Clinical and Diagnostic Imaging Manifestations of Erdheim-Chester Disease

Christina E. Borchers, M.D.[1], Roland Gazaille, D.O.[2] , Avrey Thau, M.D. [2], Alejandro Calvo, M.D. [2], Ronald Warwar, M.D. [2], William Boyce, M.D. [2], Joseph Blake, M.D. [2]

Wright State University Boonshoft School of Medicine,[1] Kettering Health Network, Dayton, OH,[2]

WRIGHT STATE UNIVERSITY

Background & Objective

Erdheim-Chester Disease (ECD) is a rare form of non-Langerhans-cell histiocytosis. Since its first description in 1930 by Jakob Erdheim and William Chester, approximately 1500 cases have been reported world-wide. Despite the majority of literature comprised by case reports, a predilection for males in their 5th and 7th decade of life with multisystem involvement that may include dermatologic systems, central nervous system, skeletal, cardiovascular, renal systems have been frequently reported. The presenting symptoms most commonly include fatty nodules on the eyelids (xanthelasma) and cutaneous xanthomas-like lesions of the skin, proptosis, diabetes insipidus, dysarthria, headache, lower extremity bone pain and imbalance, although many others have been described.

Case Presentation

A 58 year-old male presented to a local emergency department with a one day history of severe dizziness, diaphoresis, dyspnea, intermittent diplopia, and xanthelasma.

Past medical history: obesity, hypertension, hyperlipidemia, diabetes mellitus type 2, and asthma. The patient stated that the dizziness had been worsening over the past several weeks, and he had experienced headaches for the past year. The patient's wife stated she felt his eyes had been "bulging" over the past six months.

Review of Systems: Right knee and leg pain, which had been ongoing for five years. Xanthelasma for the past 5 years.

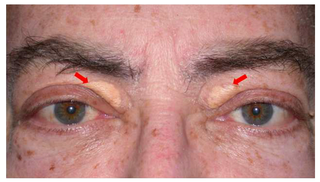
Physical Exam: Bilateral xanthelasma noted over the medial upper eyelids.Visual acuity was 20/30 OU. Mild deficit in abduction bilaterally. Funduscopic examination normal.

Studies/Labs: The patient underwent a right retrobulbar 20 gauge core needle biopsy approximately two weeks later. A few days following the biopsy, the patient returned to the emergency department with new onset 102.9 temperature, tachycardia with HR of 131bpm, tachypnea with RR of 25bpm, leukocytosis of 19,000/mm3 and procalcitonin level of 7.61ug/L. The new presentation was concerning for sepsis, but no source of infection was identified on the initial work-up.

The biopsy results returned and demonstrated bilateral symmetric retrobulbar masses. Subsequent imaging as well as orbital and bone marrow biopsies lead to the diagnosis of Erdheim-Chester disease, which is a rare non-Langerhans cell, non-familial, multisystemic histiocytosis. The condition is noted to have widespread manifestations and can be of highly variable severity.

Figures

Figure 1. Bilateral xanthelasma over the medial upper eyelids.



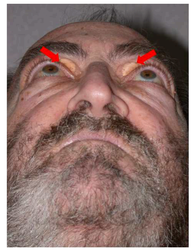


Figure 2. CT of the head and orbits with contrast. Revealed bilateral exophthalmos due to symmetric bilateral retrobulbar masses encasing the bilateral optic nerves.

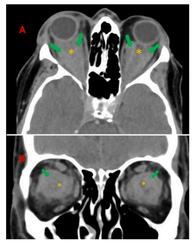


Figure 3. CT of the abdomen and pelvis with contrast due to complaint of abdominal pain. Infiltrative changes and enlargement of the bilateral adrenal glands and kidneys was found.

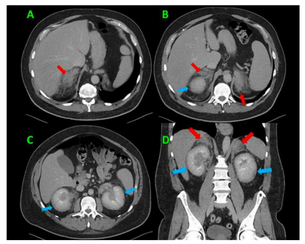


Figure 4. Skeletal survey: symmetric pattern of cortical thickening and sclerosis involving the bilateral distal femoral metadiaphyses.

