46th ANNUAL DIAGNOSTIC SLIDE SESSION 2005.

CASE 2005-1

Submitted by: Kathy L. Newell, MD, Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, Kansas 66160.

Clinical History: This 2½ year-old girl presented to the Emergency Department in partial complex status epilepticus with shaking of the right arm and leg. Initial CT and MRI scans of the brain were unremarkable. Laboratory studies, including assays for lactate, very long chain fatty acids, amino acids, ammonia, ceruloplasmin, viral serologies, and spinal fluid studies were unremarkable. Pyruvate was elevated (0.14 mM) with a normal lactate:pyruvate ratio. On day 6 of hospitalization, due to no improvement in controlling the seizures with conventional anticonvulsant therapy, she was placed in a pentobarbital coma, with the addition of Trileptal for complete control. Pentobarbital was discontinued on the 14th day of hospitalization, at which time she was observed to have occasional choreoathetoid movements and left leg weakness. MRI performed 10 days after the initial MRI study showed abnormal T2 and FLAIR hyperintensity involving bilateral caudate nuclei, globus pallidus, and putamen. MRI obtained 28 days after the initial study showed cystic changes in the globus pallidus bilaterally. The seizures were controlled and despite initial difficulties with eating and drinking, she received rehabilitation, improved, and was discharged to her home approximately 56 days after admission.

Three days prior to this presentation, the child was seen at another hospital for clenching of her body, urinary incontinence, and 5-10 minutes of unconsciousness. Lab studies and a head CT were reportedly unremarkable. She had a medical history of asthma requiring occasional albuterol and one past hospitalization for pneumonia. She lived with her mother and two healthy siblings. A brother died at 5 months of age with situs inversus and complex congenital heart defects. At age 7 months, a sister had died of sudden infant death syndrome as determined by autopsy examination.

Four days following discharge, the child was seen in the Emergency Department in cardiopulmonary arrest. Resuscitation efforts ceased after 25 minutes of asystole. A complete autopsy was performed.

Necropsy findings: No external abnormalities were identified. The peripheral organs appeared normal with the exception of petechiae involving the thymus and epicardial surface of the heart. The brain, weighing 1160 grams, and its coverings were normal externally. After formalin fixation, coronal sections revealed softening, cystic change, and dark tan discoloration involving both segments of globus pallidus bilaterally with apparent sparing of the medial medullary lamina. Softening and red-brown discoloration of bilateral putamen was also noted. Microscopic lesions in the left primary motor cortex and both substantia reticulata consisted of gliosis and macrophages with some neuronal loss. Mild to moderate neuropil vacuolation and scattered pyknotic neurons were present. Hippocampi were unremarkable. No abnormalities were revealed in the spinal cord. Sections from peripheral muscle and nerve, pituitary gland, and eye were histologically unremarkable. No mitochondrial ultrastructural abnormalities were detected in a sample from cerebellar cortex. Purkinje cells were well preserved and contained cytoplasmic crystalloid-like inclusions.

Toxicology studies were negative for alcohols, Trileptal, and other drugs tested. Enterovirus was cultured from stool.

Materials submitted: 2 x 2-inch projection slide, and an H&E section of the right or left pallidum.

Points for discussion: 1. Diagnosis; 2. Differential diagnosis

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CASE 2005-2

Submitted by: William W. Pendlebury, M.D.
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Clinical History:

The patient was a 25 year old, highly functioning college student who developed progressive cognitive and motor decline beginning in 2003. After a successful initial college career, he dropped out of school and, while traveling in Europe, was hit by a car. Although the extent of injuries was described as minor, his grandmother reported that "he wasn't the same after the accident". He began to manifest a progressive language impairment, gait disturbance, and social isolation. His living situation deteriorated such that he became homeless, and shortly thereafter he was admitted to the Neuropsychiatric Service at Maine Medical Center (MMC) in October 2004. An MRI of the brain with and without gadolinium demonstrated low signal involving the caudate nucleus, globus pallidus, and putamen bilaterally. High T2 signal also was noted to "surround" the basal ganglia, and to involve the thalami. A subsequent CT scan of the brain was interpreted as "consistent with iron deposition within the basal ganglia". The patient was discharged on medical treatment that included sertraline, carbidopa/levadopa, mirtazapine, and olanzapine. Because of a deteriorating neurologic condition and additional laboratory data, the patient was readmitted to MMC two months later and appropriate therapy was begun. Physical examination demonstrated no spontaneous language and choreiform movements of the extremities. Shortly after admission, the patient decompensated, developed an aspiration pneumonia, and required assisted ventilation. He died after his family made a decision to withdraw care.

