American Association of Neuropathologists

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Diagnostic Slide Session

Saturday, June 10, 2023

Learning Objectives:

1. *Describe advancements in diagnostic criteria and techniques for diseases of the central nervous system.*
2. *Apply diagnostic criteria to develop differential diagnoses.*
3. *Recognize the underlying causes of diseases of the central nervous system.*

64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-1

Submitted By:
Simmi Patel, M.D. and Thomas Pearce, M.D. PhD.
Department of Pathology, Division of Neuropathology
UPMC Presbyterian Hospital, Pittsburgh PA

Clinical History:
The patient is a woman in her mid-50s with history of a pituitary adenoma resected approximately two years prior, who now presents with an expanding lesion of the skull base involving Meckel's cave. A biopsy of the Meckel's cave lesion was received in consultation, together with the prior pituitary lesion. No other significant past medical history was contained in the medical records received at our institution.

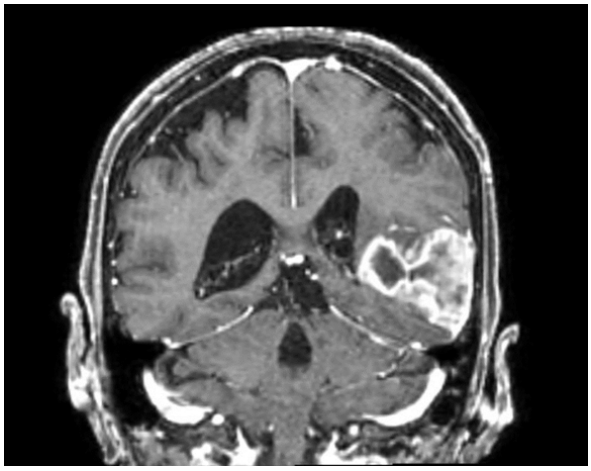
Material submitted:
1. H&E section of the Meckel's cave lesion biopsy.

Points for discussion:
1. Differential diagnosis and work-up of lesions with these histologic features.
2. Review the literature relevant to the diagnostic entity.

64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-2

Submitted By:
William Humphrey, M.D. and John C DeWitt, M.D., Ph.D.
Department of Pathology and Laboratory Medicine
University of Vermont Medical Center, Burlington, VT

Clinical History:
Eighty-two-year-old female who presented with acute neurocognitive decline. MRI revealed an intracranial mass show in the accompanying image.



Material Submitted:
1. MRI w/ contrast (T1W) images
2. H&E, IDH, ATRX, p53, CD20, PAX-5 IHC
3. One H&E slide

Points for Discussion:
1. Describe the pathophysiology and epidemiology of this entity.
2. Describe the clinical course, treatment, and prognosis for this entity.

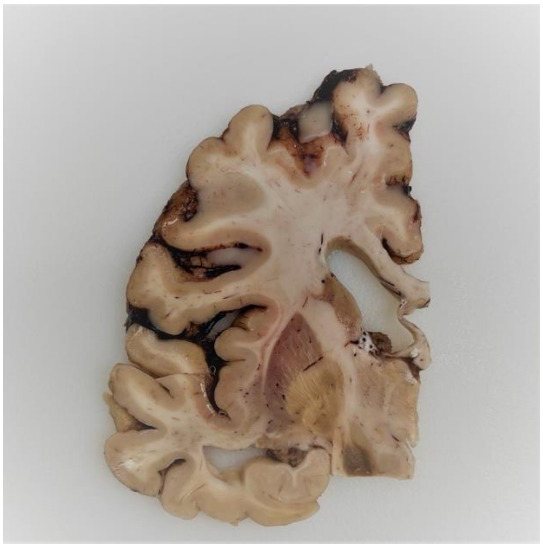
64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-3

Submitted By:
Anfisa Baiandurova, M.D., Randy Woltjer, M.D., Ph.D.
Department of Pathology
Oregon Health & Science University, Portland, OR

Clinical History:
18-year-old male who achieved developmental milestones during early infancy but then failed to develop normal walking skills by the end of the first year. This was followed by cognitive developmental delay, plateau in motor skills and subsequent progressive loss of cognitive and motor skills.