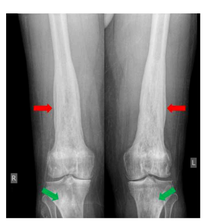


Figure 5. Bone scan: bilateral symmetric abdnormal uptake of radiotracer in the bilateral distal femoral and proximal tibial metadiaphyses.

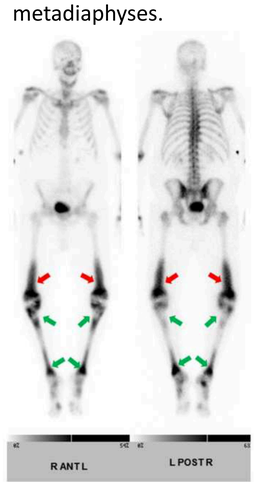
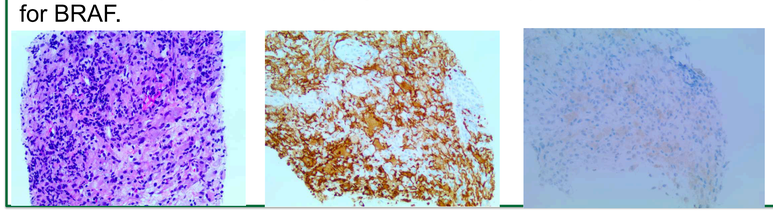


Figure 6. The core biopsy of the right retro-orbital mass demonstrated foamy histiocytes and macrophages. The histiocytes were weakly positive for BRAF.



Results

A CT of the orbits demonstrated symmetric and intraconal soft tissue masses. An abdominal CT scan showed infiltrative changes involving the bilateral adrenal glands and perirenal soft tissues. A whole body bone scan revealed symmetric areas of increased uptake of radiotracer in the metadiaphysial regions surrounding the knees in radiographic areas of osteosclerosis, which are findings pathognomonic of ECD.

The conclusive diagnosis of ECD was made by the combination of radiologic findings in conjunction with histology and immunochemistry findings of foamy histiocytes and macrophages which exhibited CD68, CD163, and Factor XIII positivity. The patient was initiated on the current first-line therapy of pegylated interferon. After experiencing medication toxicity with limited clinical improvement, treatment with pegylated interferon was halted. Although BRAF testing was unable to be completed due to limited tissue sample, the patient was started on targeted therapy with MEK inhibition. One month after the initiation of targeted therapy there was early radiologic evidence of improvement of the intraconal masses.

Conclusion

Despite its rarity, this case demonstrates clinical findings that are becoming more representative of Erdheim-Chester Disease. Radiographic and pathologic studies are of great importance in both diagnosis and choice of therapy in ECD. Nearly 95% of patients have been reported with bony involvement, noted by a pathognomonic radiologic finding of osteosclerosis involving the metadiaphyseal regions of the bones around the knees. Additionally, nearly 50% of patients describe lower extremity bone pain, which may prompt imaging studies to be performed.

The understanding of the biomolecular pathogenesis of ECD has been rapidly progressing in recent years. These advancements provide opportunity for targeted therapies. Notably in 2012, oncogenic BRAF V600E mutations were recognized in ECD histiocytes. With over 60% of cases positive for this mutation, the use of BRAF targeted therapy has emerged. Although interferon therapy is currently first-line, targeted BRAF and MEK inhibition promise for future direction.

References

1. Goyal G, Young JR, Koster MJ, et al; Mayo Clinic Histiocytosis Working Group. The Mayo Clinic Histiocytosis Working Group Censensus Statement for the Diagnosis and Evaluation of Adult Patients With Histiocytic Neoplasms: Erdheim-Chester Disease, Langerhands Cell Histiocytosis, and Rosai-Dorfman Disease. Mayo Clin Proc. 2019 Oct; 94(10):2054-2071.
2. Estraa-Veras JI, O'Brien KJ, et al. The clinical spectrum of Erdheim-Chester disease: an observational cohort study. Blood Adv. 2017; 1(6): 2054-2071.
3. Cohen-Aubart F, Emile JK, et al. Phenotypes and survival in Erdheim-Chester disease: Results from a 165-patient cohort. Am J Hematol. 2018 May; 93(5): E114-E117.

Disclosures: The author(s) have no financial relationships to disclose.