Histiocytic and Dendritic Proliferations

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NeoGenomics
CD68

• Antibodies against 110 Kd glycoprotein associated with lysosomes
• Stains monocytes/histiocytes and myeloid cells best
• Identifies true histiocytic neoplasms, acute myeloid leukemia, especially M4 and M5, mast cell neoplasms, and Langerhans cell histiocytosis
• May stain some non-Hodgkin lymphomas, malignant melanoma, MFH
CD163

- Antibodies against a 175 kD cell surface glycoprotein called hemoglobin scavenger receptor
- Thick membranous staining, often combined with some granular cytoplasmic staining
- Stains most monocytes and fixed histiocytes/macrophages
- Identifies true histiocytic neoplasms, Rosai-Dorfman disease, AML with monocytic differentiation, and some cases of LCH
- May stain fibrous histiocytomas/giant cell tenosynovial tumors (particularly histiocytes)
CD1a

- Antigen present on Langerhans cells, indeterminate cells, and immature thymocytes
- Marker for LCH and indeterminate cell neoplasms, but can also stains some cells in Rosai-Dorfman disease
- Stains some cases of T-ALL
- Stains dermatopathic lymphadenitis
CD207/Langerin

- Antibodies against Langerin, a type II transmembrane surface receptor found in Langerhans cells
- Disruption of gene abolishes Birbeck granules, but does not disrupt Langerhans cell function
- Highly specific marker for Birbeck granules
- Granular cytoplasmic pattern of staining
- Stains cells with Birbeck granules: Langerhans cells
- Stains LCH and a small subset of histiocytic sarcomas
CD123

- IL3 receptor-alpha
- Marker of plasmacytoid dendritic cells, but also stains some myeloid precursors, macrophages, dendritic cells, mast cells, basophils, and megakaryocytes
- Membrane stain
- Stains precursor plasmacytoid dendritic cell neoplasm/blastic NK-cell lymphoma-hematodermic neoplasm, but also subset of AML
Histiocytes

• Derived from monocytes
• Resident in:
  – Germinal centers (tingible-body macrophages)
  – Splenic, lymph node and marrow sinuses
  – Lymph node paracortex
  – Lamina propria of small intestine
  – Liver sinuses (Kupffer cells)
  – Lungs (alveolar macrophages)
  – Kidney and endocrine glands
  – Brain (microglia)
Histiocyte Functions: Multitasking Cell

• Produce enzymes, complement factors, coagulation factors, reactive oxygen and nitrogen species, bioactive lipids, and numerous cytokines and growth factors

• Internalize substances by pinocytosis or phagocytosis, in general fusing the internalized vesicles with lysosomes

• Mediate resistance to intracellular microorganisms and tumors through nonimmunologic mechanisms

• Gain enhanced resistance to intracellular microorganisms by activation (induced by lymphokines, particularly IF-γ)

• Important role in the recognition and clearance of apoptotic cells
Histiocytes: Phenotype

- Reactivity for nonspecific esterase, acid phosphatase, and lysozyme
- Express HLA-DR, CD45, CD15, CD33, and CD4
- Express cytoplasmic CD68 (lysosomes)
- Express CD163, CD11c, CD13, CD14, CD64, and Mac387
Clinical and Laboratory Criteria for Hemophagocytic Lymphohistiocytosis
(5/8 criteria)

• Fever
• Splenomegaly
• Cytopenia > 2 cell lines
  – Hemoglobin < 90 g/L (below 4 weeks < 120 g/L)
  – Platelets <100 x 10^9/L
  – Neutrophils < 1 x10^9/L
• Hypertriglyceridemia and/or hypofibrinogenemia
  – Fasting triglycerides > 2650 mg/L
  – Fibrinogen < 150 gm/L
• Ferritin > 500 ng/L
• sCD25 > 2400 U/mL
• Decreased or absent NK-cell activity
• Hemophagocytosis in BM, spleen, or lymph nodes
Classification and Underlying Conditions of Hemophagocytic Lymphohistiocytosis (HLH)

Genetic HLH

Familial HLH (Farquhar disease)—all autosomal recessive

Immune deficiency syndromes
  Chediak-Higashi syndrome
  Griscelli syndrome
  X-linked lymphoproliferative syndrome

Acquired HLH

Exogenous agents (infection-associated hemophagocytic syndrome, esp. EBV, toxins)