Brain MRI showed distinctive increased iron in the globus pallidus and substantia nigra and a distinctive hyperintense halo in the cerebral peduncles.

Autopsy is limited to the brain:
The brain showed mild cortical atrophy involving the frontal, parietal, and temporal lobes in addition to dark-brown discoloration of globus pallidus and substantia nigra, more prominent in the latter (fixed brain weight, 887 g).



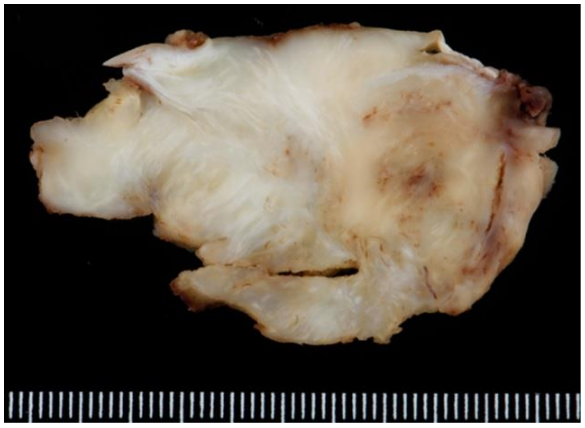
Material Submitted:
1. H&E stained slide of a representative midbrain with substantia nigra discoloration
2. Gross images of brain autopsy findings

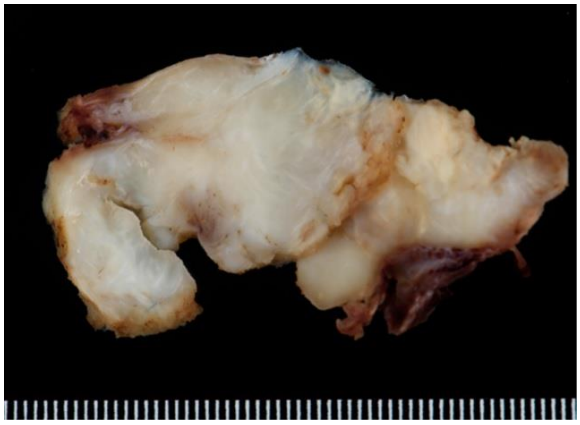
Points for Discussion:
1. What is the differential diagnosis for this type of lesion that involves the globus pallidus and substantia nigra.
2. What other stains would be helpful to establish a specific diagnosis of this disease.

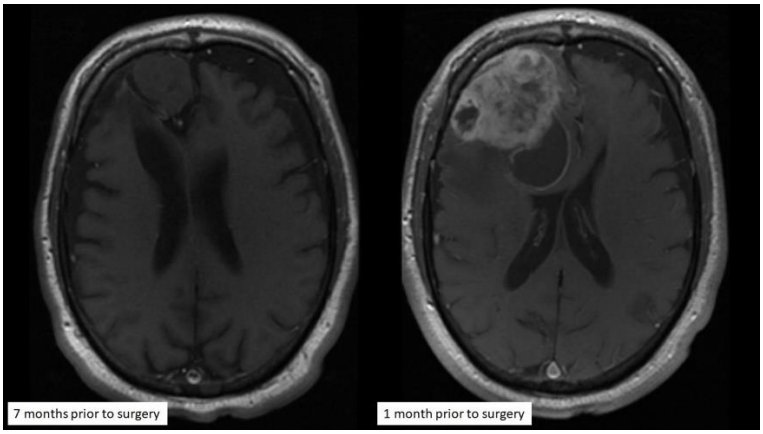
64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-4

Submitted By:
Gregory M. Chamberlin, MD and Thomas J. Cummings, MD
Department of Pathology
Duke University Medical Center, Durham, NC

Clinical History:
The patient is a 59-year-old man with a history of a right frontal grade 2 oligodendroglioma, status post resection 17 years prior at an outside hospital. 1p/19q-codeletion was reportedly present by FISH on the original resection specimen. The patient received no adjuvant chemotherapy or radiation therapy. He was followed with surveillance imaging. The lesion was radiographically stable until the most recent surveillance scan, at which time the lesion showed marked interval growth and new contrast enhancement. The patient remained asymptomatic.







