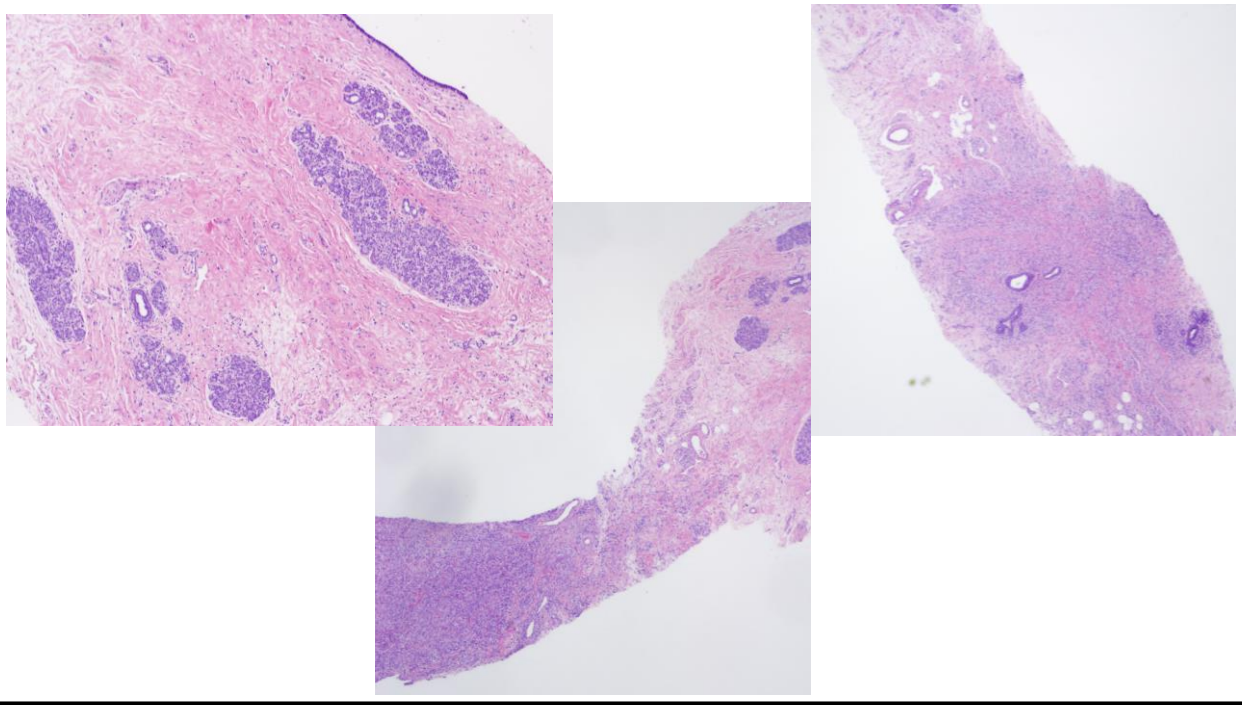
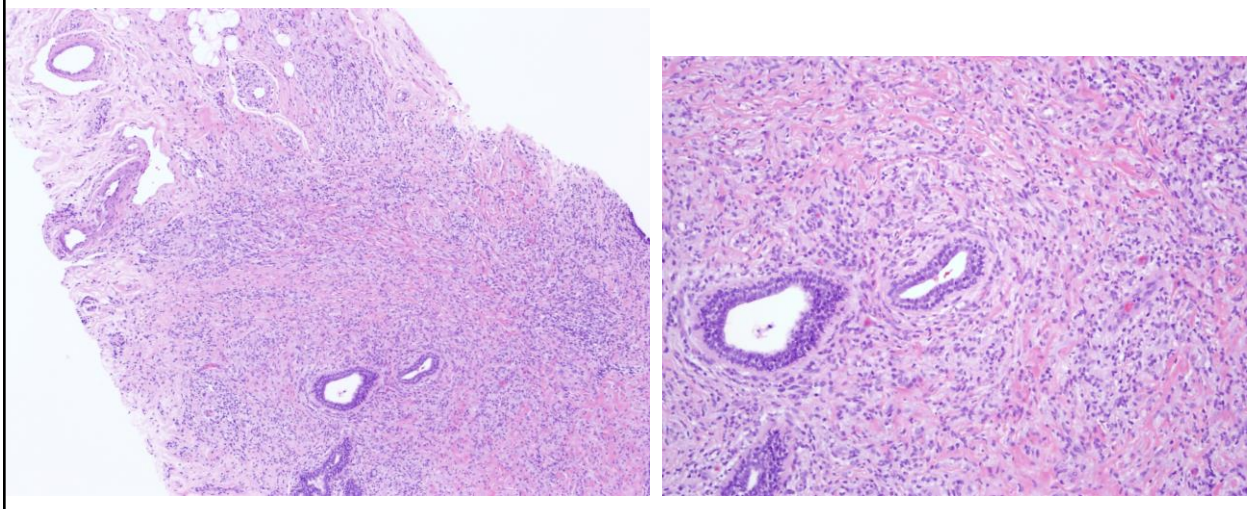
