

**Illinois Registry of Anatomic Pathology
Cases from Children's Memorial Hospital
September 21, 2009**

Case 1

Pathologist: Robert E. Ruiz, M.D., Ph.D.

CLINICAL HISTORY: The patient is a 10 day old male, delivered spontaneously at an outside hospital at 38 weeks of gestation to a 39 year old G2P2 mother. By report, prenatal ultrasound did not detect any abnormalities. He was found to have yellow nasal discharge on day of life (DOL) 1, and experienced occasional episodes of desaturation and retractions. Otolaryngology consultation revealed narrowing of the left nasal passage.

An MRI was performed and revealed an expansile heterogeneous mass in the left nasal cavity, approximately 4 cm in greatest dimension, extending through the cribriform plate into the left anterior cranial fossa, with mass effect upon the left inferior frontal lobe, left orbit, maxillary alveolar ridge, and right nasal cavity.

The patient was transferred to Children's Memorial on DOL 10. Physical exam at the time of admission showed occlusion of the left nasal passage by a mass, with rightward deviation of the nasal septum. The patient underwent nasal endoscopy with biopsy, and subsequently had two separate resections performed by Otolaryngology and Neurosurgery.

GROSS DESCRIPTION: Multiple soft tissue and bone fragments weighing 11 grams and measuring 4.5 x 2.5 x 1.5 cm in aggregate. The largest soft tissue fragment measures 4 x 1.5 x 1.5 cm. A significant portion of the largest is covered by a smooth tan capsule.

MICROSCOPIC DESCRIPTION:

Variably cellular lesion, directly underlying respiratory and squamous epithelium in some sections, with a range of morphologies, including:

- variably cellular stroma of spindle cells in a vaguely fascicular to storiform arrangement
- paucicellular myxoid areas with thin spindle cells in a haphazard arrangements
- irregular lobules of cartilage, some sharply demarcated from the stroma, others merging with it
- aneurysmal bone cyst-like spaces without an endothelial or epithelial lining
- bands of hyalinized cartilage and perivascular hyalinization
- areas of reactive new bone formation within the spindle cell stroma

DIFFERENTIAL DIAGNOSIS:

Congenital sinonasal masses:

- teratoma
- epidermoid or dermoid cyst

Case 1 (continued)

- "nasal glioma" (glial heterotopia)
- hemangioma
- rhabdomyosarcoma

DIAGNOSIS: Nasal Chondromesenchymal Hamartoma (NCMH)

REFERENCES:

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Case 2

Presenter: Natasha Berg, M.D.

Pathologist: Maria Proytcheva, M.D.

CLINICAL HISTORY: The patient is a 13-year-old male who presented with a three week history of an asymptomatic mass in his left supraclavicular area. Chest CT scan showed a 4.2 x 4 cm lobulated lymph node mass in the left supraclavicular region extending to the left upper axilla. The lymph nodes were mostly discrete and homogeneously dense with the largest measuring 2.5 x 1.5 cm causing mild compression at the junction of the left internal jugular with the subclavian vein. There was a prominent hilar adenopathy (right<left) as well as reticulonodular appearance of the lungs, and splenomegaly without focal lesions was also present. The patient denies fever or other systemic symptoms including weight loss and night sweats. A supraclavicular lymph node biopsy was performed and multiple nodes were found, the largest measuring 0.8 x 1 cm.

Case 2 (continued)

KEY FEATURES: The lymph node architecture is preserved and shows moderate follicular hyperplasia, paracortical expansion due to proliferation of numerous immunoblasts, small and medium size lymphocytes, and patchy aggregates of monocytoïd cells. Occasional large cells with round lobated nuclei and prominent intranuclear and less prominent cytoplasmic inclusions are present. These large cells are associated with the monocytoïd cells. Immunohistochemical stain with anti-CMV antibodies is positive and diagnostic.

DIAGNOSIS: Cytomegalovirus Lymphadenitis

DIFFERENTIAL DIAGNOSIS:

- **Herpesvirus lymphadenitides** such as:
 - a. **EBV lymphadenitis** (infection mononucleosis) – marked immunoblastic proliferation and Reed-Sternberg like cells, EBV is positive
 - b. **HSV lymphadenitis** – presents of extensive necrosis and karyorrhectic debris and large cells with characteristic ground glass nuclei
- **Non-Hodgkin lymphoma** such as diffuse large cell lymphoma – effaced LN architecture and sheets of immunoblasts or other obviously malignant cells
- **Hodgkin lymphoma** –Reed-Sternberg cells on the background of small lymphocytes and other inflammatory cells, lack of immunoblasts
- **Postvaccinal, measles, or drug induced lymphadenitis** – clinical history usually present.
- **Cat scratch disease**
 - a. early form – follicular hyperplasia and granulomata and necrosis containing numerous neutrophils surrounded by palisading histiocytes,
 - b. later - extensive necrosis.

