IRAP, September 26, 2011 Case #1 Maria Proytcheva, MD/ Presenter: Bryan Teruya, MD

CASE #1: Abnormal lymph node in a child with Mycosis fungoides

HISTORY: The patient is an 11-year-old female who at age 3 years developed rash in her groin initially thought to be a severe diaper rash. She was referred to dermatology where the diagnosis of cutaneous T-cell lymphoma was made. Since then, the patient was treated with topical therapy including steroids and mechlorethamine, and PUVA. Her rash consisted of nodules and papules on her palms and soles, thickening and scaling of her wrists and ankles, and a large (>8-10cm) violaceous patch on her right hip. The rash was always worst in the colder months. Throughout the course of her treatment, the patient had had intermittent self resolving lymphadenopathy mostly of her axilla and occasionally in her groin. Two-three weeks prior to her referral to Children's Memorial Hospital, the patient noted a larger node in her right groin that had persisted and was mildly tender. Lymph node biopsy was performed to rule out lymphoma.

HISTOLOGY: Markedly expanded paracortex by a proliferation of mostly CD3+ small T-lymphocytes without atypia, along with numerous histiocytes and Langerhans cells (CD1a+). Flow cytometry shows unremarkable T-cell population with no loss of a pan-T-cell marker. CD4+ T-cells predominate, however the CD4:CD8 ratio = ~4:1.

MOLECULAR GENETIC STUDIES: T-cell gene rearrangement by PCR - negative

DIFFERENTIAL DIAGNOSIS:

- Lymph node with involvement vs. without involvement by cutaneous T cell lymphoma
- Dermatopathic lymphadenopathy
- Infection with paracortical expansion
- Langerhans cell histiocytosis in lymph node

DIAGNOSIS: Dermatopathic lymphadenopathy with no atypical lymphocytes (LN0) in a child with a clinical history of mycosis fungoides

This case exemplifies the importance of the histologic evaluation of lymph nodes in patients with mycosis fungoides and the discussion is focused on the revised recommendation of the International Society for Cutaneous Lymphomas for evaluation of lymph nodes in such patients.

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CMH IRAP September 2011
Case #2 Bevan Tandon, MD; Pauline Chou, MD

Children's Memorial Hospital
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CLINICAL HISTORY:
6 year old Caucasian male with chief presenting symptom of shortness of breath, found on imaging to have very large, right sided, solid intrathoracic tumor, 16.2 x 15 x 13.5 cm. Pt. underwent needle core biopsy followed by subtotal pneumonectomy with adjuvant radiotherapy. Currently, the patient is on week 37 of IRS study-stage IV rhabdomyosarcoma chemotherapy protocol with no evidence of tumor.

MACROSCOPIC:
Grossly, tumor measured 10.2 x 4.7 x 2.6 cm, exhibited exclusively solid growth with flesh like consistency, and showed tan white, lobulated cut surface with areas of myxoid degeneration.

MICROSCOPIC:
- Initial core biopsy showed primitive appearing spindle cell sarcoma cells in fascicular arrangement with alternating areas of hyper- and hypocellularity.
- Final resection specimen showed biphasic tumor differentiation with foci of malignant embryonic cartilage associated with peripheral areas of spindle cells similar to those identified in the initial core biopsy. Large areas of necrosis and fibrosis consistent with post-chemotherapeutic effect were seen.

DIAGNOSES:
- *Initial Core Biopsy:*
SARCOMA MOST CONSISTENT WITH EMBRYONAL RHABDOMYOSARCOMA, SPINDLE CELL TYPE.

