62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

Case # 2021-1

Submitted by:

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Clinical History:

56 year-old female experienced right-sided ear pain with hearing loss beginning 3 years later. An MRI performed at age 59 showed a 2.3 cm enhancing skull-base mass at the right prepontine cistern extending to the jugular bulb; the differential diagnosis from the radiologist's report was fairly broad. Past medical history is notable for extracranial tumors for which she underwent neck dissection and open-heart surgery. She has no known history of skin cancer. The intracranial lesion was resected when the patient was age 60.

Material submitted:

Images (x2) - MRI brain (coronal and axial planes)
H&E section of the "CP angle tumor"

Points for discussion:

1. Summarize the histologic features of this tumor
2. Interpret next-generation sequencing results and clinical significance

CASE 2021 #2

Submitted by: Lorraina J. Robinson, D.O., M.S., Christian Davidson, M.D., Joshua M. Klonoski, M.D., Ph.D., Eric A. Goold, M.D.

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Clinical History: A female neonate was delivered at 39 weeks gestation via an emergency cesarean section due to non-reassuring fetal heart tones. Routine prenatal care and testing for the AB positive 35-year-old mother were unremarkable. At birth, the infant's respiratory effort was absent, and the infant was subsequently intubated. She was admitted to the neonatal intensive care unit due to concern for sepsis. An infectious work up and newborn screening test was performed with negative results. The infant died on day 3 shortly after being transitioned to comfort care.

Imaging: An MRI showed extensive areas of signal abnormality in both hemispheres and cerebellum. These areas appeared chronic in nature and included cystic lesions, architectural distortion, as well as presumed passive expansion of the left lateral ventricle. There were areas of susceptibility effect and T1 hyperintensity most likely representing hemorrhage.

Autopsy Findings: Autopsy showed a normally developed female infant and brain weight (299. 67 gm) with scattered small hemorrhages in multiple organs/tissues. Gross examination of the brain revealed diffuse hemorrhages of chronologic heterogeneity, brainstem and cerebellar hemorrhages predominately centered in the white matter, and grossly visible cystic lesions.

Material Submitted: Image of a single coronal slice of the cerebral hemispheres

Points for discussion: 1. Gross Findings, 2. Microscopic Findings, 3. Differential Diagnoses, 4. Pathogenesis, 5. Disease Phenotypes

62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

CASE 2021-3

Submitted by:
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Clinical History:
A 13-month-old term boy presented to the ER-department with a week-history of recurrent vomiting and motor regression. His antenatal history was unremarkable. On clinical examination, the patient was lethargic but no weakness. His pupils were equal and slow to react to light. CT-scan of the head showed obstructive hydrocephalus with marked enlargement of lateral and third ventricles due to a large cystic and focally calcified mass at the pineal region. Brain MRI scan revealed an acute obstructive hydrocephalous secondary to a complex large pineal region tumor. The tumor (57 x 38 x 39 mm) appeared lobulated with heterogeneous contrast-enhancement and focal cystic changes. Routine blood examination, serum alpha-fetoprotein, and beta-human chorionic gonadotropin were within normal limits. An urgent endoscopic third ventriculostomy and tumor biopsy were performed. As the tumor was not amenable to further resection, the decision was made to start 2-cycles of induction chemotherapy. Thus, the patient underwent a second surgery where they achieved a gross total resection.

Material submitted:
1. Two virtual H&E slides (the initial biopsy and the resection)
2. Representative pre-operative MRI images

Points for discussion:
1. The pathologic features and the differential diagnosis
2. Clinical prognosis and the molecular alterations

62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

CASE 2021-4

Submitted by: Rachel A. Kolster and Edward B. Lee, Department of Pathology, Hospital of the University of Pennsylvania

Clinical History:
A 67-year-old woman died with a clinical diagnosis of behavioral variant of frontotemporal dementia (bvFTD) after developing progressive cognitive and personality changes starting in her late 50s, as well as several seizure episodes (without a prior seizure history). She had a family history of several neurologic diseases, including Parkinson's disease with dementia, primary progressive aphasia, and corticobasal syndrome.

