

case report

A rare case of Erdheim-Chester disease in the breast

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Erdheim-Chester disease (ECD) is rare non-Langerhans histiocytosis with distinctive radiologic and pathologic entities. We report a rare case of which ECD was involving the breast with only eight similar cases reported in the English literature. Our patient was a 52-year-old female patient with ECD involving the breast, mesentery, left kidney, retroperitoneum and the skeleton. The diagnosis was based on distinctive imaging and histopathological findings. The patient received a new novel treatment as part of a clinical trial in the United States and showed clinical and radiological improvement.

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Erdheim-Chester disease (ECD), also known as polyostotic sclerosing histiocytosis, is a rare non-Langerhans histiocytosis with distinctive radiologic and pathologic entities. It is characterized by foamy histiocyte infiltration and was first described in 1930. There are fewer than 500 cases reported. ECD usually involves the skeleton, skin and retroperitoneum.^{1,2} Our case was unique in that it was a rare case that also involved the breast. Only eight similar cases have been reported in the English literature (**Appendix 1**).

CASE

A 52-year-old female patient complaining of multiple bilateral breast and axillary swellings with no history of trauma or nipple discharge was referred to our hospital for further workup. The patient had a past medical history of diabetes insipidus and was taking desmopressin. On initial examination, the patient was febrile, complaining of fatigue and bilateral periorbital xanthelasma. Breast examination showed multiple bilateral large hard breast and axillary masses. Laboratory tests showed decreased albumin levels, a high white blood cell count and a low red blood cell count. Diagnostic mammography for both breasts was compared to previous mammography from 2 years ago. The current study showed no obvious masses (**Figure 1A**). Complimentary breast and axillary ultrasound showed

multiple large hypoechoic breast masses (**Figure 1B**). A CT scan showed bilateral large heterogeneous breast masses extending to the axilla (**Figure 1C**). A diffuse infiltrative process involving the subcutaneous tissues was seen in the midline and perianal region (**Figure 2A, 2E**). Infiltrations of small areas were seen in the retroperitoneum, mesentery and the left kidney (**Figure 2B, 2C, 2D**). A whole body bone scan showed bilateral symmetrical increased tracer uptake in the distal part of the femur and tibia (**Figure 3A**), which correlated to sclerotic bone changes in the corresponding SPECT-CT images (**Figure 3B**).

Multiple core biopsies were taken from the breast and axilla. Histopathology showed sheets of xanthomatous histiocytes with abundant foamy cytoplasm and occasional multinucleation. The histiocytes were mixed with few small lymphocytes (**Figure 4A**). In the immunohistochemistry tests, the histiocytes were positive for CD68 and negative for CD1a and S-100 (**Figure 4B**). The samples were sent for genetic testing, which showed a BRAF codon 600 mutation.

After clinical, radiological and histopathological evaluation, the patient was diagnosed with ECD. The patient sought medical advice in the United States at Memorial Sloan Kettering Oncology Center and participated in a clinical trial. At the time of writing the patient was being treated with vemurafenib, which is B-Raf inhibitor. The patient was showing good tolerance and