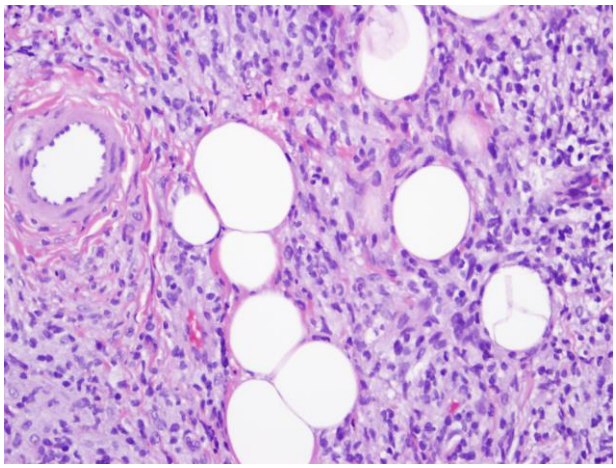
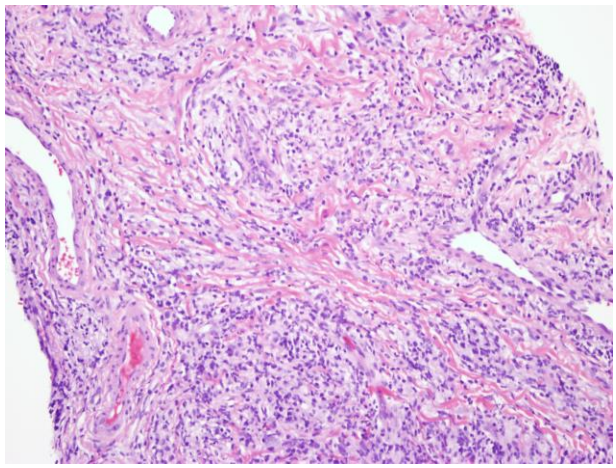
Case discussion

