ECD GLOBAL ALLIANCE
Supporting those affected by
Erdheim-Chester Disease worldwide

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Pathology Guide for Erdheim-Chester Disease Care & Diagnosis

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

DEFINITION OF ERDHEIM-CHESTER DISEASE (ECD)

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

PROTEAN 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

PATHOLOGY FINDINGS

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- 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+	CD163+
Factor 13a+	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

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

TREATMENTS

FDA Approved Treatment

- *BRAF*-inhibitor vemurafenib for *BRAF*-V600-mutation positive ECD

Options under clinical trials include:

- *BRAF* & MEK kinase inhibitors (cobimetinib, dabrafenib, and trametinib); monotherapy & combined treatments

Therapeutic options used off-label based on anecdotal experience include:

- Immunotherapy (interferon)
- Chemotherapy (cladribine, clofarabine)
- Anti-inflammatory medications (anakinra, tocilizumab, infliximab)
- Immunosuppressants (sirolimus, methotrexate, mycophenolate mofetil, azathioprine)
- Steroids (e.g., prednisone)
- Surgical debulking

Physical/Occupational Therapy

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

ECD REFERRAL CARE CENTERS

ECD Referral Care Centers are available to treat patients and/or provide consultation to local treating physicians when patients cannot travel. Find more information about these centers: http://erdheim-chester.org/care-centers/.

LEARN MORE

Contact an ECD-knowledgeable pathologist:

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