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

BASELINE & MONITORING GUIDELINES

Baseline evaluation for staging multi-system disease from clinical, radiologic, and molecular aspects is required for all patients. Response assessment (PET and CT/MRI) is performed every 3 months until best response 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
- *For some presentations, based on symptoms or organ involvement:*
  - *MRI orbit with contrast*
  - *Renal artery ultrasound*
  - *High-resolutionCT 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, testosterone (males), LH, FSH
- Vitamin B12, thiamine levels
- *BRAF*V600 genotyping
- Expanded tumor genotyping in *BRAF* V600-negative cases

ECD REFERRAL CARE CENTERS

ECD Referral Care Centers are available to treat people with ECD and or provide consultation to local treating physicians when a patient with ECD cannot travel.

WANT TO LEARN MORE?

Contact an ECD-knowledgeableneurologist.

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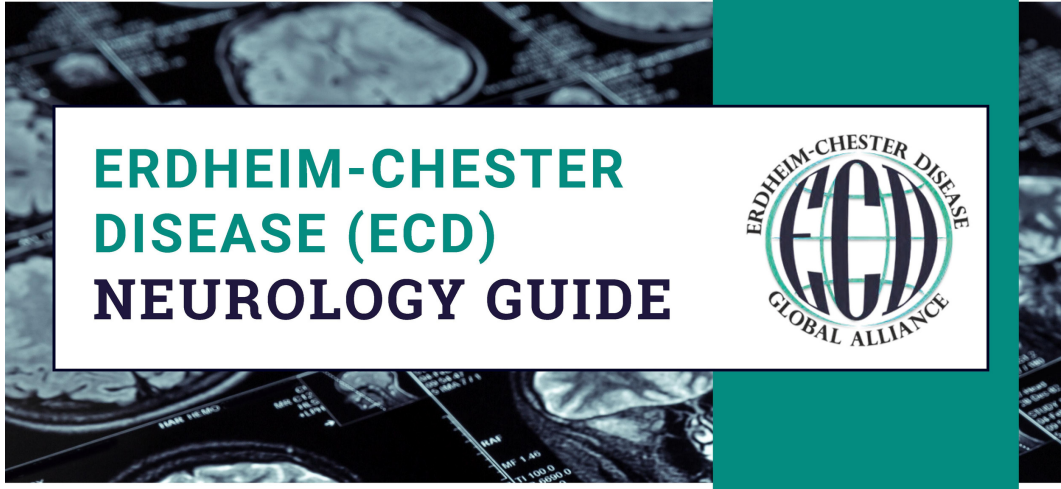


ERDHEIM-CHESTER DISEASE (ECD) NEUROLOGY GUIDE

WHAT IS ERDHEIM-CHESTER DISEASE (ECD)?

- A rare histiocytic neoplasm 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, and central nervous system
- **A rare condition with a critical need for prompt diagnosis to improve patient health outcomes**
- A blood cancer diagnosed through clinical and radiologic findings, biopsy, and molecular (e.g., *BRAF*V600E and other mutation) testing

Clinical and radiographic features are key to diagnosis.