- *Final post neoadjuvant chemotherapy resection specimen:*
SPINDLE CELL LESION WITH EXTENSIVE FIBROSIS, CALCIFICATION, AND CHONDROID DIFFERENTIATION, MOST CONSISTENT WITH POST-TREATMENT PLEUROPULMONARY BLASTOMA

TAKE HOME POINTS:
- Spindle cell tumors are rare in children and primary lung tumors are equally uncommon.
- Consider PPB in differential diagnosis, whether cystic or solid variant, especially when the results of immunostaining do not clearly fit well established patterns.
- Whereas adult pulmonary blastoma shows malignant epithelial and mesenchymal components, in pediatric pleuropulmonary blastoma only the mesenchymal component is malignant
- Type 1 PPB is cystic and shows benign epithelium overlying malignant cambium mesenchymal cells.
- Type 3 PPB is solid and shows malignant embryonic chondroid areas in association with malignant mesenchymal cell areas
- Many sarcomas may arise from the PPB malignant mesenchymal tumor cell component; our case exhibited embryonal spindle cell rhabdomyosarcomatous differentiation.
- ppbregistry.org

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CASE 3

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Hector Melin-Aldana

CLINICAL HISTORY: Male infant born at 37 weeks gestation via spontaneous vaginal delivery to a 20 year-old mother (G1P0) who had adequate prenatal care. Birth weight was 1,880 grams. Mother received treatment for urinary tract infection in her third trimester, and was admitted in labor, with rupture of membranes 5 hours prior to delivery. After birth, there were variable decelerations in fetal heart rate, thick meconium, minimal respiratory effort and floppy tone. Apgar scores were 4 at 1 minute and 8 at 5 minutes. He developed upper gastrointestinal bleeding (bright red blood from the nasogastric tube), and acute renal failure. Thrombocytopenia, prolonged coagulation times and hyperbilirubinemia were detected. Blood cultures and TORCH titers were negative. He was moderately jaundiced and had generalized severe edema. His health continued deteriorating and he expired on day 12 of life. An autopsy was performed.

MACROSCOPIC: The liver weighted 30 grams (expected 200 grams). The external surface showed a granular brown surface. Cut surface showed a dark brown to green surface with no well-defined nodules, areas of hemorrhage or necrosis.

MICROSCOPIC: Sections from the liver showed diffuse parenchymal collapse, with diffuse proliferation of reactive ductular structures. There were a small number of remaining hepatocytes, which showed severe ballooning, giant cell transformation, prominent pericellular fibrosis and variable cytoplasmic iron deposition. No regenerative nodules.

DIAGNOSIS: **NEONATAL HEMOCHROMATOSIS/GESTATIONAL ALLOIMMUNE LIVER DISEASE.**

DIFFERENTIAL DIAGNOSIS: Ischemic injury, viral infection (HSV, echovirus) or other metabolic diseases.

IMPORTANT POINT: The etiology of at least some cases of neonatal hemochromatosis is a maternal complement-mediated alloimmune response against the fetal liver. Iron deposition in the liver and other organs is secondary. The diagnosis is made by demonstrating extra-hepatic iron deposition, particularly in the pancreas, thyroid, thymus, heart or adrenal glands. It is extremely important to suspect this disease in all cases of neonatal liver failure with severe hepatocellular damage, because it has a high rate of recurrence and can be prevented by administration of intravenous immunoglobulin to the mother during pregnancy.

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Case# 4. Presenter: Agatha Bogard, M.D.

CLINICAL HISTORY: 17 year old girl with no significant past medical history, presented with an isolated seizure. Imaging demonstrated a non-enhancing signal abnormality in the left inferior frontal cortex with focal calcification, suggestive of dysplastic parenchyma versus a neoplasm. A gross total resection was performed.

MACROSCOPIC: 8.4 gm portion of frontal cortex, 5.0cm in greatest dimension was received. Cut surface demonstrates dense cortical tissue with loss of grey-white matter demarcation.

MICROSCOPIC: Sections demonstrate a hyalinized vascular proliferation with intervening disorganized white matter and interspersed neurons, as well as areas of psammomatous calcification. EMA is focally positive. Intervening glial tissue is GFAP positive. The lesion is Ki-67 negative, with occasional scattered positive lymphocytes.

