What is ECD?

- A rare multi-system, non-Langerhans Cell histiocytosis of unknown cause that usually affects adults.
- Recent findings suggest a clonal disorder, marked by recurrent BRAFV600E mutations in more than 50% of patients, with chronic uncontrolled inflammation as an important mediator of disease pathogenesis.
- Characterized by excessive production and accumulation of macrophages (histiocytes) within multiple tissues and organs. As a result the tissue becomes thickened, dense and fibrotic.
- Virtually every organ can be involved (long bones, skin, retroorbital space, lungs, brain, pituitary gland, kidney, retroperitoneum, heart, pericardium and more rarely other organs). Each patient can have a different combination of organs affected.
- Unless successful treatment is found, organ failure can result.
- Rapid advances in the treatment of ECD are being made.

The material in this publication is meant for awareness purposes only. Please send any comments or corrections to support@erdheim-chester.org.

In Loving Memory of
F. Gary Brewer, Col. USAF, Ed.D.
and
In Honor of
All Those Who Suffer from ECD

For more information, please see www.erdheim-chester.org.

Researchers interested in investigating the cause or treatment of ECD are encouraged to contact the organization about possible grant opportunities.

To donate, please send checks to:
The ECD Global Alliance
P.O Box 775
DeRidder, LA 70634 USA

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Overview for Physicians & Researchers

A non-profit patient advocacy organization supporting those affected by

Erdheim-Chester Disease (ECD)

A rare multi-system histiocytic syndrome

Symptoms

Symptoms vary, depending upon the organ(s) involved. Common symptoms may include:

- Bilateral bone pain in legs and knees
- General symptoms of weight loss; fever; night sweats; muscle and joint aches; feeling of discomfort, weakness, and fatigue (malaise); flu-like symptoms that linger or continue to return
- Excessive thirst and urination (diabetes insipidus)
- Balance issues, difficulty walking (ataxia), slurred speech (dysarthria), involuntary, rapid eye movements (nystagmus)
- Lower back, flank or abdominal pain, often associated with kidney and/or ureter involvement (retroperitoneal fibrosis); reduced kidney function
- Bulging of the eye (exophthalmos) and/or vision issues
- Sore or bump under the skin (xanthomas), rash
- Shortness of breath (dyspnea)

ECD affects different organs in different people. As a result, each person will have a different combination of symptoms. This is partly what makes ECD so difficult to diagnose. By taking a systemic view of symptoms it may be possible to test for and diagnose ECD earlier. This will potentially give patients the best chance for a successful treatment plan.

Signs

Signs are the result of histiocytic infiltration of various tissues. Depending on organ involvement, some of the following signs may be found:

- Bilateral symmetric medullary sclerosis with cortical thickening and coarsened trabecular pattern of the long tubular bones of the extremities
- Moderate anemia, increased creatinine, increased C-reactive protein and erythrocyte sedimentation rate
- Retroperitoneal thickening with possible hydronephrosis, “hairy kidney” finding on abdominal imaging
- Interstitial lung disease involving accumulations of histiocytic cells and fibrosis in a predominantly perilymphangitic and subpleural pattern
- Soft tissue masses and/or lesions
- Pericarditis, “Coated Aorta” or other cardiovascular abnormalities

Diagnosis

- Tissue biopsy contain clusters of lipid-laden, foamy histiocytes with signs of chronic inflammation and Touton type giant cells, fibrosis and possible fat necrosis
- Histiocytes are CD68 positive, CD1a negative and without Birbeck granules. S-100 staining is typically negative, but some cells in the lesions may be positive
- Bone scan classically shows a symmetrical and abnormally increased uptake of the radiotracer in the distal ends of the long bones of the lower (and sometimes also upper) limbs

Treatments

Because of the rarity of this disease, clinical trials have only recently begun or been considered.

Therapeutic option under clinical trial includes:

- BRAF kinase inhibitors (vemurafenib, dabrafenib)

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

- Immunotherapy (interferon)
- Chemotherapy (cladribine)
- Immunosuppressants (methotrexate, sirolimus)
- Imatinib mesylate (Gleevec)
- Anakinra (Kineret)
- Tocilizumab (Actemra)
- Surgical debulking (severe orbital lesions or surgically resectable intracranial lesions)

In general, the clinical course of patients with this disease is variable.

It is important to know there are patients who are living high quality lives with ECD for decades. Because ECD is so rare and publications so few, this information may not be readily available to patients or physicians.

Clinical Management

- FDG-PET should be performed every 3-6 months until stabilized
- Organ-specific imaging of affected organs every 3 months until stabilized
- Currently most treatment is recommended indefinitely as tolerated

Monitoring option under clinical trial includes:

- Urine based detection and monitoring of BRAF V600E mutational tumor load