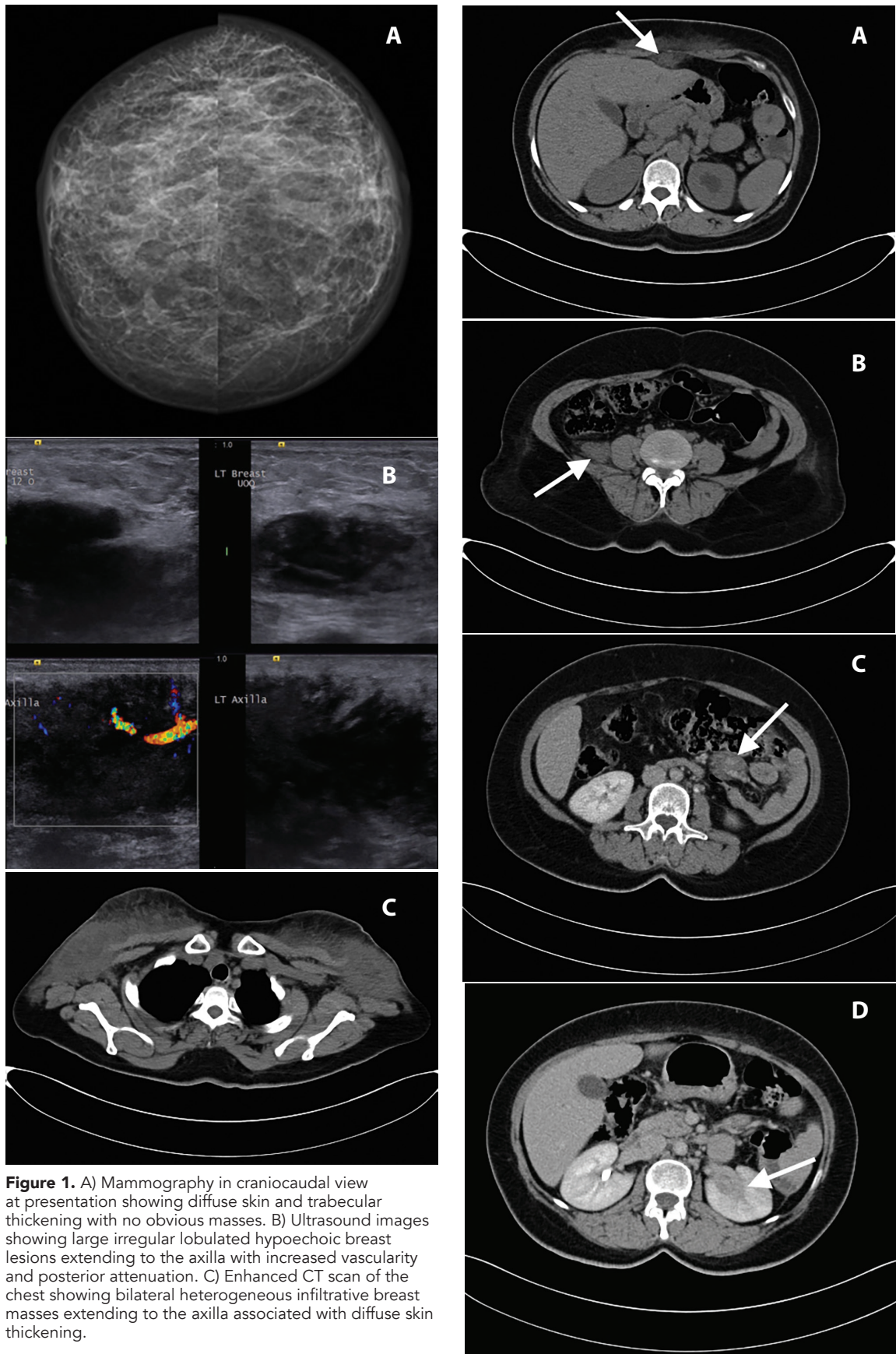


Figure 1. A) Mammography in craniocaudal view at presentation showing diffuse skin and trabecular thickening with no obvious masses. B) Ultrasound images showing large irregular lobulated hypoechoic breast lesions extending to the axilla with increased vascularity and posterior attenuation. C) Enhanced CT scan of the chest showing bilateral heterogeneous infiltrative breast masses extending to the axilla associated with diffuse skin thickening.

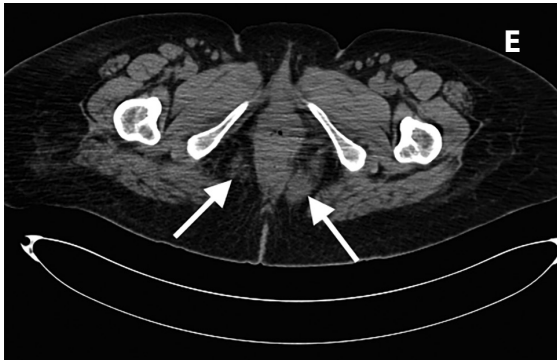


Figure 2. A) Enhanced CT scan of the abdomen showing infiltration of the anterior abdominal wall and small area of the mesentery (arrow). B) Enhanced CT scan of the abdomen showing small infiltration in the retroperitoneum adjacent to the right psoas muscle (arrow). C) Enhanced CT scan of the abdomen and pelvis showing another area of mesenteric involvement by the disease (arrow). D) Enhanced CT scan of the abdomen and pelvis showing infiltration of the left kidney (arrow). E) Enhanced CT scan of the abdomen and pelvis showing multiple subcutaneous nodules at the perianal region (arrow).