Endogenous products (product of tissue destruction, metabolic products)

Rheumatic diseases

Macrophage activation syndrome

Malignancies associated with hemophagocytosis
## Genetic Defects in Hemophagocytic Lymphohistiocytosis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Chromosome Location</th>
<th>Associated Gene</th>
<th>Gene Function</th>
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<td>FHLH-1</td>
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<td>XLP</td>
<td>Xq25</td>
<td>SH2D1A</td>
<td>Signal transduction and activation of lymphocytes</td>
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Abbreviations: FHLH, familial hemophagocytic lymphohistiocytosis; GS, Griscelli syndrome; CHS, Chédiak-Higashi syndrome; XLP, X-linked Lymphoproliferative syndrome
Hemophagocytic Lymphohistiocytosis: Histopathology

- Sinusoidal infiltration by benign-appearing histiocytes
- Histiocytes show prominent erythrophagocytosis, as well as phagocytosis of other cells, platelets, other cellular debris
- Plasma cells may be abundant, but germinal centers usually inconspicuous
- Malignant cells may be interspersed with associated with lymphoma
- Lymphocyte depletion seen late in the course
Lymphohistiocytic Hemophagocytosis: Outcome

- May resolve, particularly if there is successful treatment of the underlying condition.
- Death, when it occurs, may be due to underlying condition or to complications of the syndrome.
- Rarely, EBV-associated cases may progress to an EBV+ T-cell lymphoma.
2016 Classification of Histiocytic Neoplasms and Associated Disorders of the Histiocyte Society

A: L Group
- LCH
- ICH
- ECD
- Mixed LCH/ECD

B: C Group
- Cutaneous non-LCH
  - XG family: JXG, AXG, SRH, BCH, GEH, PNH
  - Non-XG family: cutaneous RDD, NXG, other NOS
- Cutaneous non-LCH with a major systemic component

C: R Group
- Familial Rosai-Dorfman Disease (RDD)
- Sporadic RDD
  - Classical RDD
  - Extra-nodal RDD
  - RDD with neoplasia or immune disease
- Unclassified

D: M Group
- Primary Malignant Histiocytes
- Secondary Malignant Histiocytes (following or associated with another hematologic neoplasia)
  Subtypes: Histiocytic, Interdigitating, Langerhans, indeterminate Cell

E: H Group
- Primary HLH: Monogenic inherited conditions leading to HLH
- Secondary HLH (non-Mendelian HLH)
- HLH of unknown/uncertain origin

* A proportion of PIK3CA mutant patients have concomitant BRAFV600E mutations.

Jean-François Emile et al. Blood 2016;127:2672-2681
Rosai-Dorfman Disease

- 90% of patients present with cervical nodes
- Multiple nodes most common
- Extranodal sites involved in 40% (Rosai-Dorfman); particularly bone, soft tissue, skin, nasal cavities
- Median age of 20 years; more frequent in males and in individuals of African descent
- Usually a variety of lab abnormalities
- Some patients with ALPS and the “H” syndrome (hyperpigmentation, hypertrichosis, hepatosplenomegaly, hearing loss, heart anomalies, hypogonadism, low height, hyperglycemia/diabetes mellitus and hallux valgus) may show focal R-D-like features
Rosai-Dorfman Disease: Histopathology

- Fibrotic lymph node capsule
- Massive dilation of the sinuses
- Characteristic histiocytes
- Numerous plasma cells
- Extranodal sites show identical features
Rosai-Dorfman Disease: Cytologic Features

• Characteristic nuclei: round with vesicular chromatin and one to several nucleoli
• Abundant cytoplasm, amphophilic to eosinophilic, and occasionally foamy
• Cytoplasm often contains lymphocytes (or other cells)
Rosai-Dorfman Disease: Immunohistochemistry

- S-100 protein +
- CD68 and CD163 +
- Usually CD1-, but may be focally +
- Langerin -
- Usually CD30 -, but may be focally CD30 + (up to 50% of cases in one series)
- CD21, CD23, CD35 –
- May have many IgG4 positive plasma cells
Rosai-Dorfman Disease: Molecular Studies

- Negative for clonal Ig or TCR rearrangements
- Polyclonal by HUMARA assay, supporting a reactive process
- No evidence of association with any known viruses, including EBV, HHV-6, HTLV
- No BRAF V600E mutations have been reported
Rosai-Dorfman Disease: Differential Diagnosis