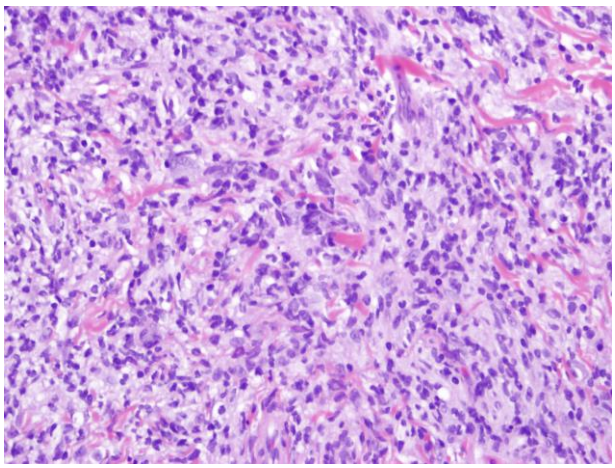
Patient details

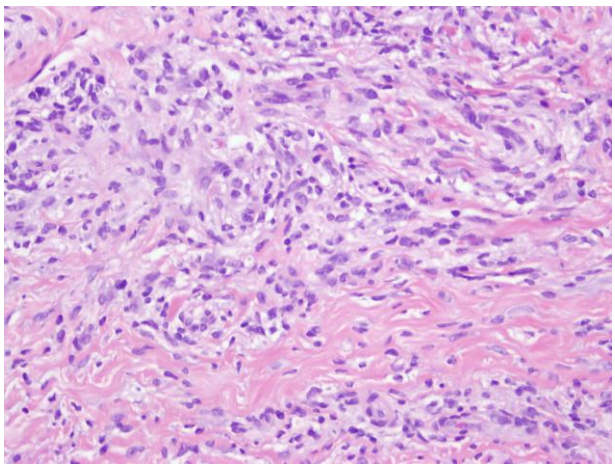


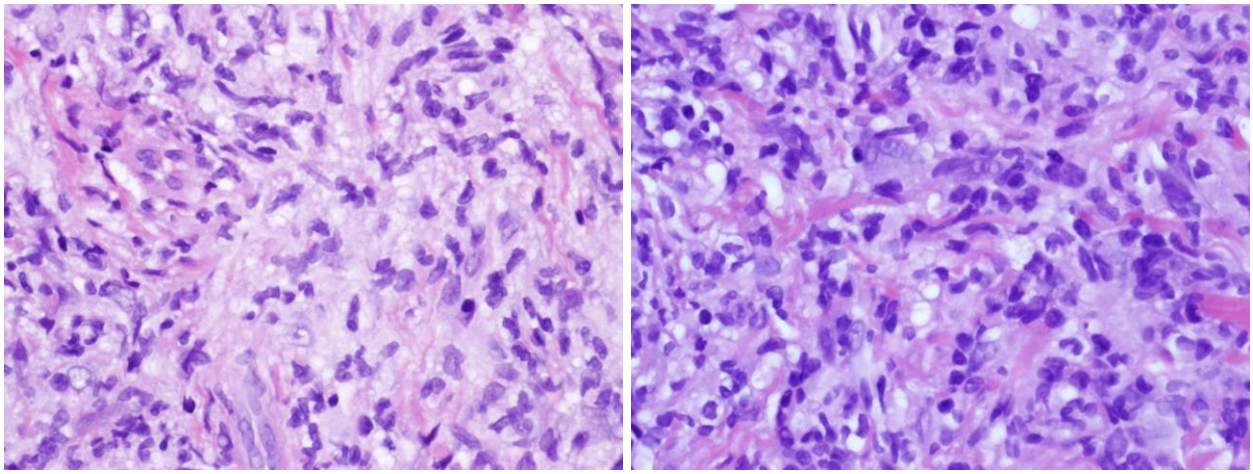








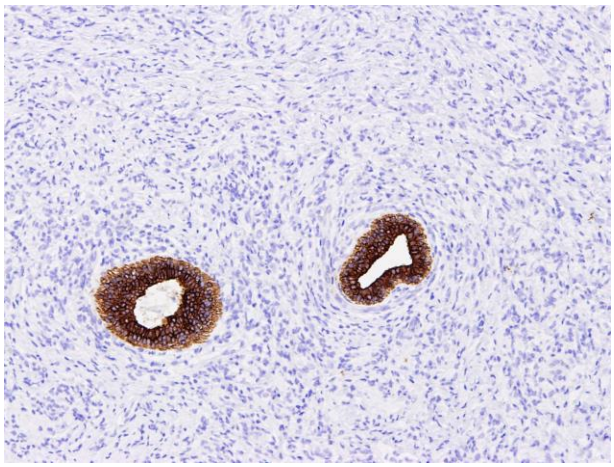


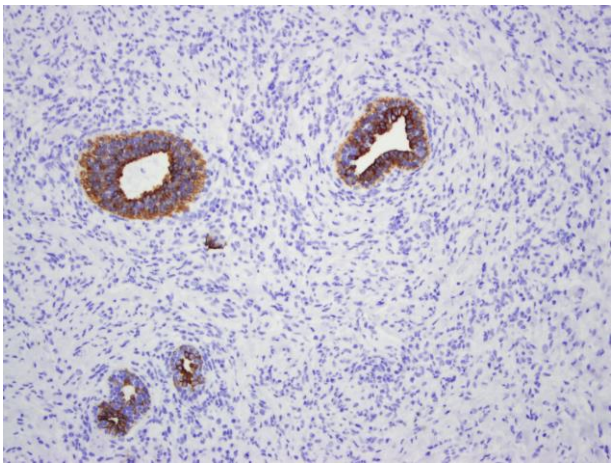


Differential Diagnosis

- Unusual carcinoma – “fibromatosis like” and other low grade metaplastic carcinomas
- Myofibroblastoma
- Fat necrosis
- Granulomatous inflammation
- Other lesions

