BASELINE & MONITORING GUIDELINES

As a multisystem disease, a baseline evaluation, along with close monitoring are required for all patients. Monitoring is typically performed every 3 months until progression is stabilized and monitoring reduces to every 6 months.

PHYSICAL EVALUATION

- HEENT: xanthelasma, exophthalmos
- Cardiac: hypertension, irregular pulse, cardiomegaly, murmurs, ECG abnormalities
- Pulmonary: diminished aeration, rales
- Neurologic: disconjugate gaze, cranial nerve palsies, dysarthria, ataxic or magnetic gait, hyperreflexia
- Psychiatric: pseudobulbar affect

RADIOLOGICAL EVALUATION

- PET/CT including distal extremities
- CT chest, abdomen, and pelvis
- MRI brain with contrast and detailed examination of the sella turcica
- Cardiac MRI
- Selected patients based on symptoms or organ involvement
  - MRI orbit with contrast
  - Renal artery ultrasound
  - High-resolution CT chest
  - Pulmonary function tests
  - Testicular ultrasound
  - Electromyography

LABORATORY EVALUATION

- Complete blood count with differential
- Comprehensive metabolic panel
- Erythrocyte sedimentation rate
- C-reactive protein
- Morning urine osmolality
- Morning serum cortisol
- TSH and free T4
- Prolactin and IGF-1
- FSH/LH with testosterone (males) and estradiol (females)
- BRAF V600 genotyping
- Expanded tumor genotyping in BRAF V600- negative cases

National Comprehensive Cancer Network®
Practice Guidelines

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/.

WANT TO LEARN MORE?

Contact an ECD-knowledgeable hematologist.

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ERDHEIM-CHESTER DISEASE (ECD)
Hematology Guide

WHAT IS ECD?

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

Clinical and radiographic features are key to diagnosis.

Erdheim-Chester Disease Global Alliance
www.erdheim-chester.org
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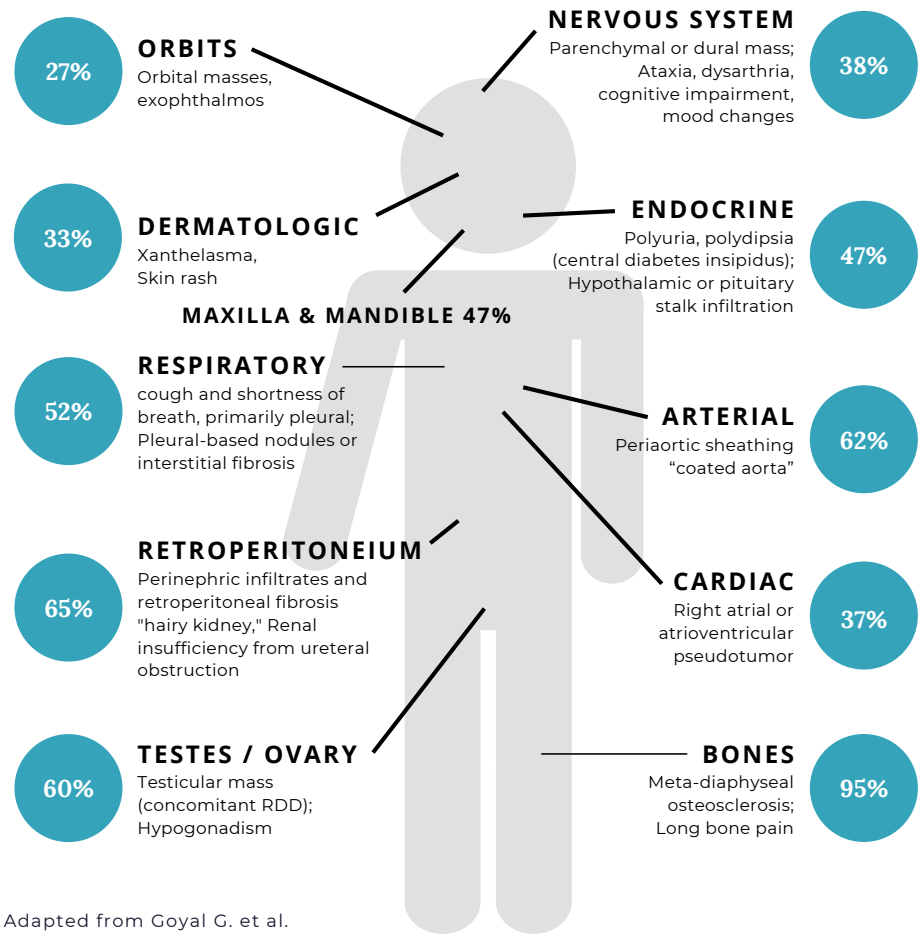
KEY FEATURES OF ERDHEIM-CHESTER DISEASE

The following diagram shows the percentage of ECD patients who experienced issues associated with each of the listed organs as reported in a 2020 publication. These numbers have been compiled using multiple existing studies. The illustration depicts clinical and radiographic features with frequencies and descriptions.



Adapted from Goyal G. et al. Blood. 28 MAY 2020 | VOLUME 135, NUMBER 22

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
- Encasing disease of organs - "hairy kidney," "coated aorta," retroperitoneal fibrosis, right atrial mass, and pericarditis

KEY POINTS FOR HEMATOLOGISTS

- None of the pathologic changes are unique to ECD – clinical and radiographic features are key to diagnosis.
- High index of suspicion for ECD in patients with typical "hairy kidney," retroperitoneal, or bone involvement, especially if concomitant diabetes insipidus.
- ECD may coexist with Langerhans Cell Histiocytosis (LCH) or myeloid neoplasm.
- Very important to pursue PET-CT scan from vertex to toe (whole body) to capture diamethaphyseal involvement around the knee joint and investigate for multi-organ involvement.
- Molecular studies increasingly play a role in diagnosis and management.

PATHOLOGY FINDINGS

- Infiltration by foamy or lipid-laden, epithelioid or spindled histiocytes, with associated fibrosis, and/or inflammatory background; foam cell change is not always present
- ECD is a clonal proliferation of histiocytes that have a xanthogranuloma (XG) phenotype.
- Touton giant cells may be present
- Immunohistochemistry - ECD histiocytes are XG family phenotype:
  CD68+ S-100+/-
  CD163+ Fascin+
  Factor 13a+ CD1a
- BRAF V600E mutations in >50% of patients – can be tested by immunohistochemistry or by polymerase chain reaction (PCR) based assay
- Other MAPK pathway alterations, including kinase fusions, in <50% of patients
- 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 and neutrophils are often present – often misdiagnosed as a reactive process.

TREATMENTS

FDA-Approved Treatments

- BRAF-inhibitor vemurafenib for BRAF-V600-mutation-positive ECD
- MEK-inhibitor cobimetinib for BRAF-V600-mutation-negative ECD

or single-agent treatment of adult patients

Options under clinical trials include:

- BRAF & MEK kinase inhibitors (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

Endocrinology evaluation and treatment