Autopsy findings:
On postmortem examination, the brain weighed 981 grams and external examination showed severe atrophy. On sectioning, the hippocampus and amygdala were atrophic. The substantia nigra and locus ceruleus were de-pigmented.

Material submitted:
2 H&E sections of the frontal lobe and hippocampus (5 images: 2 low power images of frontal lobe and hippocampus, and three high power of frontal cortex, CA1 and subiculum)

Points for discussion:
1. Diagnosis
2. Pathogenesis

62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

CASE 2021 #5

Submitted by: Nima Sharifai, MD, PhD & Sonika Dahiya, MBBS, MD

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Clinical History: The patient is a 3-year-old girl with a history of a large left shoulder hemangioma, who presented with three weeks of headache, nausea, and vomiting. Head CT showed a posterior fossa mass and ventriculomegaly. Brain MRI showed a heterogeneously enhancing, 5.1 x 4.2 x 3.2 cm, mixed solid and cystic mass centered in the cerebellum. The lesion exerted significant mass effect with partial effacement of the 4th ventricle, as well as anterior-superior displacement of the medulla and pons. Multiple faint septations were seen within the mass with evidence of diffusion restriction in the solid areas. The patient underwent suboccipital craniotomy for cerebellar tumor resection.

Material submitted:

1. One representative H&E slide
2. Brain MRI images (Axial T1 post-contrast and sagittal FLAIR)
3. Microscopic image of smear preparation (40x magnification)

Points for discussion:
1. Differential diagnosis
2. Diagnostic work-up
3. Key diagnostic findings

62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

CASE 2021 [6]

Submitted by:

Changhong Xing and Chunyu Cai
Department of Pathology, University of Texas Southwestern Medical Center
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Clinical History:
37 years old right-handed Caucasian male with a history of end stage renal disease status post two renal transplants in 1993 and 2005 has developed progressive bilateral hand weakness and muscle atrophy for two years, with no preceding trauma or illnesses. He is a body builder and is not able to grip the weight when weight lifting. He also has dysphagia, balance problems and poor vision. On exam, he has marked distal hand weakness and atrophy, extensors>flexors. He also has bulbar weakness and nasal dysarthria. He does not have proximal weakness or lower extremity distal weakness. EMG shows myopathy in hand and forearm muscles. A biopsy of extensor carpi radialis longus (ECRL) is performed.

Material submitted: One H&E and one Gomori trichrome slide

Points for discussion:

1. Differential diagnosis
2. Histochemical and EM findings

62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

CASE 2021-7

Submitted by: Kathryn Eschbacher MD, Eleni Constantopoulos, MHS, PA(ASCP), and Aivi Nguyen MD
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Clinical History:

This 65-year-old woman presented in 2010 with a 2 year history of intermittent headaches, a 6-month history of worsening ataxia, word-finding difficulties, tremor, confusion, and hallucinations followed by a more rapid onset of confusion and disturbed spatial perception and progressive left visual field loss. Cerebrospinal fluid (CSF) studies, cerebral angiogram, and an electroenceophalogram were unrevealing. MRI demonstrated abnormal T2 signal centered in right temporoparietal cortex and subcortical white matter, and minimal cortical enhancement on postcontrast images, which was overall concerning for vasculitis or mitochondrial encephalopathy.

In 2015, she subsequently underwent a right parieto-occipital brain biopsy, which did not render a specific diagnosis. Following her surgery, she had a comprehensive mitochondrial DNA analysis and MRI spectroscopy performed, both of which were unrevealing. In 2016, she had multiple episodes, lasting up to 3 days, in which she developed severe headache, slurred speech, arm heaviness and numbness, decrease in vision, and mild confusion. Head imaging studies did not demonstrate evidence of disease progression. She underwent whole exome sequencing, which identified a variant of unknown significance in *MACF1*. In 2016, her brother began experiencing stroke-like and encephalitis-like episodes similar to his sister. In 2017, both siblings underwent skin biopsy which further directed clinical work-up.