- Lymphohistiocytic hemophagocytosis/sinus histiocytosis
  - Phagocytosis of RBCs rather than lymphocytes
  - Cytologic features differ
  - Only focally S-100 +, if at all
- Langerhans cell histiocytosis
  - Cells are smaller
  - Cytologic features differ
  - CD1a and Langerin +
Rosai-Dorfman Disease: Outcome

- Spontaneous resolution occurs in most patients
- Some patients have a protracted course
- Surgery reserved for disfiguring lesions or those with functional consequences
- Some patients die (5-10%), due to organ involvement or consequences of immunologic abnormalities
Disseminated (Visceral) JXG

- Most occur by age 10
- May have multiple lesions, often in combination with skin lesions
- Most often occurs in soft tissue
- Often involves mucosa sites, particularly the upper aerodigestive tract
- May involve CNS, dura, pituitary stalk, eye, liver, lung, lymph node and bone marrow
Disseminated Juvenile Xanthogranuloma: Disease Associations

- Some cases associated with Langerhans cell histiocytosis
- Also associated with NF1 (particularly café au lait spots) and NF2 (particularly schwannomas)
- As many as 1 in 5 children with NF1 may develop JXG before the age of 3
- JMML is associated with multiple JXGs, particularly in patients with NF1
- JMML/NF1/JXG may be particularly common
Disseminated (Visceral) JXG

- Histopathology and phenotype identical to typical JXG, although usually greater fibrosis and less Touton giant cells
- Again, no consistent molecular findings
- Generally a benign disease, although lesions in critical areas (e.g., brain, pituitary) may cause significant morbidity or even mortality
Erdheim-Chester Disease

- Median age of 55-60 years, with a 3:1 male predominance
- Near universal involvement of long bones; often bilateral and symmetrical, involving diaphyseal and metaphyseal regions
- About 50% have extraskeletal involvement, including heart, kidney, peri-renal soft tissue, skin, brain, lung, orbital region, pituitary gland
- Histopathology and immunophenotype identical to JXG
- No standard treatment: 50% three-year survival
Erdheim-Chester Disease: Molecular Features

• BRAF V600E mutations in about 50% (no mutations in JXG)
• Other cases may have MAP2K1, NRAS, KRAS, ARAF, and PIK3CA mutations
• In-frame fusions involving several kinases, including BRAF, ALK, and NTRK1 may be present in cases without point mutations
• It may be that all cases have at least one mutation activating the MAP-kinase pathway
Histiocytic Sarcoma

- Very rare neoplasm that is greatly overdiagnosed
- Need to do a complete workup to exclude B and T cell lymphoma
- Most suspected cases turn out to be CD30+ ALCL
- When term strictly applied, less than 0.2% of NHL
Histiocytic Sarcoma: Clinical

- Occurs in all age groups, adults > children
- No gender predilection
- Most often involves extranodal sites, including GI tract, skin, and soft tissue
- Also commonly occurs in LNs
- Patients usually present with a solitary mass or lymphoma symptoms, although a “systemic” presentation may be seen
- Prognosis generally poor
- Occasionally complicates mediastinal germ cell tumor (malignant teratoma, w/ or w/o yolk sac tumor)
- Some cases associated with malignant lymphoma, particularly ALL or low grade B-cell lymphomas
Histiocytic Sarcoma: Histopathology

• Involved nodes may be partially (patchy, paracortical, or sinusoidal) or completely replaced
• Neoplastic cells generally cytologically malignant, but resemble histiocytes
  – Eosinophilic or vacuolated cytoplasm
  – Large, eccentric, bean-shaped nucleus
• May see multinucleated cells
• May see vacuolization
• May see hemophagocytosis
Histiocytic Sarcoma: Immunophenotype

- Must express two (one) or more monocyte/macrophage lineage antibodies (CD14, CD11c, CD13, CD68, CD163)
- CD4 (cytoplasmic), CD15, CD43, CD45, CD45RO, CD33, lysozyme, PD-L1 +/-
- S-100 may be focal +
- CD30, specific B or T cell markers -
- CD1a, CD21, CD23, CD35 -
Histiocytic Sarcoma: Molecular