Necropsy Findings:

The general autopsy showed hepatosplenomegaly with macronodular cirrhosis, focal acute pneumonia, and ascities. Gross and microscopic features of the brain will be presented at the slide session

Material submitted: One H&E section of the lesion.

Points for discussion: 1. Diagnosis
2. Prognosis

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CASE 2005-3

Submitted by: Kathryn McFadden, M.D. and Clayton Wiley, M.D., Ph.D.
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Clinical History:

The patient was a normally developing boy who noted hand tremors at 7.5 years of age, approximately 3 weeks after his last mumps, measles and rubella vaccine. One month later, he exhibited difficulty walking, leg pain and weakness. His gait became stiff legged with the right leg rotated outwards. He was found to have significant action and intention tremor, bilateral lower leg weakness (tibialis anterior), decreased deep tendon reflexes and pes planus. He also exhibited impaired speech articulation.

Despite continued neurological progression, extensive clinical evaluation over the next year demonstrated limited abnormalities. Nerve conduction studies showed slowing of motor and sensory conduction velocities. Electron myography showed giant motor unit potentials suggestive of previous denervation followed by reinnervation. Sural nerve biopsy showed mild axonal degeneration and regeneration suggesting neuroaxonal dystrophy. A skin biopsy was unremarkable. Laboratory values for copper, ceruloplasmin, creatine kinase, lactate, erythrocyte sedimentation rate, anti-nuclear antibody, Lyme serology, thyroid panel, lipoprotein electrophoresis, lysosomal enzymes and complete Charcot-Marie-Tooth Disease DNA panel were normal. Urine amino acids were normal. An EKG was normal. CSF showed 60 leukocytes (99% mononuclear), 0 RBC, protein 31, glucose 56 and lactic acid 1.0. Brain MRI showed mild enlargement of cerebellar sulci and vermian atrophy.

He became wheelchair bound by 9 years of age and was unable to produce speech or control secretions. His tremor became coarser and tongue fasciculations, extensor plantar reflexes and oculogyric crises were noted. Cognitive function remained intact and there was no discernible abnormality of sensation, vision or hearing. A trial of L-dopa produced no noticeable improvement of symptoms. Amantadine was initiated with marked albeit temporary improvement. At 13 years of age, he developed an intercurrent respiratory infection and died of respiratory failure.

Necropsy Findings:

Significant findings were generalized muscle atrophy and emaciation, bilateral pulmonary lobar consolidation and pericardial effusion. The fresh brain weighed 1425 grams. Examination of the fixed hemisected brain was unremarkable except for mild atrophy of the cerebellar hemisphere and vermis. The substantia nigra was not grossly pigmented. Mild atrophy of the ventral roots of the spinal cord was evident. Multiple cross sections of the spinal cord showed no other gross abnormalities

Material Submitted: 1 H&E stained slide of cerebral cortex and cerebellum
1 Unstained slide of cerebral cortex and cerebellum

Points for Discussion: 1) Diagnosis
2) Pathogenesis

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CASE 2005-4

Submitted by:

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Clinical History

A 2 month old female presented with right facial weakness (asymmetric crying). MRI demonstrated a large mass of posterior and middle fossa which was resected.

Material submitted
1 H and E of tumor
1 unstained slide

Points for discussion
Diagnosis

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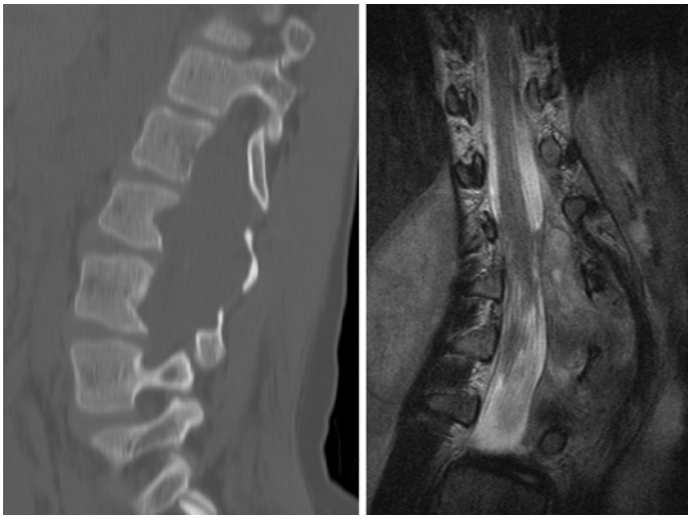
CASE 2005-5

Submitted by: Fausto Rodriguez[1], Robert J. Spinner[2], Caterina Giannini[1].
[1]Departments of Laboratory Medicine and Pathology, and [2]Neurosurgery Mayo Clinic, Rochester MN 55902.