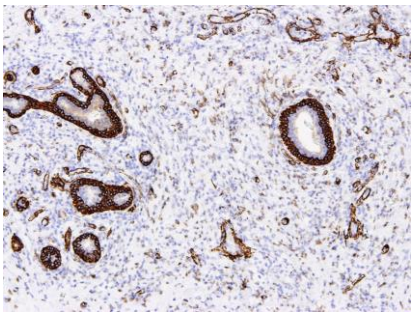
Keratins

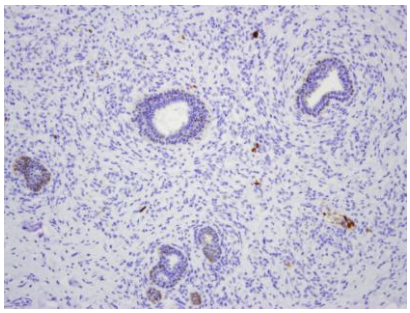


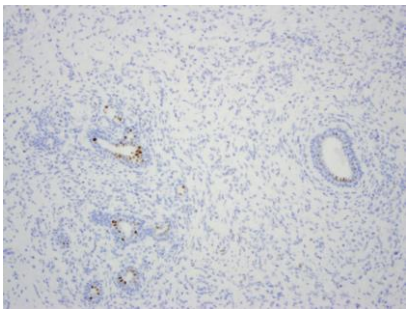


Differential Diagnosis

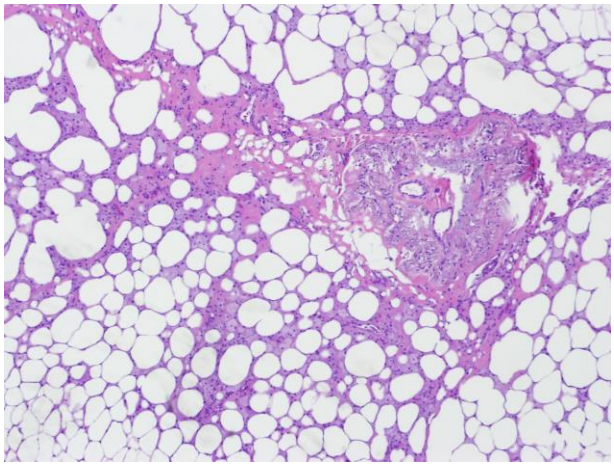
- Unusual carcinoma
- Myofibroblastoma

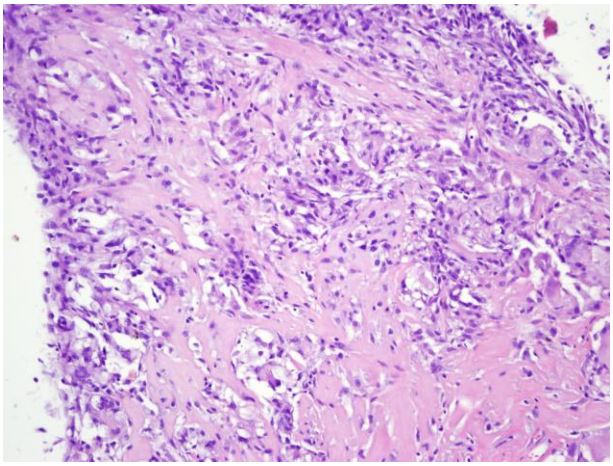






Fat necrosis



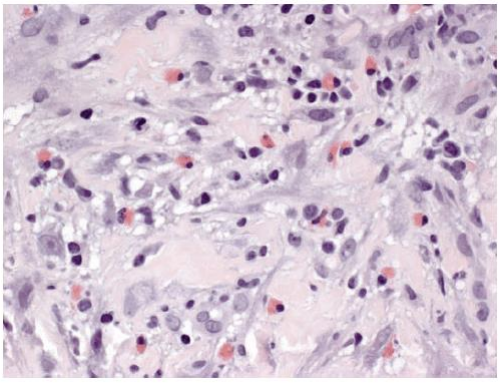


Granulomatous inflammation

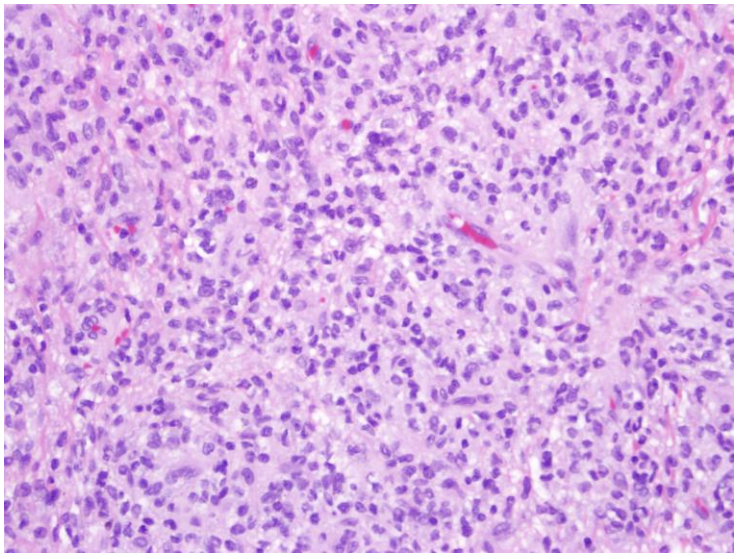
- Tuberculosis
- Fungal
- Post lactational inflammation
- Parasites
- Idiopathic

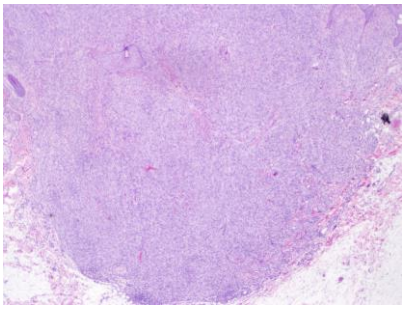
Idiopathic Granulomas – Indiana

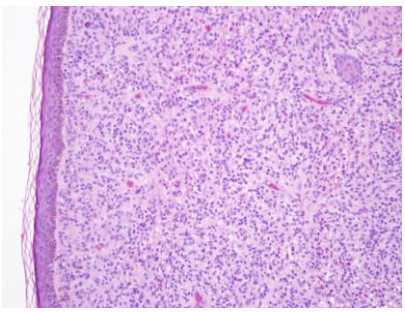
All seven biopsy specimens were sent to CDC for additional histopathologic evaluation.† This testing confirmed IGM in all seven patients, each with noncaseating granulomas, acute and chronic inflammation, and absence of foreign body material in breast biopsy tissue. Eosinophilia was noted in specimens from five patients (Figure). Special stains revealed no evidence of mycobacteria, spirochetes, other bacteria, fungi, or trypanosomes. Immunohistochemistry (IHC) on the tissue specimens for mycobacteria and *Trypanosoma cruzi* were negative. IHC using polyclonal antibodies for *Corynebacterium diphtheriae* showed rare epithelial staining in four of seven cases, although this test has unknown specificity. However, polymerase chain reaction (PCR) assays on DNA extracts from the formalin-fixed tissues using broad-range panbacterial 16S rDNA primers were negative.