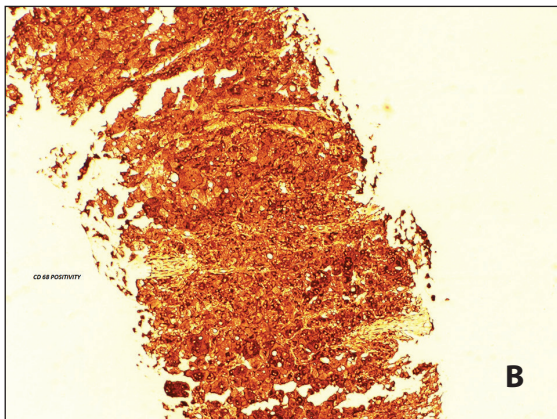
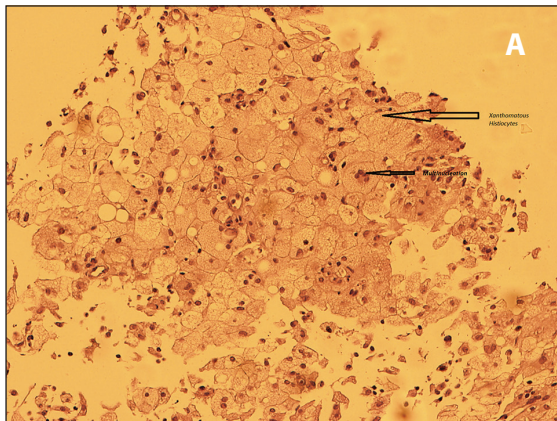


Figure 4. A) Histopathology slides in hematoxylin and eosin (H&E) stain and 10-power magnification, showing the characteristic xanthomatous histiocytes (large arrow) and multinucleated Touton type giant cells (small arrow). b. Immunohistochemistry studies showing the CD68 positivity.

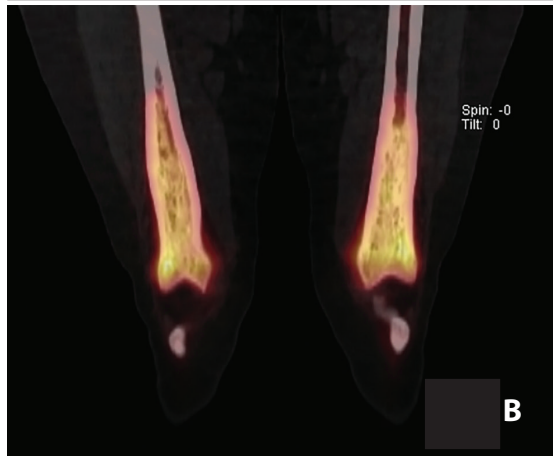
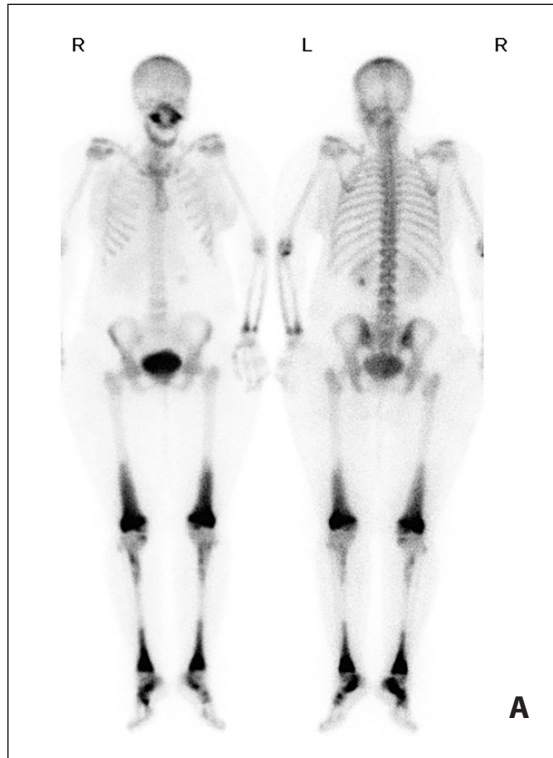


Figure 3. A) Technetium 99m MDP bone scan showed bilateral symmetrical increased tracer uptake in the distal aspects of the femora and tibiae. B) Complimentary SPECT-CT scan showing bilateral symmetrical sclerosis of the distal Femora with increased tracer uptake.

an excellent clinical and radiological response (**Figure 5A, 5B**).