DIAGNOSIS: Meningioangiomatosis

KEY POINTS: This is a rare entity, which may be confused with an infiltrating meningioma. It most commonly presents sporadically in younger patients, with a history of new onset seizures or headaches. It is also found in NF2 patients, as an incidental finding or at autopsy, and in these cases it is asymptomatic. Rare cases of meningioangiomatosis are associated with meningiomas. Immunohistochemical and molecular testing has not resolved whether this is a neoplastic process.

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IRAP September 26, 2011 Presenter: Bevan Tandon MD, PhD

CASE #5: Case of spindle cell lesion of the lung/diaphragm.

HISTORY: 6 year old Caucasian male with a right sided chest mass which on CT scan demonstrated a heterogeneously enhancing mass in the inferior aspect of the right hemi-thorax measuring 16.2 x 15 x 13.5 cm with opacities within the right lung, and prominent jugular chain lymph nodes.

DIAGNOSIS: RHABDOMYOSARCOMA, SPINDLE CELL TYPE ARISING IN A PLEUROPULMONARY BLASTOMA.

KEY POINTS: Pleuropulmonary blastoma (PPB) are rare tumors arising from the pleura or lung parenchyma. They can be cystic or solid and unlike the adult pulmonary blastoma, only the mesenchymal element is malignant. The histology is composed of hypo and hypercellular areas in a myxoid background. Embryonic chondroid tissue if present is very helpful in making this diagnosis. Many intrathoracic embryonal rhabdomyosarcoma may have represented the solid type III PPB.

DIFFERENTIAL DIAGNOSIS: Embryonal rhabdomyosarcoma, synovial sarcoma, leiomyosarcoma.

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Case# 6 Presenter: Larry Jennings, M.D., Ph.D.

CLINICAL HISTORY: A 14-month old female presents with an abdominal mass. The mass was asymptomatic and identified incidentally. CT of the abdomen shows a large, multi-cystic, enhancing mass associated with the right upper pole of the kidney.

MACROSCOPIC: A nephrectomy specimen is received that is grossly distorted by a large renal mass (15x10x8 cm). The mass is lobulated with fibrous bands and mostly solid with a yellow/ tan cut surface that is gelatinous in consistency. There are areas of hemorrhage and small foci of necrosis.

MICROSCOPIC: Sections demonstrate a well-circumscribed, non-encapsulated tumor with invasion involving renal tubules and vascular structures. There is sheet-like growth of tumor cells that are predominantly plump spindle cells with open chromatin, inconspicuous nucleoli, and scant eosinophilic cytoplasm. Some areas show myxoid stroma and other areas show clearing of the extracellular matrix. Mitoses are frequent and there are scattered lymphocytes. Immunostains are negative for NGFR and CD31 highlights an unremarkable vascular pattern. FISH studies show loss of part of the *ETV6* gene and RT-PCR confirms the presence of the fusion transcript, *ETV6-NTRK3*.

DIAGNOSIS: Congenital Mesoblastic Nephroma, Cellular Variant

KEY POINTS: This case is a nice example of one of the more common pediatric renal tumors occurring in infancy. Congenital mesoblastic nephroma (CMN) has histological variants (classic, cellular, and mixed) that behave differently with the cellular variant being more likely to recur and metastasize. The cellular variant is characterized by the balanced translocation t(12;15)(p13;q25) resulting in a recurrent fusion transcript, *ETV6-NTRK3*. Identification of the fusion transcript is very useful to distinguish cellular variant CMN from other common pediatric kidney tumors. However, it should be recognized that perhaps 25% of the cases will not exhibit the translocation by RT-PCR or FISH. The *ETV6-NTRK3* fusion transcript is also characteristic of infantile fibrosarcoma, secretory carcinoma of the breast, mammary analogue secretory carcinoma of the salivary glands, mammary-type secretory carcinoma of the skin, and has also been identified in few cases of acute myeloid leukemia.[1-4]

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