Clinical and Surgical History: An 8-year-old girl was first seen at our institution in the summer of 2004 for evaluation of progressive scoliosis. Her mother and school nurse noted mild trunk asymmetry beginning at age 6 as well as progressive enuresis. Recently she developed prominent daytime urinary urgency and frontal headaches, progressively increasing in frequency and severity. Her past medical/surgical history was remarkable for prematurity with a birth weight of 1 pound and 13 ounces. She required an extended neonatal ICU stay, apparently without sequelae.
On physical examination her left leg length was 1 cm shorter than the right. She showed a 1.5 cm left thoracolumbar prominence on forward bending. The neurologic exam was negative. Imaging of the thoraco-lumbar spine demonstrated an extradural mass within the left side of the spinal canal involving T11 to L3. The mass extended through remodeled left neural foramina at multiple levels into adjacent psoas muscle. Spinal cord was not compressed.



CT MRI (T2)

Radiologically, the mass was thought to be to a nerve sheath tumor, most likely a plexiform neurofibroma. MRI of the head was normal.
Debulking of the tumor was undertaken in two separate stages with posterior and anterior approaches.

Material submitted: Representative H&E section of the resected tumor.
Points for discussion:

1. Diagnosis
2. Rationale for classification

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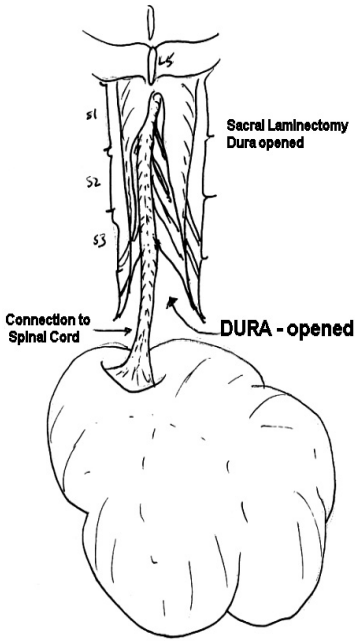
CASE 2005-6

Submitted by:

Edward S. Johnson[1], M.D., Keith E. Aronyk[2], M.D., and Gordon M. Lees[2], M.D.
Departments of Laboratory Medicine and Pathology[1] and Surgery[2], University of Alberta, Edmonton, Alberta, Canada T6G 2R7

Clinical History:

A one year old girl presented for investigation of an enlarging sacral mass noted since the age of two weeks and associated with the symptoms of chronic constipation and pain upon bowel movements. Although the neurological examination was normal, anal stenosis was found on rectal examination. Pertinent clinical laboratory studies included an alpha fetoprotein of 12 and 13 kU/L (normal <7) and beta HCG of <5 U/L (normal <5). A MRI scan disclosed a malformed sacrum and coccyx associated with a 6.5 x 4 x 2 cm, multicystic sacral mass that anteriorally displaced the rectum, bladder and uterus. These findings were confirmed at surgery, which revealed the mass to be in continuity with the dura of the spinal canal and attached to the spinal cord by a tethered filum, as illustrated in the diagram.



Pathologic examination of the 28.4 gm pseudoencapsulated mass showed an opened 4 x 2.5 cm glio-ependymal lined cyst that had been connected to the filum terminale and extended to the opposite polar margin of an asymmetrically placed solid component. Included among the heterologous tissue elements of this component were rare niduses of cartilage and occasional cysts lined with squamous epithelium, simple cuboidal to columnar epithelium, or ependyma.