SPECIAL STUDIES: Immunohistochemical stain with anti-CMV antibodies – positive. In situ hybridization with EBV encoded RNA – negative. CD20 and PAX5 – B lymphocytes in the follicles, monocytoïd cells, and a small number of interfollicular immunoblasts – positive. CD3 – most of the interfollicular T small lymphocytes and immunoblasts.

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1. Ioachim, H. L. M. L. J. Ioachim's lymph node pathology: Philadelphia, Wolters Kluwer Health/Lippincott Williams & Wilkins, 2009: 83-86.
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Case 3

Presenter: Elaine Cham, M.D.

Pathologist: Veena Rajaram, M.D.

CLINICAL HISTORY: Six week old girl with a garment type congenital nevus involving the buttocks and lower extremities with a 6.5 cm ulcerated nodule on her posterior trunk. Following treatment, the ulcer healed but the nodule increased in size. The patient underwent resection of the mass.

GROSS DESCRIPTION: The specimen consisted of a 12.2 x 3.9 cm skin ellipse with a pink to red hypopigmented, lobulated myxoid nodule measuring 5.5 x 4.6 x 2.0 cm. There were multiple satellite nodules ranging from 0.2-2.5 cm.

MICROSCOPIC DESCRIPTION: Sections demonstrate a large cellular nodule with a myxoid and heterogeneous morphology arising in a congenital nevus. The large nodule showed a variety of patterns including: 1) poorly differentiated small round blue cells; 2) rhabdomyoblasts; 3) cartilage; and 4) spindle cells. The satellite nodules demonstrated proliferative nodules without evidence of melanoma.

DIAGNOSIS: Embryonal Rhabdomyosarcoma arising in a Giant Congenital Nevus

IMPORTANT POINT: Giant congenital nevi are rare maldevelopmental lesions of the neural crest. The most common malignant neoplasm that can arise in a giant congenital nevus is melanoma. However, since neural crest cells are pluripotent cells that can differentiate along mesenchymal lines (i.e. skeletal muscle, bone, fat, and cartilage), into so-called ectomesenchyme, a variety of neoplastic patterns can arise in giant congenital nevi, including rhabdomyosarcoma. It is thought that the prognosis and management of lesions arising in giant congenital nevi should depend on the malignant component(s) present.

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Case 3 (continued)

5. Cohen MC, Kaschula ROC, Sinclair-Smith C, Emms M, Drut R. Pluripotential melanoblastoma, a unifying concept on malignancies arising in congenital melanocytic nevi: Report of two cases. *Ped Path Lab Med.* 16:801-812, 1996
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Case 4

Pathologist: Hector Melin-Aldana, M.D.

CLINICAL HISTORY: Eighteen month-old boy with progressive hepatomegaly and physical signs of portal hypertension. He had progressive liver synthetic dysfunction and poor growth. CT scan of the head, EMG and echocardiogram were normal. A liver biopsy was obtained, and a liver transplant was performed shortly afterwards.

GROSS DESCRIPTION: An 1170 gram liver was received, with no significant changes on the external aspect. Cut surface was beefy red with no obvious fibrosis or nodularity.

MICROSCOPIC DESCRIPTION: A sample from the native liver showed prominent lobular disarray, predominantly due to fibrosis, which was portal and pericellular. There were many portal-to-portal bridges as well as nodules, but not following a homogeneous pattern of cirrhosis. Mild lymphocytic inflammation, non-specific, was present in areas of fibrosis. Hepatocytes were enlarged and contained well circumscribed cytoplasmic inclusions of pale eosinophilic, finely granular, “fluffy” material. This material was positive with PAS stain, and also positive with PAS-diastase stain.

ELECTRON MICROSCOPY: The cytoplasmic inclusions consisted of glycogen, present in two forms: fibrillar and in rosettes, the former being more abundant.

DIAGNOSIS: Glycogen Storage Disease, Type IV

DIFFERENTIAL DIAGNOSIS: The cytoplasmic inclusions resemble those in Lafora's disease, but this disease shows a much different clinical history, with significant neurological symptoms.

IMPORTANT POINT: This rare disease has very characteristic light and electron microscopic features in the liver. It is important to remember that this is indeed a disorder of glycogen metabolism, despite a histologic appearance which is much different than the rest of the glycogen storage diseases, including positivity with PAS stain after diastase digestion. The definitive diagnostic test is measurement of the deficient enzyme (glycogen branching enzyme) in liver, white blood cells, cultured fibroblasts or amniotic cells.

