of the mass.

Points for discussion:

1. What is the final integrated histomolecular diagnosis of this left CPA mass?

2. What is the most common molecular genetic alteration in lesions of this type?

59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018.

CASE 2018 - 6

Submitted by: Jason A. Gregory, CPT USA, MD, Meggen Walsh, MD and Jesse Lee Kresak, MD

University of Florida
Department of Pathology, Immunology, and Laboratory Medicine
1600 SW Archer Rd
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Gainesville, FL 32610

Clinical History:
A twenty-year-old male presents for esophagogastroduodenoscopy for persistent dysphagia with a specific chief complaint of "I'm unable to chew because I can't open my mouth and my teeth hurt." He has a history of hypertension, obstructive sleep apnea, and a congenital musculoskeletal disorder. During the procedure, the patient was noted to have airway instability with subsequent desaturation. Resussitative efforts were unsuccessful and the patient expired.

Autopsy findings:
General autopsy revealed a thin man of short stature weighing 75 lbs. He had various musculoskeletal abnormalities including scoliosis, pes planus, and asymmetrical muscular atrophy. The brain weighed 1,560 grams. Gross examination revealed an enlarged brainstem with a markedly stenotic aqueduct. The medulla appeared ovoid rather than the normal "papilionaceous" shape. Internal architecture of the brainstem appeared distorted. The dentate nucleus of the cerebellum was difficult to delineate grossly. The remainder of the cerebrum and cerebellum appeared normal.

Material submitted:
H&E-stained section of the medulla

Points for discussion:
1. Differential diagnosis and ancillary studies
2. Pathogenesis

59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018.

CASE 2018-7

Submitted by:

Kyle Conway, Theodore Brown, David Gordon, John Kennedy, and Sriram Venneti
University of Michigan Department of Pathology
1301 Catherine St.
Ann Arbor, MI 48109

Clinical History: The decedent is a 50 year old female who presented with hemiparesis, expressive dysphasia, headaches, visual disturbances, and paresthesias. Imaging showed multifocal frontal and temporal lesions crossing the corpus callosum. A frontal lobe biopsy at this time demonstrated only reactive gliosis and perivascular inflammation. Several months later, she presented to the emergency department with acute worsening of symptoms. Repeat imaging showed findings consistent with an ischemic stroke. Serologic workups for autoimmune disease and infection were negative. She was discharged, and her neurologic condition worsened over the course of a year. She passed way after an acute deterioration in neurologic status.

Autopsy findings: Gross autopsy findings included multiple areas of softened parenchyma in the left frontal, right fronto-parietal, right superior parietal, left mid parietal, and left occipital lobes. The lumina of the carotid arteries were grossly narrowed (approximately 0.1 cm in diameter).

Material submitted:

1. MRI images
2. Gross photographs of cortex and base of brain
3. H&E stained slide of cortical lesion
4. Trichrome stained slide of carotid artery

Points for discussion:

1. Explain the differential diagnosis of this clinical history and workup
2. Understand the classification and subtyping for this disease

59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018.

CASE 2018-8

Submitted by:

Angela N. Viaene, MacLean P. Nasrallah, and Zissimos Mourelatos

Hospital of the University of Pennsylvania, Department of Pathology and Laboratory Medicine, Division of Neuropathology, 6th Floor Founders, 3400 Spruce Street, Philadelphia, PA 19104

Clinical History:

A 38 year old female with no significant past medical history presented with headache, nausea and photophobia for three days. She subsequently developed visual loss and aura in both eyes which prompted imaging studies. A large, predominantly cystic left parietal mass measuring 6.4 x 4.3 x 5.2 cm associated with irregular and nodular peripheral enhancement and areas of hemorrhage around its periphery was seen on brain MRI. There was mass effect including 7-8 mm rightward midline shift and partial effacement of the basal cisterns. The patient underwent left craniotomy for gross-total resection of the enhancing mass.