Material Submitted:
1. Two H&E slides

Learning Objectives:
1. List differential diagnoses for this tumor.
2. Utilize ancillary testing and published literature to establish a definitive diagnosis for this tumor.

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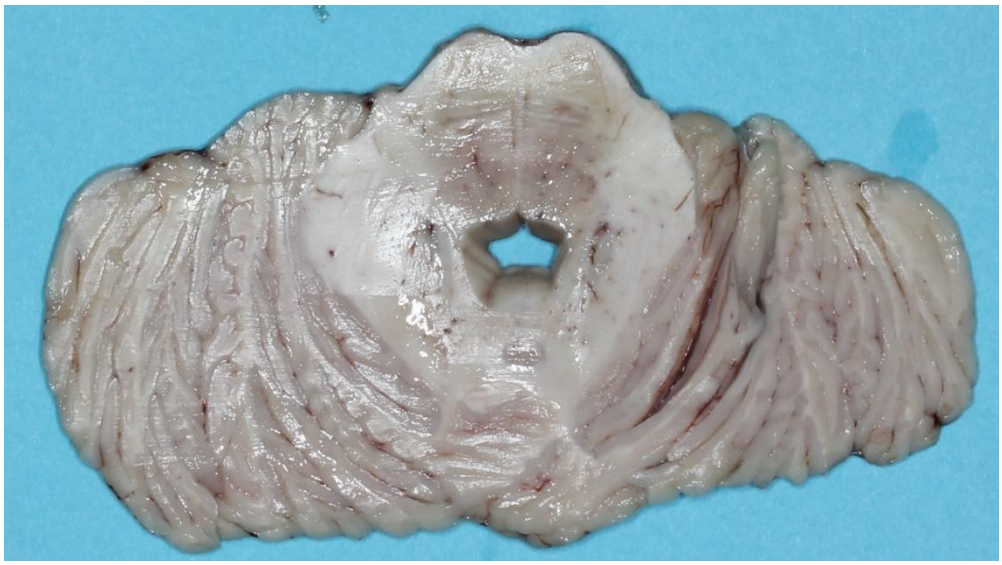
CASE 2023-5

Submitted By:
Dr. Avneesh Gupta, M.D., Dr. Rebecca Folkerth, M.D.
New York City Office of Chief Medical Examiner, New York, NY

Clinical History:
This 3 1/2-year-old girl had a history of Hirschsprung Disease, diagnosed soon after birth (born preterm at 26 gestational weeks). She had repeated enterocolitis alternating with chronic constipation, treated by her parents at home with over-the-counter enema preparations.
She had undergone a "pull-through" procedure as well as placement of an intraosseus line for treatment of dehydration (6 and 2 months prior to death, respectively). The latter procedure was complicated by osteomyelitis, detected and treated 2 weeks prior to death. Four days prior to death, the child had continued vomiting and poor fluid intake. Her parents administered saline enemas the night prior to death. After the parents found her lethargic, she was brought into hospital and died despite resuscitation efforts.