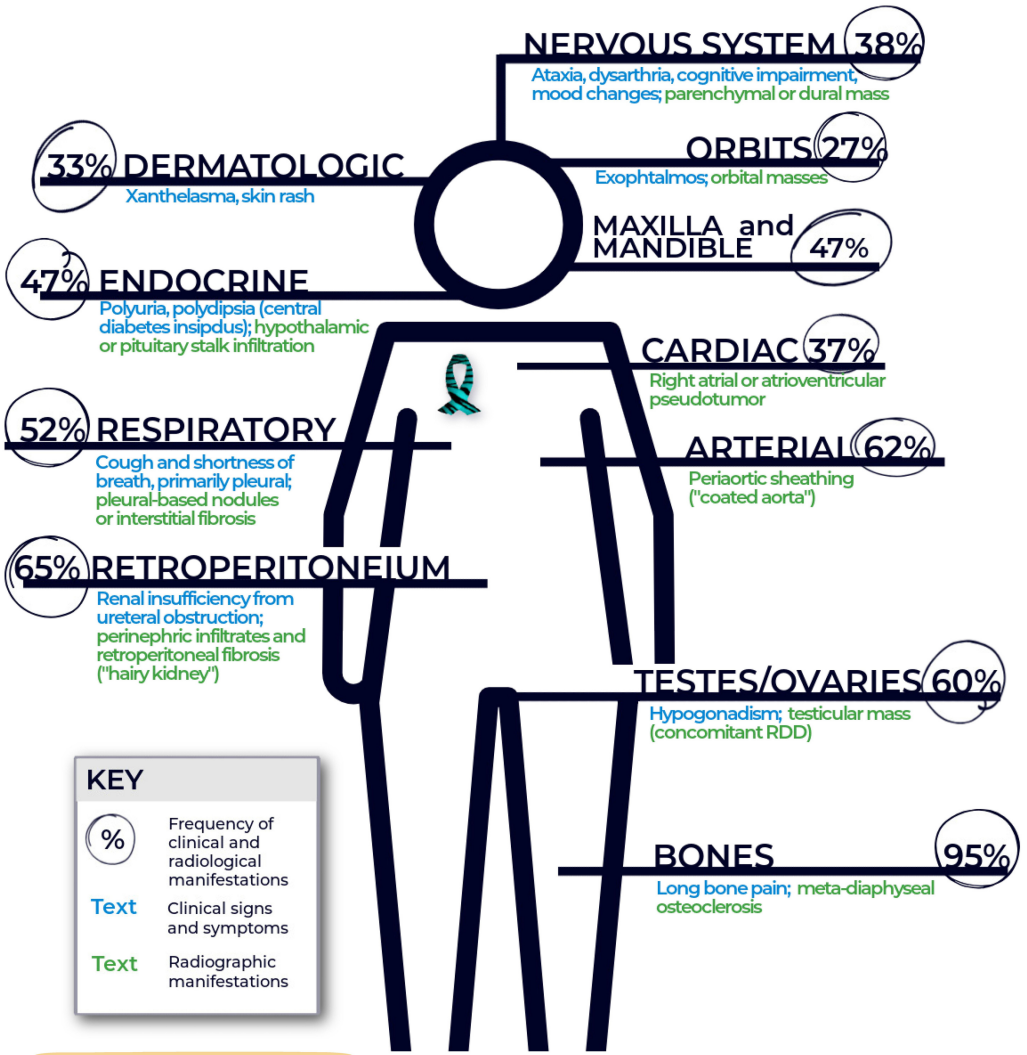
2020 CONSENSUS RECOMMENDATIONS

Goyal G, Heaney ML, Collin M, Cohen-Aubart F, Vaglio A, Durham BH, Hershkovitz-Rokah O, Girschikofsky M, Jacobsen ED, Toyama K, Goodman AM, Hendrie P, Cao XX, Estrada-Veras JI, Shpilberg O, Abdo A, Kurokawa M, Dagna L, McClain KL, Mazor RD, Picarsic J, Janku F, Go RS, Haroche J, Diamond EL. Erdheim-Chester disease: consensus recommendations for evaluation, diagnosis, and treatment in the molecular era. Blood. 2020 May 28;135(22):1929-1945. doi: 10.1182/blood.2019003507. PMID: 32187362.

WWW.ERDHEIM-CHESTER.ORG

HOW PATIENTS EXPERIENCE ECD

This illustration is based on the 2020 Consensus Recommendations. It identifies the percentage of ECD patients with disease involvement of the listed organs. Summarizing data from multiple ECD studies, the illustration includes both clinical and radiographic features with frequencies and descriptions.



FURTHER READING

National Comprehensive Cancer Network (NCCN) Guidelines for Histiocytosis

Histiocytosis and the Nervous System: From Diagnosis to Targeted Therapies

Neurological Manifestations of Erdheim–Chester Disease

KEY POINTS FOR NEUROLOGISTS

- ECD typically affects the HPA axis, infratentorial brain parenchyma, and meninges
- HPA axis involvement can lead to neuro-endocrinopathies (most commonly diabetes insipidus), hypersomnia, and visual impairment
- Infiltration of the brainstem and cerebellum can cause ataxia, dysarthria, cranial neuropathies, and motor impairment
- Pachymeningeal thickening can mimic a nodular meningioma or cause diffuse plaque-like expansion of dural structures

PATHOLOGY FINDINGS Infiltration by foamy or lipid-laden, epithelioid or spindled histiocytes, with associated fibrosis, and/or inflammatory background; foam cell change 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+ CD163+
  Factor 13a+ S-100+/-
  Fascin+ 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% 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, neutrophils is often present–often misdiagnosed as a reactive process

TREATMENTS

FDA-Approved Therapies

- BRAF-inhibitor vemurafenib for *BRAF*V600-mutation-position ECD
- MEK-inhibitor cobimetinib for *BRAF*V600-mutation-negative ECD

Clinical Trial Options

- BRAF & MEK kinase inhibitors (dabrafenib, and trametinib); monotheraphy and combined treatments

Physical/Occupational Therapy

Endocrinology Evaluation and Treatment

Other Therapeutic Options
(Off-Label, Based on Anecdotal Evidence)

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

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