DISCUSSION

ECD is an extremely rare disease of unknown etiology. ECD affects both genders with a male predominance and mean age of 53 years.^{1,2} The most commonly affected site is the skeleton, mainly the long bones.

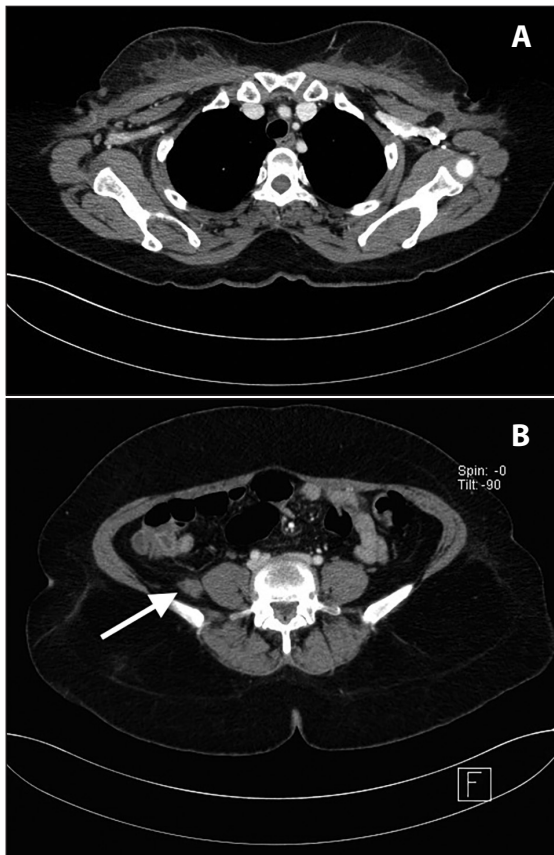


Figure 5. A) Enhanced CT scan of the chest showing nearly complete resolution of the breast lesions. B) Enhanced CT scan of the abdomen and pelvis showing small area of residual infiltration in the retroperitoneum (arrow).

These lesions usually appear as bilateral symmetrical heterogeneous sclerosis of the affected bones from bone marrow replacement with infiltrative foamy histiocytes. These lesions show significant radiotracer uptake in bone-targeting nuclear studies.^{1,2} Most cases of ECD show at least one extra-skeletal involvement at the time of diagnosis. Most commonly affected extra-skeletal sites in descending order are the retroperitoneum, heart, lung, central nervous system, skin, then pituitary gland and orbits.^{1,2}

The patient's clinical manifestations vary and depend on the site of involvement. The most common symptom is juxta-articular pain, particularly of the lower extremity.^{1,2} Abdominal and back pain were also reported due to involvement of the retroperitoneum.^{1,2} However, the most debilitating symptoms are caused by cardiac and pulmonary involvement and are a significant cause for mortality and morbidity.^{1,2} CNS involvement is less common and it is predominantly periorbital and presents with exophthalmos and visual changes.

Other symptoms include, diabetes insipidus from pituitary gland involvement and periorbital xanthelasma from skin involvement.^{1,2}

There are many non-Langerhans histiocytotic diseases; however, the foamy cytoplasm of the histiocytes with Touton type giant cells is characteristic of ECD. Furthermore, the positive immunohistochemistry for CD68 and negativity for S-100 are distinctive for ECD. A few scattered lymphocytes and plasma cells and possibly surrounding areas of fibrosis could frequently be seen with no cytologic atypia or increased mitotic activity.^{1,2}

In the eight previously reported cases of ECD involvement of the breast, all the patients were females with a mean age of 57 years except for one case in a 60-year-old male patient reported by Ferrozzi et al.³ In five of the eight reported cases, the lesions were unilateral with more right breast predilection in one patient. The remaining three cases showed bilateral involvement. Most patients presented with a history of breast lumps. However, in the case reported by Ferrozzi et al, the patient presented with gynecomastia and skin ulcerations.³ ECD involvement of the breast can be incidentally discovered as it was reported by Furuta et al.⁴ In all cases, extramammary involvement was found at the time of presentation except for one recent case reported by Basara et al, where there was bilateral isolated breast involvement.⁵