Material Submitted:

- Transparency of rostral surface of the mass with opened cystic attachment to the filum terminale
- H&E stained section of solid component of mass

Points for Discussion:

1. Diagnosis
2. Pathogenesis of the mass and sacral defect

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CASE 2005-7

Submitted by:
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Clinical history:
Forty-three year-old male who has lived in Michigan for the past eight years, presented with a two year history of myalgias and mild weakness. The myalgias started in the lower extremities, and subsequently worsened to also involve the upper extremities. CPKs were consistently elevated in the 1000-2000 mU/mL range (normal 40-230). No myoglobinurea was detected. Rheumatology consult was obtained. Laboratory studies including metabolic and rheumatologic markers were negative. A muscle biopsy was performed to evaluate the possibility of an inflammatory myopathy.

Material submitted: 1 split kodachrome of hematoxylin and eosin stained frozen section and paraffin block section

Points for discussion:
Diagnosis:
Differential:

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Case 2005-8

Submitted by: Rebecca D. Folkerth, MD, and Jason F. Schmidt, MD, Brigham and Women's Hospital, Dept. of Pathology (Neuropathology), 75 Francis Street, Boston MA 02115, rfolkerth@partners.org

Clinical History:

The patient is a 66-year-old man who presented with a "large palpable mass" of the right thigh, which had been present for approximately one year, without apparent enlargement during that time. When he first noticed it, he thought he may have "pulled a muscle" while exercising. Since it did not seem to be resolving, MR was performed, showing a mildly infiltrative, increased T2 signal and enhancement in the rectus femoris muscle, extending approximately 6cm craniocaudal. This was interpreted as a possible muscle strain or contusion. A fine needle aspirate revealed "atypical cells possibly consistent with inflammation".

At operation, the surgeon found a 3.5cm "ball" of distinctly abnormal tissue within the muscle belly, but surrounded by a loose areolar plane. The abnormal tissue was excised.

Material submitted: 1 H&E slide of formalin-fixed, paraffin embedded skeletal muscle

Points for discussion:

1. Differential diagnosis
2. Pathogenesis
3. Prognosis

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Case 2005-9

Submitted by: Stefanie Freeman M.D., and Anat Stemmer-Rachamimov M.D.
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Clinical History:
The patient is a 50 year-old male, native of Guatemala who presented with localized left thigh tightness, swelling, and pain in September of 2004. He had associated weakness and numbness with limited range of motion in the left leg, and walked with the aid of a cane or walker.

His past medical history included carcinoma of the gastrointestinal tract diagnosed in December of 2003 and treated with chemotherapy (Taxotere), and acute renal failure with bilateral hydronephrosis. He had been in good health prior to October of 2003.

MRI of the left thigh revealed increased T2 signal involving the muscle of the adductor and anterior compartment, the pectineus, sartorius, visualized portion of the iliopsoas, and semitendinous muscles. There was enhancement in the adductor compartment and in the obturator externus. The underlying bones demonstrated normal signal characteristics, with no evidence of cortical destruction. The differential diagnosis included polymyositis, myonecrosis, or an atypical denervation process. The patient was referred for a muscle biopsy.

Material Submitted: 3 images of left vastus medialis muscle biopsy. 1 low power H&E, 1 intermediate power H&E and 1 high power H&E

Points for Discussion:
1. Differential Diagnosis
2. Your diagnosis

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Case 2005 #10

Submitted by: Cindy Welsh, M.D.
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Clinical History:

The patient is a 25 year-old right handed female with one month history of headache, double vision, and slowness of thought and speech. She had also reportedly lost her appetite and significant weight. She had had a motor vehicle accident two months prior to this admission. She was seen in an outside ER, where on exam, she had difficulty finding words, but did answer questions appropriately. Her visual fields were intact to confrontation. Cranial nerve testing, peripheral motor and sensory exams, and examination of her reflexes showed no deficits. Head CT at the outside institution showed a bi-frontal intraparenchymal mass which heterogeneously enhanced. She was transferred to Medical University of SC for definitive care, where a subtotal resection was performed. Three days after surgery she developed lower extremity weakness with anterior cerebral artery distribution hypodensities on CT; the weakness improved slightly with a hypertensive hypervolemic hemodilution protocol. A percutaneous gastrostomy tube was required for dysphagia and she was unable to initiate speech. She spent several weeks in the transitional care unit postoperatively, during which time radiation therapy was begun, and was eventually discharged from there, intact neurologically. On the resected material received in pathology, immunohistochemical stains and ultrastructural evaluation were performed.

Material submitted: One H&E stained section, one unstained section

Points for discussion:

1. Differential diagnosis