Autopsy Findings:
Hirschsprung Disease:

- Status post "pull-through" procedure (intact)
- Dilated large colon filled with liquid stool
- Full-length, full-thickness colitis

Material Submitted:

1. Gross image of mid-pons
2. H&E- and LFB/PAS-stained sections of pons

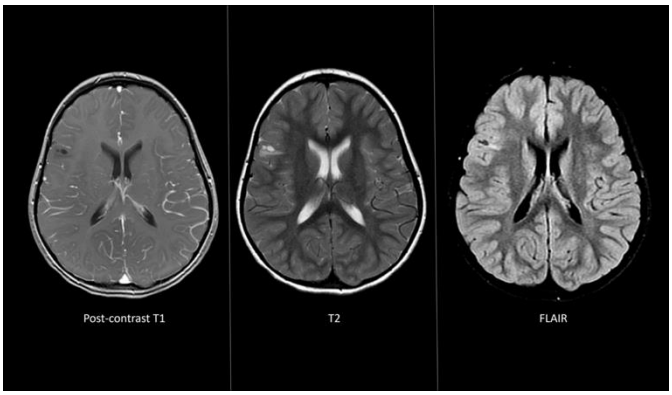
Points for Discussion:

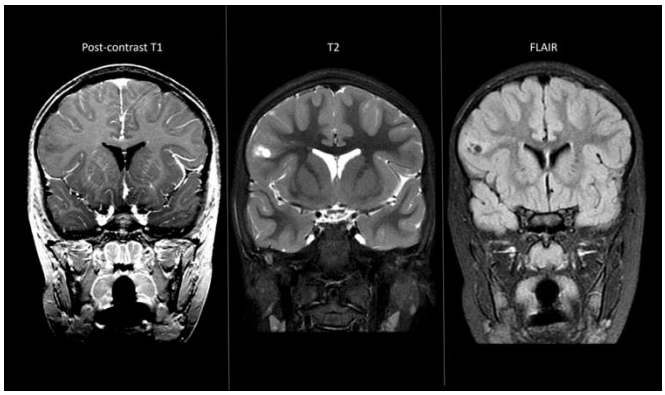
1. Diagnosis
2. Pathogenesis

64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-6

Submitted By:
Ekin Guney, M.D. and Arie Perry, M.D.
Department of Pathology
University of California, San Francisco, San Francisco, CA

Clinical History:
The patient is an 8-year-old girl with a history of autism, developmental delay, 15q11.2 deletion syndrome and immune thrombocytopenic purpura. She has no history of headaches, nausea, vomiting or change in vision. Brain MRI shows a T2 hyperintense, FLAIR hypointense and non-enhancing cystic lesion in right frontal lobe, which has increased in size. She underwent right frontal craniotomy for resection of the mass. On histopathologic evaluation, the perivascular spindled cells were negative for EMA, SSTR2A, PR, E-cadherin, SMA, and CD34.





Material Submitted:
1. One (1) H&E-stained section from the right frontal lobe mass specimen
2. One (1) axial brain MRI with post-contrast T1, T2 and FLAIR sequences
3. One (1) coronal brain MRI with post-contrast T1, T2 and FLAIR sequences

Points for Discussion:
1. Differential diagnosis.
2. Ancillary studies and molecular findings.

64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-7

Submitted By:
Rufei Lu, M.D., Ph.D. and Marta Margeta, M.D., Ph.D.
Department of Pathology
University of California, San Francisco, San Francisco, CA

Clinical History:
A 48-year-old man with a "Marfanoid" body habitus (tall, with long arms and pectus carinatum) and a thin sharp face presented with right heart failure and mixed hypoxic/hypercapnic respiratory failure several months following an asymptomatic COVID infection. Although the patient denied muscle weakness, he reported longstanding difficulties reaching things overhead and jumping. There was no family history of a neuromuscular disorder. Physical examination showed slightly weakened facial muscles, mild bilateral tongue weakness, bilateral scapular winging, high steppage gait, inability to heel walk, positive Trendelenburg sign, and reduced muscle bulk in legs, pectoralis, deltoid, triceps, and biceps muscles. The pulmonary function tests showed a restrictive pattern. The severity of hypercapnia raised the possibility that his respiratory failure had neuromuscular etiology, so the neurology and genetics teams were consulted. Electrodiagnostic testing provided evidence for a myopathic process without membrane irritability, affecting both the upper and lower extremities. CK levels were within normal limits. The patient was evaluated for Marfan syndrome when he was 14 years old, but the tests done at the time were unrevealing. Genetics recommended a muscle biopsy to guide the further genetic testing strategy, and a deltoid muscle biopsy was performed.