Imaging findings of ECD in the breast vary considerably. Most reported descriptions of mammographic findings are non-specific with two cases showing irregular speculated masses. However, all sonographic examinations showed irregular lobulated hypoechoic lesions. In the five reported cases where CT scans were performed, the lesions were diffusely infiltrative and heterogeneous associated with skin thickening and calcifications, except for Furuta et al where the lesion appeared as a well-defined rounded mass.⁴ Unfortunately, MRI studies, which varied in their findings, were performed in only two cases.

In our case, the breast lesions were indeterminate and were considered BIRAD 4 lesions. Lymphoma was suggested at first due to the diffuse nature of the disease, but was discounted after the histopathology results. Based on the histocytological findings, a reactive process such as granulomatous mastitis, fat necrosis and panniculitis were first considered, but the lack of traumatic history and absence of inflammatory signs on examination made these entities unlikely. Other histiocytic infiltrative diseases like Langerhans histiocytosis and Rosai-Dorfman disease were excluded based on the immunohistochemistry tests.^{1,2-6} Histiocytoid variant of inva-

sive lobular carcinoma was the main differential diagnosis. However, the distinctive skeletal radiologic features lead to the diagnosis of ECD.

The rarity and variable presentation of this disease usually leads to delayed diagnosis, which combined with a lack of definite treatment leads to high mortality rates

from associated complications. In conclusion, ECD in the breast is very rare and its imaging findings vary considerably. Other systemic imaging findings combined with the histopathological findings facilitate the final diagnosis. B-Raf inhibitors like vemurafenib are promising new treatments for ECD patients with BRAF mutation.

REFERENCES

1. Roei D Mazor, Mirra Manevich-Mazor, Yehuda Shoenfeld. Erdheim-Chester Disease: a comprehensive review of the literature. *Orphanet J Rare Dis.* 2013;8:137.
2. Giulio Cavalli, Barbara Guglielmi, Alvise Berti, Corrado Campo Chiaro, Maria Grazia Sabbadini, Lorenzo Dagna. The multifaceted clinical presentations and manifestations of Erdheim-Chester disease: comprehensive review of the literature and of 10 new cases. *Ann Rheum Dis.* 2013;72:1691-5.
3. Ferrozzi F, Bova D, Tognini G, Zuccoli G. Pseudotumoral bilateral involvement of the breast in Erdheim-Chester disease: CT appearance. *J Comput Assist Tomogr.* 2000;24:281-3.
4. Furuta T, Kiryu S, Yamada H, Hosoi M, Kurokawa M, Morikawa T et al. Erdheim-Chester disease with an 18F-fluorodeoxyglucose-avid breast mass and BRAF V600E mutation. *Jpn J Radiol.* 2014;32:282-7.
5. I. Basara, E. Yavuz, P. Balci, E.B. Tuna, I. Sari. Erdheim Chester disease presented isolated breast and axillary involvement. *JBR-BTR.* 2015;98:82-4.
6. Guo S, Yan Q, Rohr J, Wang Y, Fan L, Wang Z. Erdheim-Chester disease involving the breast-a rare but important differential diagnosis. *Hum Pathol.* 2015;46:159-64.
7. Provenzano E, Barter SJ, Wright PA, Frouhi P, Allibone R, Ellis IO. Erdheim-Chester disease presenting as bilateral clinically malignant breast masses. *Am J Surg Pathol.* 2010;34:584-8.
8. Barnes PJ, Foyle A, Haché KA, Langley RG, Burrell S, Juskevicius R. Erdheim-Chester disease of the breast: a case report and review of the literature. *Breast J.* 2005;11:462-7.
9. Andrade VP, Nemer CC, Prezotti AN, Goulart WS. Erdheim-Chester disease of the breast associated with Langerhans-cell histiocytosis of the hard palate. *Virchows Arch.* 2004;445:405-9.
10. Tan AP, Tan LK, Choo IH. Erdheim-Chester Disease Involving Breast and Muscle: Imaging Findings. *AJR Am J Roentgenol.* 1995;164:1115-7.