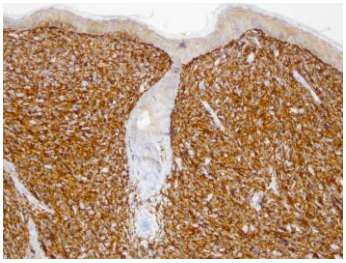
Additional history - Skin lesions

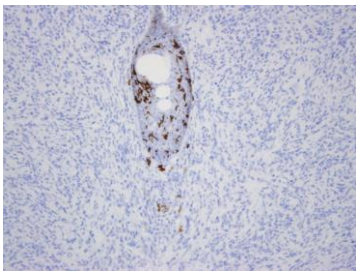


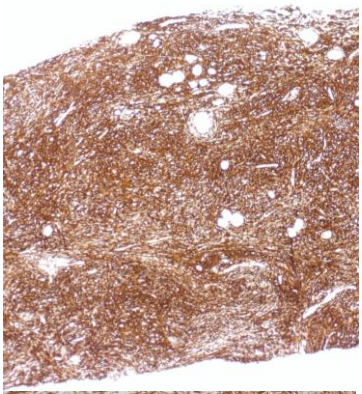


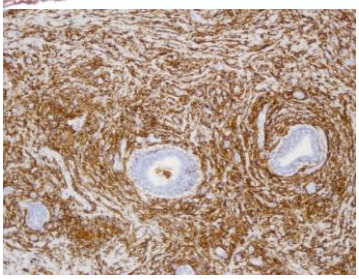


Diagnostic IHC CD68+/CD1a-



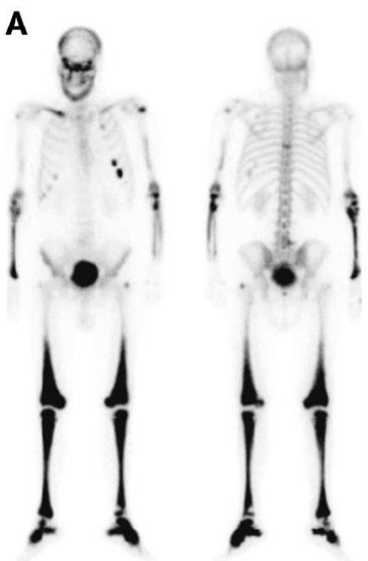






Erdheim Chester Disease

- Disease of adults (M>F)
- Non –Langerhans cell histiocytosis
- Bone involvement is classical
  - Bilateral symmetric long bone involvement
- CNS involvement is prognostic
- Other organs variably involved.



Erdheim Chester Disease 2

Table 1
Organ involvement, signs and symptoms and imaging features of Erdheim-Chester disease. The absolute frequency of each organ involvement is indicated parenthetically. Among the imaging features, those underlined are nearly pathognomonic for Erdheim-Chester disease.

Organ involvement	Signs and symptoms	Imaging features
Skeletal (90%)	Invalidating bone pain (especially lower limbs)	Plain radiography: symmetrical cortical osteosclerosis of the diaphysis and/or metaphysis of long bones ^{99m}Tc-bone scintigraphy: symmetrical uptake of lower limbs
Neurological (50%)	Diabetes insipidus Cerebellar ataxia Panhypopituitarism Papilledema	Brain MRI with contrast: Gadolinium-enhancing lesions; involvement of dentate nuclei of cerebellum and pons
Orbital (25%)	Exophthalmos Diplopia Visual impairment	Orbital MRI with contrast: intraorbital T2-hypointense enhanced pathological tissue
Endocrine (5%)	Hyperprolactinemia Gonadotropin insufficiency Deficiency of IGF	Brain MRI with contrast (detailed examination of sella turcica): enlargement and abnormal enhancement of pituitary gland and stalk
Renal (30%)	Dysuria Abdominal pain Chronic kidney failure Nephrovascular hypertension	Abdomen CT scan/MRI: retroperitoneal and perirenal space infiltration ("hairy kidney"); hydroureteronephrosis Angio-CT or Doppler-US Renal arteries compression
Pulmonary (20%)	Cough Chest discomfort	Spirometry: Restrictive pattern with normal or reduced DLCO High-resolution CT Chest: Interstitial infiltrates, ground-glass opacities, centrilobular opacities
Cardiovascular (45%)	Pericardial pain Cardiac tamponade Cardiac failure Myocardial infarction	Cardiac MRI and cine-MRI: pseudotumoral lesion of the right atrium or right atrio-ventricular sulcus; pericoronarial infiltration; circumferential infiltration of the thoracic and abdominal aorta ("coated aorta")
Skin (30%)	Xanthelasma Xanthoma	
Constitutional (22%)	Fever Fatigue Weight loss	