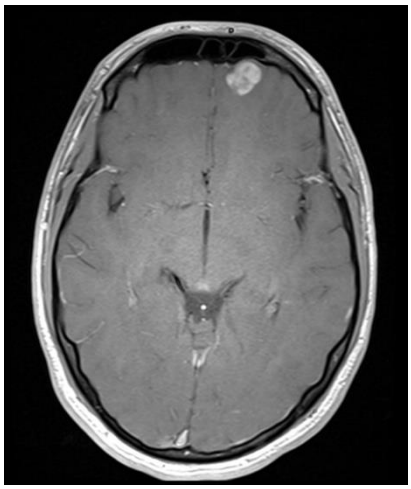
Material Submitted:
1. One (1) H&E-stained cryosection
2. One (1) modified Gomori trichrome-stained cryosection

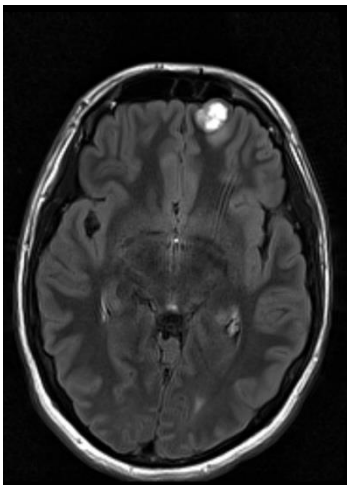
Points for Discussion:
1. Differential diagnosis.
2. Ancillary studies and molecular findings.

64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-8

Submitted By:
Sara Stone M.D., Ph.D., Amir Banihashemi M.D.
Department of Pathology and Laboratory Medicine
Hospital of the University of Pennsylvania, Philadelphia, PA

Clinical History:
A previously healthy 20 year-old male presented to the emergency department following syncopal episode. Upon arrival to the emergency department, the patient had a witnessed seizure. The patient reported recent forgetfulness and his friends noted periods of "zoning out." CT of the head revealed an area of hypodensity in the left frontal lobe with punctate peripheral calcifications and possible scalloping of the overlying calvarium. Subsequent MRI revealed a 16 mm circumscribed, cortically based intra-axial, heterogeneously enhancing mass lesion in the left anteroinferior frontal lobe. The patient underwent left frontal craniotomy for tumor resection.





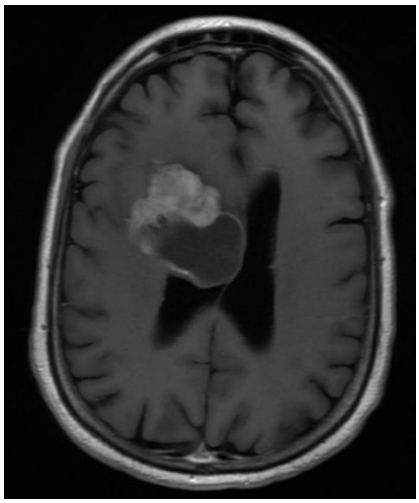
Material submitted:
1. H&E section of lesion
2. MRI T1 post-contrast
3. MRI T2 FLAIR

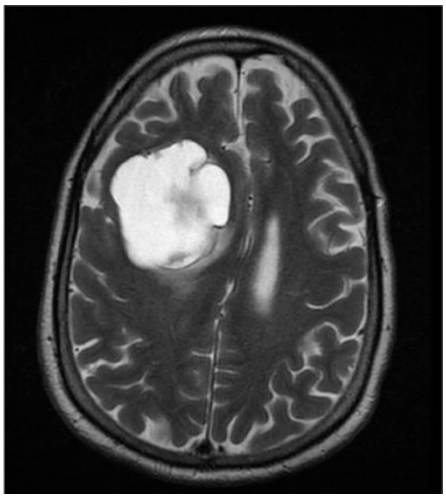
Points for Discussion:
1. Differential diagnosis
2. Ancillary studies and molecular findings