Autopsy findings:

At the time of autopsy, the brain appeared normally developed with mild hydrocephalus ex vacuo with a brain weight of 1026.4 grams (fixed). There was evidence of a right parietooccipital biopsy site defect and a right inferior parietal lobe laminar necrosis with associated softening. Mild depigmentation of the substantia nigra was present.

Material submitted:

1. H&E section of amygdala
2. H&E section of midbrain
3. H&E section of right leg skin

Points for discussion:

1. Differential diagnosis
2. Ancillary immunohistochemical/additional stains
3. Useful ante-mortem tests

62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

CASE 2021 #8

Submitted by:
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Clinical History:
The patient is an infant boy born at gestational age 37 weeks and 2 days with a vascular brain lesion noted on prenatal imaging. Other prenatal screens were negative, and maternal history was significant only for hypertension. Delivery was via cesarean section with APGAR scores of 9 and 9. He was neurologically intact with no focal deficits or seizures. Magnetic resonance imaging at 1 week of age showed a 7 cm hypervascular right parieto-occipital lesion with significant mass effect on the cerebellum and midbrain. He underwent preoperative embolization and subtotal resection at 2 weeks of age. Intraoperative findings include a large, white, and highly vascular tumor occupying the right parieto-occipital space.

Material submitted:

1. H&E-stained section (right parieto-occipital lesion).
2. Pre-operative MR imaging (sagittal T1 post-contrast, axial T2 FLAIR).

Points for discussion:

1. Differential diagnosis.
2. Ancillary studies and molecular findings.

62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

CASE 2021-9

Submitted by: Tiffany Baker, MD PhD
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Clinical History: 60 year old female non-smoker with no prior history of malignancy or occupational exposures presented with headache and new onset vision loss in left eye. Symptoms did not resolve following a course of antibiotics and steroids. Imaging revealed a midline skull base lesion centered within the ethmoid sinus with involvement of the cribriform plate and orbital apex. Due to mass effect on the orbital contents an emergent endonasal debulking was performed with some subsequent vision improvement.

Material submitted: H&E stained slide of anterior skull base tumor.

Points for discussion: 1. Criteria for pursuing the diagnosis
2. Clinical significance of making the diagnosis

62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

CASE 2021-10

Submitted by: Thomas Zaikos, M.D., Ph.D., Peter Burger, M.D., Jason Savell, M.D., Fausto Rodriguez, M.D., and Meaghan Morris, M.D., Ph.D.

Clinical History:
The patient is a 43-year-old female with HIV who presented with generalized weakness, dizziness, and mild incoordination. Imaging revealed obstructive hydrocephalus with an ill-defined mass-like T2 hyperintensity in the left cerebellar hemisphere with progressive irregular contrast enhancement. A biopsy of the cerebellar lesion was performed.

Material submitted: 1 H&E stained section and pre-operative MRI images

Points for discussion:
1. Differential diagnosis
2. Pathogenesis

Case 2021-11

Submitted by:

Peter J Kobalka[1]

1. Neuropathology, Ohio State University, Columbus, OH.

Clinical History: The patient is a 57-year-old female who presented with a DVT, as well as decreased eye vision with proptosis and blurring. Imaging revealed a 3.5 cm mass involving the left frontal calvarium with an extra-axial dural based component and compressing the left ocular globe. The mass appears to abut the frontal lobe with local mass effect. Her past medical history is significant for a prior surgery to resect an anterior mediastinal mass. A gross total resection was performed.

Material submitted:
H&E slide from resection of left orbital/frontal lobe mass

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