ERDHEIM-CHESTER DISEASE (ECD)
A rare histiocytic neoplasm

DEFINITION
• A non-Langerhans cell histiocytic neoplasm that accumulates and infiltrates organs and tissue
• Multisystem disease affecting virtually any combination of organ systems, including ophthalmic/periorbital, pulmonary, cardiovascular, renal, musculoskeletal, and central nervous system
• Prompt diagnosis is critical for more favorable outcomes
• Usually diagnosed through biopsy, scans (bone, PET, MRI), and clinical symptoms

PROTEAN CLINICAL PRESENTATIONS
• Depends on organs involved
• Non-specific symptoms of bone pain, fevers, night sweats, weight loss, fatigue, and/or weakness are often present
• Findings may include diabetes insipidus, ataxia, diplopia, proptosis, angina, dyspnea on exertion, xanthelasmas, and renal failure
• Typical onset between 40 and 70 years of age, although documented cases in all age groups
• Slight preponderance of males

TYPICAL RADIOLOGY FINDINGS
• Bilateral cortical sclerosis of the long bones involving the diaphyseal regions
• Strong bilateral long bone uptake of radioactive tracer on 99mTc bone scintigraphs or PET scans
• Infiltrative disease of organs - "hairy kidney", "coated aorta", retroperitoneal fibrosis, right atrial mass, and pericarditis

PATHOLOGY FINDINGS
• Infiltration by foamy or lipid-laden, epithelioid or spindled histiocytes, with associated fibrosis, osteosclerosis and/or inflammatory background; foam cell change not always present
• Touton giant cells may be present
• Immunohistochemistry: ECD histiocytes are XG family phenotype:
  - CD68+
  - Factor 13a+
  - Fascin+
  - CD163+
  - S-100+/−
  - Fascin−
  - CD1a−
• BRAF V600E mutations in >50% of patients
• Other MAPK pathway alterations, including kinase fusions, in <50% patients
KEY POINTS FOR PATHOLOGISTS

1. None of the pathologic changes are unique to ECD – clinical radiographic features are key to diagnosis.
2. ECD is a clonal proliferation of histiocytes that have a xanthogranuloma (XG) phenotype.
3. ECD may coexist with Langerhans Cell Histiocytosis (LCH).
4. Foamy nature of histiocytes is a helpful clue, but is not required. ECD has a varied morphology including epithelioid and spindled histiocytes.
5. Fibroinflammatory background of lymphocytes, plasma cells, neutrophils is often present – often misdiagnosed as a reactive process.
6. Molecular studies increasingly play a role.

WANT TO LEARN MORE?
Contact an ECD-knowledgeable pathologist

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