- May see heavy chain and/or light chain Ig or rearrangements
- Cases associated with B-cell lymphoma may share same pattern of Ig gene rearrangements
- Do not see ALK translocation or ALK expression
- No consistent cytogenetic abnormalities seen; frequent chromosomal gains or losses are typical
- About 60% of cases reported to have BRAF V600E mutations
Histiocytic Sarcoma: Differential Diagnosis

- Any expression of CD30 or specific T or B-lineage markers more consistent with malignant lymphoma
- Most cases previously called “malignant histiocytosis” represent ALCL with involvement of sinusoids
- Monocytic leukemia may share similar phenotype, but is usually associated with bone marrow involvement, has a more blastic appearance, and may be + for CD34 and/or CD117
Myeloid Dendritic Cells: Stages of Maturation

DC Precursor/Indeterminate cell → Langerhans cell (DC Immature) → Interdigitating dendritic cells (DC Mature) → Apoptosis

- Cytokines
- Pathogens
- T cells
- IL-10

Cytokines

Pathogens

T cells
Dendritic Cells: Unitasking Cells

- Antigen capture
  - Macropinocytosis
  - Fcε and Fcδ receptors
  - Mannose receptor and C-type lectin receptor
  - Engulfment of apoptotic bodies

- Antigen presentation to antigen-specific T-cells
  - MHC-II loading
  - MHC-I loading
Dendritic Cells

- Cytokines
- CD40
- Adhesion molecules
- MHC Class II
- Antigen peptides
- B7(CD80/CD86)
- Cytokine receptors

T Cells

- Cytokine receptors
- CD40L
- Adhesion molecules
- CD3
- TCR
- CTLA-4/CD28
- Cytokines
# Dendritic Cells: Immunohistochemical Features

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<tr>
<th></th>
<th>CD45</th>
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<tr>
<td>Interdigitating dendritic cells</td>
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<td>+</td>
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<td>Follicular dendritic cells</td>
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Langerhans Cell Histiocytosis

• Unifocal disease (solitary eosinophilic granuloma)
• Multifocal unisystem disease (Hand-Schuller-Christian)
• Multifocal multisystem disease (Letterer-Siwe)
• Langerhans cell sarcoma
Langerhans Cell Histiocytosis: Unifocal Disease

- 50-60% of cases
- Most commonly affects bone (skull, femur, rib) of older children and young adults below 30 years
- Lung involvement occurs in male smokers between 20 and 30 years (may be different disease)
- Lymph node involvement usually affects cervical or inguinal region; may be painful
- Other sites: skin, thymus, soft tissue, vulva, spinal cord
Langerhans Cell Histiocytosis: Multifocal Unisystem Disease

- 20-40% of cases
- Usually affects infants between 2 and 5 years
- Bones affected include skull, ribs, pelvis, scapula
- May get hypothalamic involvement, diabetes insipidus, tooth problems, exophthalmos, bone involvement
Langerhans Cell Histiocytosis: Multifocal Multisystem Disease

• 10% of cases
• Usually affects infants less than 3 years
• Generally involves skin, lymph nodes, lung liver
• Numerous generalized symptoms
• Numerous laboratory abnormalities
Langerhans Cell Histiocytosis: Pathology

• Key feature
  – Identification of Langerhans cells in the appropriate milieu

• Langerhans cells
  – Mononuclear cells with folded, grooved, or lobulated bland nucleus with moderate amount of eosinophilic cytoplasm

• Milieu
  – Eosinophils, mononuclear and multinucleated histiocytes, neutrophils, small lymphocytes

• Older lesions
  – Fibrosis, foamy histiocytes, lymphocytes, plasma cells
LCH: Pathology in Lymph Nodes

- Nodes enlarged in primary involvement, but small in secondary involvement

- Primarily affects sinuses (involvement of paracortical region more likely to be dermatopathic), but may be patchy

- May be associated with malignant lymphoma, including Hodgkin lymphoma, non-Hodgkin lymphoma, and leukemia; usually as small focus not in sinus
LCH: Immunohistochemistry

- S-100, CD1a, Langerin +
- Cyclin D1+ (normal LCs are cyclin D1 -)
- CD45 +/- (negative in my experience)
- CD68, PLAP +/- (normal LCs are PLAP -)
- CD163 -
- CD35 -
Langerhans Cell Histiocytosis: Molecular Studies