Material submitted:

1. One representative H&E slide
2. Representative pre-operative MRI image

Points for discussion:

1. Differential diagnosis
2. Molecular findings

DSS 2018 Case 9 Protocol

Missia Kohler, M.D., Jamie Walker, M.D., Ph.D., Qinwen Mao, M.D., Ph.D., and Eileen Bigio, M.D.
Northwestern University Feinberg School of Medicine
Department of Pathology
710 North Fairbanks Ct
Chicago, IL 60611

Clinical History:
The patient initially presented in 2009 at the age of 72 to neuropsychiatry with a two-year history of minor memory problems. His cognitive exam revealed memory issues that were primarily amnestic, moderate executive dysfunction and a MoCA score of 20/30. His sensory and motor exam were unremarkable. His MRI demonstrated more atrophy than expected for his age. His *APOE* allele status was ε4/ε4. In 2016, he was still driving, but experienced bowel and bladder incontinence and was having a "hard time fixing things" in the home. By 2017, he was displaying more word-finding difficulties and required instructions for most daily tasks. In the autumn of 2017, he had a few falls and hospitalizations for infections. Thereafter, he rapidly declined, and died at the age of 80 in October of 2017.

Material submitted
1. One H&E stained slide

Points for discussion:
1. Differential diagnosis
2. Immunohistochemical work-up

59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018.

CASE 2018 #10

Submitted by: M. Adelita Vizcaino M.D.[1], Verena Staedtke M.D.[2], Allan Belzberg, M.D[2]., Fausto J. Rodriguez M.D.[1]

Division of Neuropathology[1], and Department of Neurology and Neurosurgery [2], Johns Hopkins University School of Medicine.

Clinical History:
An 11-year-old boy was previously healthy until approximately the year prior, when the family noticed that he was walking on the lateral aspect of his right foot, resulting in callus formation and closed pressure ulcer. During physical examination, it was noted that the patient had a high arch of the right foot as well as a 3 cm. leg length discrepancy. Several subtle café-au-lait spots were also identified. Subsequent radiographs demonstrated multiple stress fractures, which prompted MRI of the spine and lower extremities demonstrating enlargement of the right lumbosacral plexus and right sciatic nerve extending distally down the thigh, progressing to include the tibial nerve and common peroneal nerve to the bifurcation with continued involvement of the deep and superficial peroneal nerve branches to the foot. At the time of surgical intervention for orthopedic corrections, a biopsy of the tibial nerve was performed.

Material submitted: Virtual H&E image of tibial nerve biopsy

Points for discussion:

1-Differential Diagnosis
2-Pathogenesis
3-Role of molecular genetics

59th ANNUAL DIAGNOSTIC SLIDE SESSION 2018

CASE 2018-11

Submitted by: Isaac Solomon, M.D., Ph.D.; Sandro Santagata, M.D., Ph.D.
Department of Pathology, Brigham and Women's Hospital, 75 Francis Street, Boston, MA, 02115, USA.

Clinical History:
A 53-year-old man from Cape Verde presented following an acute onset of vertigo, nausea, and vomiting. His past medical history was notable for a brain lesion resected in his 20s, Hodgkin's lymphoma treated with ABVD chemotherapy seven years earlier, and latent tuberculosis treated with nine months of anti-mycobacterial drugs. At the time of presentation, he lived in Massachusetts and had last visited Cape Verde two years earlier. He had recently traveled to Mexico. A neurological examination of the patient revealed ataxic gait, up-beating nystagmus, and right-sided dysmetria. No abnormalities were identified by routine blood testing that included a complete blood count, a basic metabolic panel and liver function tests. HIV antibody, cysticercosis IgG, and tuberculosis interferon gamma release assay were negative. Toxoplasma IgG antibody was positive. A 4-cm lobular, cystic, rim-enhancing lesion in the right hemisphere of the cerebellum was identified using MRI. The patient was taken to the OR for resection.

Material Submitted:
H&E section of cerebellar mass

Points for Discussion:
1. Histologic characteristics
2. Differential diagnosis (imaging, histology)
3. Short review/summary