ERDHEIM-CHESTER DISEASE (ECD)

A rare histiocytic neoplasm

Pathology investigations are vital to ECD diagnosis and proper life-saving treatment.

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, xanthelasma, 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 diametaphyseal 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+/- CD1a-

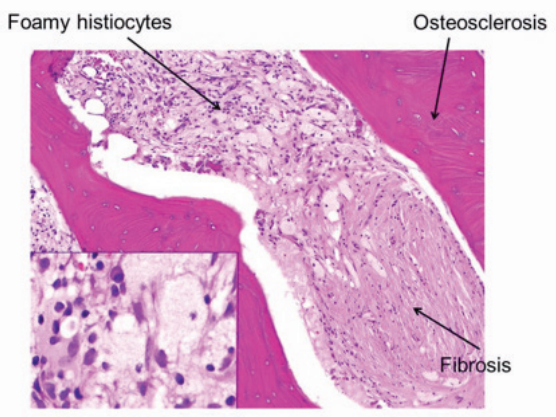
- BRAF V600E mutations in >50% of patients
- Other MAPK pathway alterations, including kinase fusions, in <50% patients

ERDHEIM-CHESTER DISEASE GLOBAL ALLIANCE

A 501c3 organization | Supporting those affected by ECD

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

JENNIFER PICARSIC, MD
University of Pittsburgh School of Medicine
picarsicj@upmc.edu

ELAINE S. JAFFE, MD
National Cancer Institute
ejaffe@mail.nih.gov

BENJAMIN H. DURHAM, MD
Memorial Sloan Kettering Cancer Center
durhamb@mskcc.org

KAREN L. RECH, MD
Mayo Clinic
Rech.Karen@mayo.edu

AHMET DOGAN, MD, PHD
Memorial Sloan Kettering Cancer Center
dogana@mskcc.org