Cases #13-16

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August 8, 2014
Case #13 -

- 4 week old girl with a history of neck mass, for two days prior to admission, rapidly growing
- Minimal response to antibiotics after one week
- Imagining demonstrated extensive lymphadenopathy of neck and chest
- A cervical lymph node is excised.
Groovy nuclei
A limited immuno panel was performed
CD68 KP-1
Factor 13
Case #13 - Diagnosis

Langerhans cell histiocytosis
Langerhans Cell Histiocytosis

- Proliferative disease of cells that share characteristics with Langerhans cells of the epidermis
- Incidence of 4.6 per million
- Median age at diagnosis is <5 years
  - Peak 1-3 years
- M:F of 2:1
- Variable clinical spectrum
  - Single site
  - Multiple sites within a single organ system
  - Multiple organ systems
LCH: Clinical Spectrum

- Unifocal (solitary eosinophilic granuloma)
  - 2/3 of cases
  - Single site involved – bone (most common), lymph node, lung (smokers), thymus, rarely thyroid
    - Skull, femur, pelvic bones, ribs most common sites, appear lytic, diaphyseal with cortical erosion
  - Most commonly seen in children
  - 2/3 in males
LCH: Clinical Spectrum

- Multiple sites within a single organ system (Hand-Schüller-Christian syndrome)
  - Bone most common
  - M>F
  - Younger patients than unifocal disease

- Multifocal, multiple organ systems (Letterer-Siwe)
  - M>F
  - Infants, young children
  - Bone, lymph nodes, skin, thymus, lung, liver, bone marrow, CNS, GI tract, spleen
LCH: Pathogenesis

- Not fully understood
- Debate immune mediated versus neoplastic
  - Neoplastic may be winning
    - Clonality by HUMARA studies in females
      - (except pulmonary LCH in smokers)
    - Higher rate in monozygotic twins
    - Rare familial cases
    - *BRAFV600E* mutations
LCH: Mutations

- *BRAF* V600E mutations found in 35-64% of LCH cases
- Recent study found *MAP2K1* mutations in 50% of *BRAF* negative LCH cases
  - Mutations mutually exclusive
- Both are members of the MAPK pathway

High prevalence of somatic *MAP2K1* mutations in *BRAF* V600E negative Langerhans cell histiocytosis

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Blood 2014 June 30 epub ahead of print
LCH: Morphology

- LCH cells
  - 10-12 um in size
  - Oval shape
  - Folded, indented, lobulated nuclei with “coffee bean” groove
  - Minimal atypia, inconspicuous nucleoli
  - Mitotic figures rare

- Background
  - Eosinophils (not always), histiocytes, neutrophils, multinucleated giant cells, small lymphocytes
  - May have necrosis
    - Eosinophilic microabscesses
  - Late lesions fibrotic
Lymph Nodes in LCH

- Sinusoidal pattern of involvement
  - In contrast to dermatopathic lymphadenopathy
  - Starts subcapsular and moves into medullary, may extend into paracortex
  - Nodal architecture usually preserved
  - Rarely foci of LCH may be seen associated with lymphoma in the same node
    - Hodgkin’s as well as non-Hodgkin’s
LCH: Immunophenotype & EM

- Identical to normal Langerhans cells
- S100, CD1a, CD207 (Langerin) are positive
  - CD207 very specific (component of Birbeck granule)
- Also positive for PLAP, vimentin, low amount of fascin, patchy CD68
- Negative for CD163, Factor 13a, CD45, lysozyme, EMA, CD30, CD15
- CD4 +/-
- EM – Birbeck granule
  - If have CD1a and CD207, may not need to prove it
LCH: LN Differential Diagnosis

- Dermatopathic lymphadenopathy
  - Paracortical involvement – not sinusoidal, melanin and hemosiderin pigment
  - Langerhans cells will be there (beware immunos)
  - Negative for \textit{BRAF} mutations
  - History of rash or chronically itchy skin

- JXG (disseminated juvenile xanthogranuloma)
  - Factor 13a positive

- Rosai-Dorfman
  - S100+ but CD1a and CD207 negative
  - Emperiplolesis

- ALCL (CD30+)

- Melanoma
Dermatopathic Lymphadenopathy
Be careful doing a CD207 in a lymph node: normal pattern of staining in sinusoids
LCH: Prognosis

- Unifocal disease – benign behavior, generally does not disseminate
  - Even without treatment
- Multifocal, multiorgan (disseminated) disease– generally poor
  - Mortality of almost 20% in children <2 yrs
- Patients are stratified into high or low risk
  - Higher risk if involve liver, lung, bone marrow, spleen, and onset <2 years
Our Case: Follow Up

- CSF, bone marrow exams negative
- LFTs, CBC normal
- MRI of brain/abd/pelvis negative
  - Patient developed stridor after intubation during MRI, treated with racemic epinephrine and decadron with rapid resolution of symptoms
- Skeletal survey negative for lytic lesions

- 9 months later, patient healthy with complete resolution and no further evidence of LCH
  - Has received no further therapy
Case #14 -

- 15 year old girl with lymphadenopathy, hypergammaglobulinemia, hyperuricemia, and hypoplastic anemia

- Bone marrow biopsy shows polyclonal plasmacytosis (14.5%), but negative for lymphoma

- An inguinal lymph node is excised.
4 month history of fatigue, dizziness and found to have severe anemia (Hgb = 6.4 g/dL) with inappropriately low retic count (2.2%)

Also had pruritic rash, back pain

Cervical, axillary, and inguinal lymphadenopathy

Splenomegaly on US

Markedly elevated ESR with high IgG (>10,000), rouleaux on PBS, elevated uric acid