Erdheim-Chester disease involving the breast—a rare but important differential diagnosis

Shuangping Guo PhD [a], Qingguo Yan PhD [a], Joseph Rohr PhD [b], Yingmei Wang MD [a], Linni Fan PhD [a], Zhe Wang PhD [a,*]

Table 2 Erdheim-Chester disease involving breast as reported in English literature

Report	Sex/age	Location	Clinical features	Outcome
Provenzano et al [4]	Female/78	Bilateral breast masses	Associated cerebrovascular disease with carotid artery stenosis	Progressive changes in the breast and new masses in the axillae at 28 mo
Tan et al [5]	Female/59	Multisystem disease involving the breast	Associated lesions in pericardium, retroperitoneum, kidneys, and abdominal wall	Stable disease after treatment with combination chemotherapy
Andrade et al [6]	Female/40	Right breast lump	History of Langerhans cell histiocytosis of the hard palate 1 y previous	Corticosteroid therapy. Patient underwent an autologous hematopoietic stem cell transplant. ECD recurred at 3 y with additional orbital and retroperitoneal involvement
Barnes et al [7]	Female/49	Right breast mass	Developed further breast lesions. Developed systemic and neurologic symptoms at 3 y	No response to prednisolone. Significant reduction in the lesions' masses with cladribine
Ferrozzi et al [8]	Male/60	Enlargement of both breasts with gynecomastia	Heterogeneous enlargement of both breasts and mixed sclerotic and lytic lesions of both tibiae	Refused treatment and follow-up
Furuta et al [9]	Female/49	Left breast mass	Multiple osteosclerotic lesions in the metaphysis and epiphysis of the femora and tibiae and left breast mass	Received symptomatic treatment without systemic corticosteroids, immunotherapy, or chemotherapy
Present case	Female/61	Right breast mass	Abdominal wall mass 1 y previous. Further developed multiple masses/nodules in right breast, abdominal wall, and cerebellum bilaterally	Total resection of the lump. The patient was treated with interferon α and remained alive at 2 years

Erdheim Chester Disease 4

A B S T R A C T

Erdheim-Chester disease (ECD) is rare form of non-Langerhans cells histiocytosis with multiorgan involvement. Individuals are more frequently affected in their fifth decade and there is a slight male prevalence. Recent studies have demonstrated that ECD patients bare mutations in the proto-oncogene BRAF (and more rarely in other genes involved in the MAPK activation pathway), suggesting a critical role of this pathway in the pathogenesis and a possible clonal origin of the disease. Clinical manifestations are extremely protean and virtually every organ system can be affected. The most common clinical features include skeletal involvement with typical bilateral osteosclerotic lesions of long bones of the lower limbs, diabetes insipidus, cardiovascular involvement with circumferential thickening of the aorta ("coated aorta"), and retroperitoneal fibrosis ("hairy kidney"). Cardiovascular and central nervous system (CNS) involvement are associated with the worst prognosis. Biopsy is necessary to establish a definite diagnosis with the identification of CD68 +/CD1a −/S100 − foamy histiocytes. Currently, interferon-α is the first-line treatment in ECD, as it has been clearly demonstrated to increase overall survival. Anakinra and infliximab have also led to encouraging results and should be taken into consideration when treatment with interferon-α fails. More recently, the BRAF-inhibitor vemurafenib has been used in small groups of ECD patients with optimal efficacy in all treated cases. Nevertheless, its adverse effects and the scanty data on its long-term efficacy and safety still discourage its use as a first-line option. Further studies are still warranted to better understand and treat this neglected and overlooked disease.

Campochiaro et al Eur J Int Med 2015