64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-9

Submitted By:
Janna Shold, D.O. and Nelli Lakis, M.D., MSc.
Department of Pathology and Laboratory Medicine
The University of Kansas Medical Center, Kansas City, KS

Clinical History:
62-year-old male who presented to ED after experiencing two syncopal episodes and a headache. His past medical history included Hemophilia A. His neurologic exam was within normal limits. MRI of the brain showed a large, partially cystic, calcified, and solid enhancing mass involving the right lateral callosal body and frontal white matter with a wide differential diagnosis including a low-grade glioma (such as pilocytic astrocytoma or oligodendroglioma), solitary cerebral metastasis or an atypical high-grade glioma. The patient underwent craniotomy and resection of the tumor.





Material Submitted:

1. H&E section of the right frontal mass

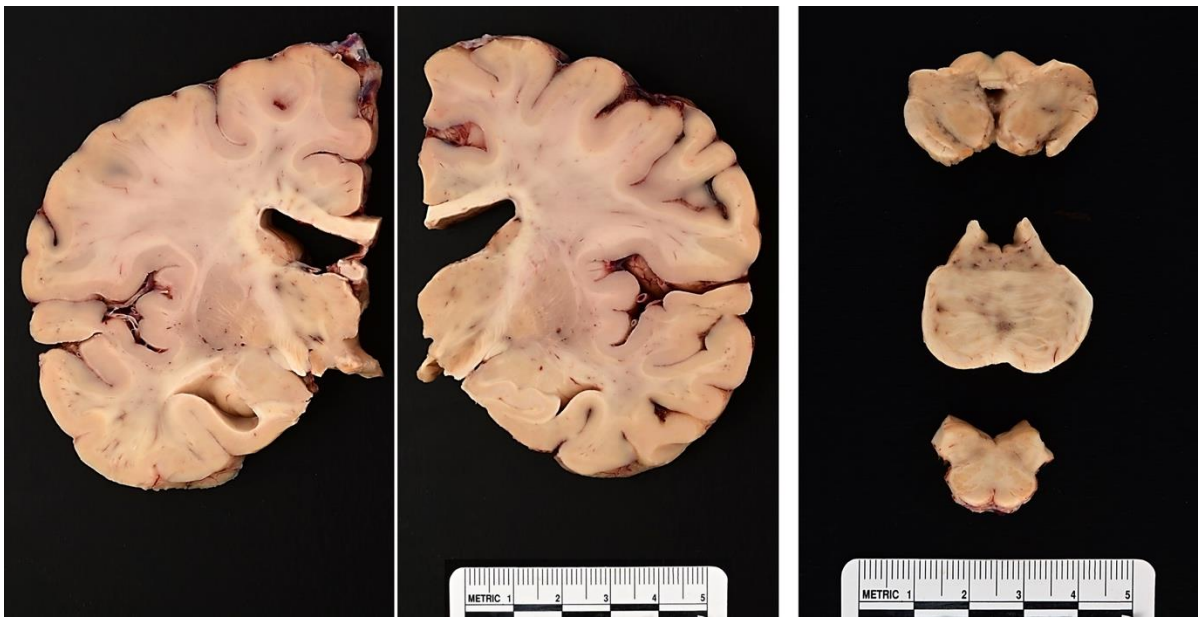
Points for Discussion:

1. Discuss the differential diagnosis
2. Compare the clinical and histopathological findings with the molecular findings

64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-10

Submitted By:
M. Adelita Vizcaino, MD[1], Divyanshu Dubey, MBBS [2], R. Ross Reichard, MD [1]
Departments of [1]Laboratory Medicine and Pathology and [2]Neurology, Mayo Clinic Rochester, MN

Clinical History:
A 76-year-old woman presented with gradually progressive symptoms for over 10 years. She debuted with facial tightening and throat pulsations. Later on, she developed dysphagia, dysarthria, ophthalmoplegia, obstructive sleep apnea and REM sleep behavior disturbance, followed by ataxia and choreiform movements. Copper, ceruloplasmin, erythrocyte sedimentation rate, TSH, and CPK levels were within normal limits. A myasthenia gravis panel and antibodies to acetylcholine and N-methyl-D-aspartate receptors and thyroid peroxidase resulted negative. Serial brain MRI and electromyography showed no significant abnormalities. She ultimately died of pneumonia.



