ERDHEIM-CHESTER DISEASE (ECD)

A rare histiocytic neoplasm

ECD is a rare disorder with variable presentations, delayed diagnosis, and the potential for poor outcomes.

A multidisciplinary approach is necessary

DEFINITION

- A rare histiocytic disorder with infiltrates throughout the body's organs and tissues
- A multi-system disease affecting virtually any combination of organ systems, including ophthalmic/periorbital, pulmonary, cardiovascular, renal, musculoskeletal, dermatologic, hypothalamic/pituitary, and central nervous system
- A rare disease with a critical need for prompt diagnosis to improve patient health outcomes
- Classified as a blood cancer, diagnosed through clinical and radiologic findings, biopsy, and molecular (e.g., BRAF V600E and other mutation) testing

PROTEAN CLINICAL PRESENTATIONS

- Depends on organs involved
- Generalized symptoms of bone pain, fevers, night sweats, weight loss, fatigue, and/or weakness are often present and can be severe
- Findings may include diabetes insipidus, ataxia, dysarthria, diplopia, proptosis, dyspnea on exertion, xanthelasma, and renal failure
- Typical onset between 40 and 70 years of age, although there are 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
- Encasement of organs - "hairy kidney," "coated aorta," retroperitoneal fibrosis, right atrial mass, pericardial thickening or effusion

PATHOLOGY FINDINGS

- Infiltration by foamy or lipid-laden, epithelioid or spindled histiocytes, with associated fibrosis and/or inflammatory background; foam cell finding 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 (e.g. MAP2K1, KRAS), including kinase fusions, in nearly all patients without ***BRAF***V600E mutation

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Erdheim-Chester Disease (ECD): Key Considerations for Dermatologists

ECD is a rare histiocytic disorder that can mimic many other conditions. Prompt recognition can prevent misdiagnosis and delays in targeted therapy.

KEY FACTS FOR DERMATOLOGISTS

- **Cutaneous involvement**(~20–30%): xanthelasma (yellow plaques on eyelids/intertriginous areas); xanthomas (red–brown papules/nodules or yellow–brown plaques); subcutaneous nodules; less commonly GA-like or panniculitis-like lesions
- **Genetics & therapy**: BRAFV600E in ~50–60%; other MAPK pathway mutations seeen. **Targeted therapy** (BRAF inhibitors e.g., vemurafenib; MEK inhibitors e.g., cobimetinib) is central to mortality reduction and should be genotype-directed

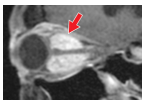
Multisystem Involvement in ECD

Dermatologic 25%

- Xanthelasma-like lesions
- Periorbital lesions
- Foamy histocytes

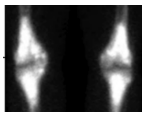
Orbits 30%

- Orbital masses

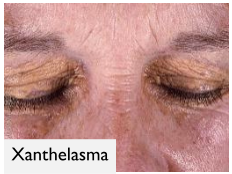


Bones 95%

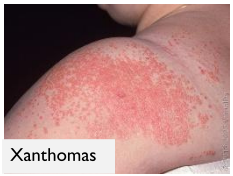
- Osteosclerosis of long bones and pain around the knees



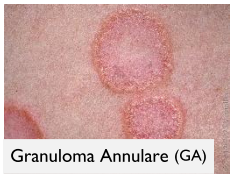
Scan For Other Body Systems



Xanthelasma



Xanthomas



Granuloma Annulare (GA)

Panniculitis-like lesions

THERAPY CONSIDERATIONS

BRAFInhibitors

- Morbilliform eruption (~20%,weeks–months); usually mild → topical steroids; monitor for SJS/TEN
- Photosensitivity / phototoxicity → strict sun protection
- Hyperproliferative lesions (↑ without MEK): verrucous keratoses, KA, cSCC→ surveil, biopsy/excise
- Hyperkeratosis ± early hand–foot skin reaction
- Other: alopecia, mucositis, HFSR (palms > soles), paronychia, onycholysis

MEK Inhibitors

- Acneiform eruption (face/chest/back; papules–pustules, no comedones) within weeks → emollients, topical steroids, BPO wash ± oral tetracyclines; severe: isotretinoin ± short steroids
- Xerosis and pruritus → emollients, antihistamines; refractory: gabapentin/aprepitant
- Erythema multiforme–like eruptions reported

Goyal, G et al. Mayo Clinic Proceedings, Volume 94, Issue 10, 2054 - 2071