- Most cases germline for Ig and TCR genes, unless associated with B-cell (usu. follicular) lymphoma
- Clonal by HUMARA assay (most forms)
- Merkel cell polyoma virus has been identified in some cases
- BRAF V600E mutations seen in about 50-60% of cases (better detected by IHC)
- About one-half of the BRAF mutation negative cases may have mutations in MAP2K1, and other cases may have occasional ARAF, MAP3K1, ERBB3, PICK1, PICK3R2 mutations
- Mutations detected in dendritic cell precursors may correlate with high-risk disease
Langerhans Cell Histiocytosis: Differential Diagnosis

• Dermatopathic lymphadenitis
  – Paracortical rather than sinusoidal or patchy
  – No cytologic atypia
• Langerhans cell sarcoma
  – Cytologically malignant
Langerhans Cell Sarcoma

- LCH with malignant cytologic features
- Male predominance, predilection for multisystem involvement, and a rapidly progressive course
- Most cases do poorly, although some cases do well
Follicular Dendritic Cells

• Antigen-processing cells of the germinal center
• Not clearly bone marrow-derived
• CD21 +, CD23 +, CD35 +, clusterin +, D2-40 +, CXCL13+, desmoplakin +
• S100 -/+ 
• CD45-, CD1a-
Follicular Dendritic Cell Sarcoma

- Rare but underdiagnosed
- Most common in cervical and axillary nodes
- Extranodal sites include mucosa and soft tissue
- May occur as complication of Castleman disease
- Local excision usually adequate, local recurrences occur
Follicular Dendritic Cell Sarcoma: Histopathology

- Spindle cell neoplasm
- May see fascicular, nesting or storiform pattern
- Admixture of small lymphocytes
- Bland oval nuclei with low mitotic rate commonly seen
- Some cases may show atypia; correlates with clinical aggressiveness
Follicular Dendritic Cell Sarcoma: Immunohistochemistry

- CD21, CD23, CD35, D2-40, CXCL13, clusterin, desmoplakin +
- PD-L1 and PDL2 +/-
- S-100, CD68, CD20 +/-
- CD45, CD163, lysozyme, CD1a -
Inflammatory Pseudotumor-Like Follicular/Fibroblastic Dendritic Cell Sarcoma

- Occurs predominantly in young to middle-aged adults, with a marked female predominance; lesions may recur
- Found in liver, spleen, or rarely the GI tract
- Spindle cells in a lymphoplasmacytic background
- SMA +; focal CD21 and CD35 may be seen
- Uniformly EBER positive
Follicular Dendritic Cell Sarcoma: Differential Diagnosis

- Interdigitating dendritic cell sarcoma
- Fibroblastic reticulum cell sarcoma
- Palisaded myofibroblastoma
- Other sarcomas
Follicular Dendritic Cell Sarcoma: Molecular Findings

• BRAF V600E mutations found in 20%

• Recurrent loss-of-function alterations found in tumor suppressor genes involved in the negative regulation of NF-KB and cell cycle regulation

• Focal copy-number gains of chromosome 9p24 (area including PD-L1 and PD-L2 genes)
Interdigitating Dendritic Cells

- Antigen-processing cells of T-zones
- Similar nuclei to Langerhans cells
- CD45, S-100 +
- CD1a -/+, Langerin -
- CD163 -
- CD21, CD23, CD35, clusterin, desmoplakin -
Interdigitating Dendritic Cell Sarcoma: Clinical

- Very rare neoplasm; children and adults
- Usual presents as solitary mass, but there may be systemic symptoms
- Most often presents in LN and skin, although other sites occur
- Some may behave benign, but the majority are aggressive; probably more aggressive than FDC sarcoma, with one-half dying of the disease
Interdigitating Dendritic Cell Sarcoma: Histopathology

• Spindled to round cell neoplasm
• Some mimic FDC sarcoma, some mimic lymphoma, most are somewhat in between
• Nuclei range from bland with Langerhans cell appearance to pleomorphic
Interdigitating Dendritic Cell Sarcoma: Immunohistochemistry and Molecular

• S-100 +
• CD21, CD23, CD35, clusterin -
• CD1a, Langerin -
• CD163 -
• PD-L1, CD68, CD45, lysozyme -/+ 
• SOX-10, HMB-45, Melan-A, MITF, tyrosinase –
• BRAF V600E mutations have been identified; incidence unknown
Indeterminate Cell Tumors: Epidemiology and Presentation