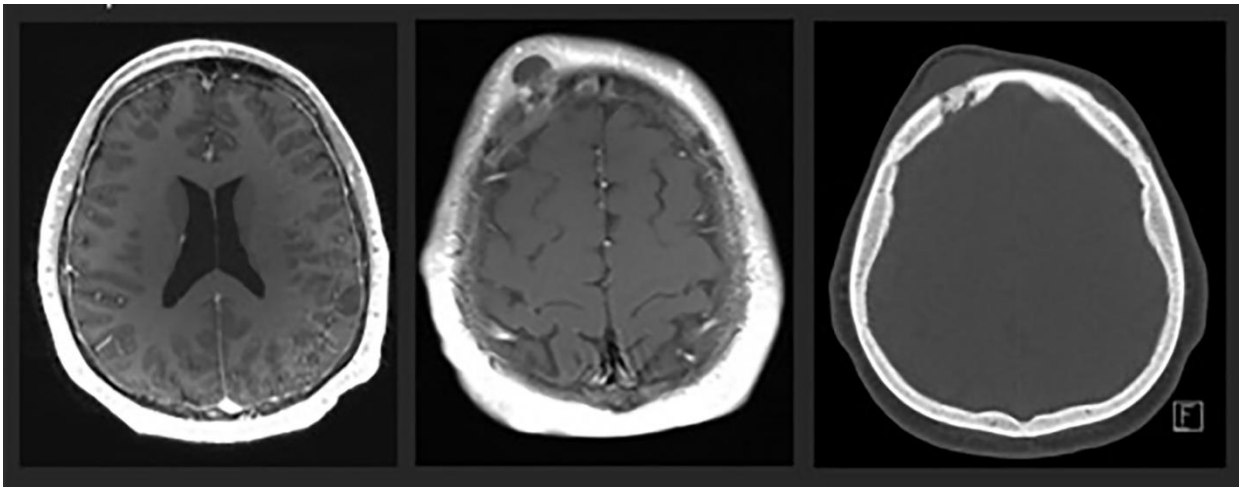
Material Submitted:
1. Virtual H&E slides
2. Macroscopic brain autopsy photographs

Points for Discussion:
1. Differential diagnosis
2. Proposed pathogenetic mechanisms

64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-11

Submitted By:
Cassie B. MacRae, M.D. and Isaac Solomon, M.D., Ph.D.
Department of Pathology
Brigham and Women's Hospital, Boston, MA

Clinical History:
A 25-year-old man in his normal state of health experienced a first lifetime seizure. He was playing video games with some friends when his roommate heard a noise and discovered him at the base of the stairs. MRI demonstrated a 1.6 cm mildly enhancing cystic intraparenchymal lesion in the peripheral left inferior parietal lobe. He was treated with antiepileptics and followed with serial imaging and planned for surgical resection. Five months later, the patient presented with a new scalp lesion (initially tender to touch without associated erythema or skin ulceration). Repeat brain imaging showed a 1.2 x 1.6 cm right frontal lesion with enhancement of the adjacent scalp, loss of the subjacent right frontal calvarial cortex, and thickening and enhancement of the underlying right frontal dura. His previously documented intracranial left parietal lobe lesion was unchanged/stable in appearance. He underwent surgical biopsy and resection of the right frontal scalp mass.