Case 4 (continued)

REFERENCES:

1. Portmann BC, et al. Genetic and metabolic liver disease, in MacSween's Pathology of the Liver, 5th. Edition, 2007. Churchill Livingstone Elsevier, Ed. p. 205.
2. Moses SW, Parvari R. The variable presentations of glycogen storage disease type IV: A review of clinical, enzymatic and molecular studies. Curr Mol Med 2002; 177-88.

Case 5

Pathologist: Pauline Chou, M.D.

CLINICAL HISTORY: The patient is a 17 yr 8 mo old female who presents with history of abdominal pain and anemia. The pain was described as aching and stinging, had started a few months back and is located in the midline from the epigastrium to the periumbilical region. She has lost approximately 12-15 pounds since the onset of symptoms. The pain is particularly worsened by acidic foods such as citrus. She has occasional vomiting in the morning, before eating. There is no visible blood but it has been positive for occult blood on testing in the past. She has intermittent fevers, up to 102 degrees F.

Prior to the onset of abdominal pain, she was diagnosed with anemia (went to donate blood, noticed to be anemic). She was placed on iron therapy, without improvement. After the onset of abdominal pain, she was referred to a gastroenterologist. She had an upper and lower endoscopy, which failed to show the etiology of her bleeding. She was diagnosed with gastritis and an extramucosal mass in her fundus. Her colonoscopy, including terminal ileal biopsies, was normal. She was not placed on any medication after this procedure.

In May she was referred to a CMH hematologist due to iron resistant anemia. She has had an extensive laboratory evaluation and bone marrow biopsy which failed to show the etiology of her anemia, but did confirm iron deficiency as well as hypoalbuminemia and reactive thrombocytosis. Due to concerns of IBD, she underwent an upper GI series with small bowel follow-through which was suboptimal due to the patient's inability to tolerate an adequate amount of barium. In addition to the above, the patient had an abdominal CT in April, which was normal apart from a cystic lesion in right adnexal region.

DIAGNOSIS: Osteoclast-Rich Clear Cell Sarcoma-Like Tumor of the Gastrointestinal Tract

Case 5 (continued)

DIFFERENTIAL DIAGNOSIS:

1. GIST (Gastrointestinal stromal tumor)
2. Leiomyosarcoma
3. Melanoma with clear cell features
4. Epithelioid malignant peripheral nerve sheath tumor

KEY MORPHOLOGIC FEATURES:

Gross: Tumor centered in the bowel wall extends to the overlying mucosa and through muscularis propria into mesenteric soft tissue.

Microscopic: Cellular neoplasm growing in sheets or nests, pseudoalveolar pattern with monomorphic intermediate to large cells, round to oval nuclei and small chromocenters. The cytoplasm is abundant and clear and accompanied by osteoclast-like giant cells.

SPECIAL STUDIES:

Immunohistochemical stains: Positive for S-100, CD57 and weakly bcl-2, and negative for CD117 (C-kit), HMB45, Melan A, SMA, desmin and CD34. Giant cells positive for CD68.

FISH analysis: t(12;22)(q13;q12) (EWS-ATF1) fusion transcript

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5. Tamenilli L., et al. Primary clear cell sarcoma of the ileum. *Virchows Arch* 447(4):772-7, 2005
6. Joo M., et al. Primary gastrointestinal clear cell sarcoma: report of 2 cases, one associated with IgG4-related sclerosing disease. *Ann Diagn Pathol* 13(1):30-5, 2009
7. Efkers TO et al. Clear cell sarcoma of tendons and aponeuroses in the duodenum. *Histopathol* 22:255-9, 1993.

Case 6:

Pathologist: Larry Jennings, M.D., Ph.D.

CLINICAL HISTORY: 22 month-old male presented with a right frontotemporal mass. Patient's mother had noted the lesion had been increasing in size over the preceding 6 weeks. Swelling was thought to be secondary to possible trauma. CT of head showed a "well-circumscribed, high density superficial right frontotemporal mass. The high attenuation and fluid levels are most suggestive of an evolving hematoma."

GROSS DESCRIPTION: Excisional biopsy was performed. The mass consisted of one firm brown-tan fragment measuring 5.5 x 5.5 x 2.3 cm and weighing 36 g.

MICROSCOPIC DESCRIPTION: Sheets of monomorphous cells with perivascular rosettes, frequent mitoses (14/10 hpf) and scattered cells with dense eosinophilic cytoplasm. Most cells are positive for myogenin and scattered cells also are positive for desmin.

DIAGNOSIS: Alveolar Rhabdomyosarcoma, Solid Variant

DIFFERENTIAL DIAGNOSIS:

Embryonal Rhabdomyosarcoma

IMPORTANT CLUES: Clinically this presented like ERMS but histologically like ARMS, solid variant. Molecular studies showed this to be *PAX7-FOXO1* positive, confirming the diagnosis¹⁻⁵.

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