• Extraordinarily rare
• May be a female predominance, although numbers of reported cases are low
• May be more common in adults, although cases have been reported in children
• May be an association with prior B-cell lymphoma
• Generally presents a solitary skin and less often multiple skin lesions, although primary lymph node involvement may occur
Indeterminate Cell Tumor: Histology and Ultrastructure

- Histocytic to Langerhans-cell appearing
- Relatively bland nuclei with minimal cytological variation; may see multinucleated cells
- Cytoplasm typically abundant and usually eosinophilic
- Lacks significant eosinophilic infiltration
- By EM, may see complex interdigitating cell processes, but no Birbeck granules or desmosomes
Indeterminate Cell Tumor: Immunophenotype and Molecular

- Expression of S-100 and CD1a
- Consistently negative for Langerin/CD207
- Variable weak expression for CD163, CD68, lysozyme, CD45, and CD4
- Negative for FDC and specific lymphoid markers
- BRAF V600E mutations identified; incidence unknown
- Recently, ETV3-NCOA2 translocations were detected in 3/3 cases of ICT and in no cases of LCH, GXG, or RDD studied by FISH
Indeterminate Cell Tumor: Association with B-Cell Lymphoma

- Has association with B-cell lymphoma (similar to other dendritic and histiocytic neoplasms)
- Lesional cells show same clonal changes as cells of B-cell lymphoma
- May be due to sharing of a common precursor with B-cells, the presence of a factor that causes loss of B-cell identity, altering their normal pathway of differentiation and maturation (? PAX-5 in the absence of PCR signalling), or cell fusion
Indeterminate Cell Tumor: Clinical Outcome

- Not clear in small numbers of cases reported
- At least one reported case terminated as AML
- Death in occasional cases due to presence of underlying lymphoma
- Prognosis probably good in cases limited to skin involvement and not associated with B-cell lymphoma
Fibroblastic Reticular Cells

- Not marrow-derived
- Probably represent myofibroblastic structural elements
- Probably do not function in the immune system
- Rare tumors have been reported as primary lymph node sarcomas
- S-100, CD1a, Langerin, CD21, CD23, CD35 –
- May have markers of myofibroblasts (SM actin), may be desmin +, and may be CK oscar +
Precursor Plasmacytoid Dendritic Cell Neoplasm

• AKA blastic NK-cell lymphoma
• AKA CD4+, CD56+ hematodermic neoplasm
• AKA lymphoblastoid variant of NK-cell lymphoma
• AKA monomorphomic NK-cell lymphoma
• Now thought to be tumor of precursor plasmacytoid dendritic cells (of lymphoid lineage), due to expression of CD123, CD4, and other markers
Precursor Plasmacytoid Dendritic Cell Tumor: Epidemiology

- Rare
- Most patients are older adults, but has been described in children and teenagers
- No sex predilection
- No association with Asian population
- No association with EBV
Precursor Plasmacytoid Dendritic Cell Neoplasm: Clinical Presentation

- Patients usually present with multiple sites of disease, but a skin presentation is most common.
- Skin lesions may be single or multiple, and forms tumors and plaques.
- Lymph node, blood, bone marrow, soft tissues, and CNS are also commonly involved.
- Most patients present in high stage.
Precursor Plasmacytoid Dendritic Cell Neoplasm: Histopathology

- Dermis shows diffuse infiltrate, usually with extension to subcutaneous tissue, with sparing of epidermis
- Monomorphous population of blastic cells
- High mitotic rate
- No to few accompanying host cells
Precursor Plasmacytoid Dendritic Cell Neoplasm: Immunophenotype

- CD4, CD56, CD123, and CD43 +
- CD2 +/-, cytoplasmic CD3 +/-
- TDT +/-, CD34 +/-
- Surface CD3, CD33, myeloperoxidase –
- Negative for clonal B and TCR gene rearrangements
Precursor Plasmacytid Dendritic Cell Neoplasm: Prognosis and Progression

- Most patients initially respond to therapy, but a poor prognosis is ultimately seen for patients treated with current regimens
- Patients treated for ALL protocols may fare slightly better than patients treated on AML or lymphoma protocols, often followed by SCT
- Patients with disease limited to skin may do slightly better
Histiocytic and Dendritic Neoplasm: Conclusions

• Most entities are quite rare
• There may be inter-relationships and overlaps between entities, and even inter-relationships with malignant lymphoma
• BRAF and similar mutations may help provide a unifying framework
• Good luck with your cases!