Material Submitted:
1. H&E section of right frontal scalp mass
2. MRI images of right frontal scalp lesion and left parietal lobe mass

Points for Discussion:
1. Discuss the differential diagnosis for these histological findings
2. List appropriate ancillary testing to confirm the diagnosis

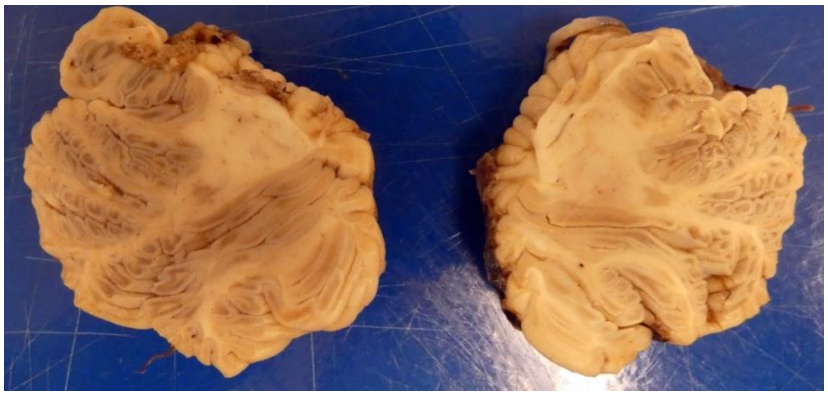
64th ANNUAL DIAGNOSTIC SLIDE SESSION 2023
CASE 2023-12

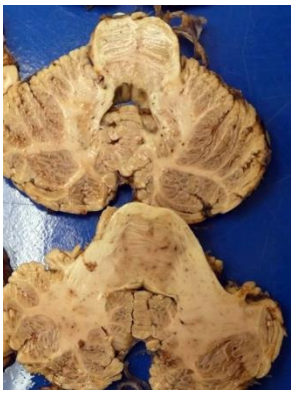
Submitted By:
Lena Young, D.O., MS and M. Beatriz Lopes, M.D., Ph.D.
Division of Neuropathology, Department of Pathology
University of Virginia, Charlottesville, VA

Clinical History:
The decedent was a 79-year-old male with history of prostate cancer and squamous cell carcinoma of the skin, admitted to the hospital for sepsis, acute kidney injury, rhabdomyolysis, confusion, fever, leukocytosis, hypothermia, and rash in the setting of a recent bite/sting by an unknown insect. He eventually developed a morbilliform rash covering the trunk and extremities. A lumbar puncture showed no elevated white blood cell count, with normal glucose and protein. With treatment there appeared to be improvement, however 2 days after admission he was dysarthric with left facial droop and was not stable enough for MRI evaluation. He became more acidotic, oliguric with increasing fevers, decreased mentation, and intubated on the third day, continued to worsen and died on day 4 following admission.

Autopsy Findings:
Postmortem examination was consistent with end-stage shock that appears to be most likely septic in nature. Histopathological analysis shows acute tubular necrosis of the kidney, diffuse ischemic enterocolitis (small intestine, large intestine, and rectum), and signs of coagulopathy with disseminated petechial hemorrhages, all findings consistent with shock. The skin was remarkable for diffuse lesions suggestive of a small vessel vasculitis or leukocytoclastic vasculitis with sweat duct necrosis. However, these findings seem nonspecific and most likely representing a vascular reaction pattern secondary to shock and end-stage coagulopathy.

The brain and dura weighed 1430 gm and were grossly normal with questionable subarachnoid hemorrhage over the right parietal cortex. Microscopic examination did not show signs of encephalitis or meningitis Additional findings include cerebral amyloid angiopathy, neuropathologic changes consistent with Alzheimer disease, low probability, (A1, B1, C1), as well as atherosclerotic cerebrovascular pathology. Testing of the postmortem blood and CSF for tickborne illnesses, sent to the CDC for analysis, resulted negative for Rickettsia, Ehrlichia, Powassan, Bourbon, and Heartland viruses.





Material Submitted:
1. Gross photos of the brain
2. H&E section of cerebellum

Points for Discussion:
1. Histopathologic features and differential diagnosis.
2. Diagnosis and clinical significance.