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ERDHEIM CHESTER DISEASE PRESENTED ISOLATED BREAST AND AXILLARY INVOLVEMENT

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Erdheim-Chester disease (ECD) is a rare non-Langerhans cell histiocytosis of unknown aetiology. The most common sites of involvement are the long bones, skin, orbit, pituitary and retroperitoneal space. Isolated breast involvement is rare in the literature. ECD of the breast has been rarely reported. ECD should be considered in the differential diagnosis of histiocytoid breast lesions, including fat necrosis and histiocytoid invasive mammary carcinoma. In this case report, we present an unusual presentation isolated breast involvement of ECD with radiological and histopathology findings.

Key-word: Liopogranulomatosis.

Erdheim-Chester disease (ECD) is a rare non-Langerhans cell histiocytosis. The aetiology of this disease is unknown (1, 2). The disease was first described as "lipoid-granulomatous" in two patients by William Chester and Jakob Erdheim in 1930 (2). Histologically, ECD is characterized by infiltration by foamy non-Langerhans cell histiocytes, Touton-type giant cells and mixed lymphoid infiltrates (3). The commonest involvement sites are bone, skin, orbit, pituitary, retroperitoneal space, pericardium, and lung (1, 2). Perivascular region, central nervous system, thyroid, testis, liver, and spleen are the rarer sites of ECD involvement (4). The symptoms of the disease include bone pain, diabetes insipidus, exophthalmos, dyspnoea, and neurologic symptoms. The prognosis of the disease depend on extend and severity of extraskeletal findings. Of 57% patients die secondary to pulmonary or cardiac involvement (2). Isolated breast involvement in ECD has been rarely described. To the best of our knowledge, there are only a few case reports of ECD of the breast. We present a case of ECD presenting as bilateral clinically malignant breast and axillary masses, with imaging findings suggestive of bilateral breast cancer.

Case report

In September 2013, a 62-year-old woman presented with palpable breast masses in the upper outer quadrant of both breasts and axillar regions. She did not have any trauma and did not report nipple discharge. The patient had been admitted to the hospital with a complaint of nodular lesions on her eyelids 6 years ago. At that time these lesions were evaluated and biopsy was performed. Histopathology result was xanthomatous granuloma. In the meantime she did not have any specific complaints except cervical and lumbar pain. Blood and biochemical examinations, abdominal ultrasonography (US), cervical and lumbar magnetic resonance imaging (MRI) examinations were normal. In radiology department of our institute, the patient was evaluated with mammography. There were irregular opacities on both outer quadrants and axillary regions (Fig. 1A). After that she was examined with US. In US evaluation there were multiple, hypoechoic, macrolobulated solid nodular lesions. Also there were hypoechoic nodular lesions with hyperechogenic area which were thought as central hilum of lymph nodes at her both axillary regions (Fig. 1B). After these evaluations the patient was investigated with MRI examination. On MRI images there were well defined but irregular lesions in her both breasts extending to the axillary regions (Fig. 1C). The lesions were located on the anterior part of pectoral muscle and they were separated from the muscle. After contrast material administration, the lesions were enhanced and in pharmacokinetic evaluations type 2 curves were obtained (Fig. 1D). The lesions had diffusion restrictions in diffusion weighted MRI (Fig. 1E).

After these evaluations the patients was referred to biopsy procedure and with 18G needle, tru-cut biopsy was applied to the lesions on her axillary regions. In the histopathology evaluation, the histiocytes had positive staining with antibodies for CD68 and were negative for S-100 protein (Fig. 2). After clinic, radiologic and histopathology evaluations of breasts, additionally systemic radiological and clinic evaluations were applied but there was no sign of ECD involvement in any other part of the body. As a result a diagnosis of isolated breast involvement of ECD was then proposed.

Discussion

ECD is an extremely rare disease of unknown aetiology, with distinct clinic, pathologic, and radiological findings in the absence of detectable serum lipid abnormalities. The clinical manifestations of ECD are not well defined, but men and women in the 50th through 70th decades of life appear to be affected (2). The clinical presentation is largely determined by the sites of involvement as a result of mass lesions, local pain, or functional compromise. Usually the most commonly reported symptoms are juxtaarticular bone pain of knee and ankle. There is no response to analgesics. Other symptoms include exophthalmos, diabetes insipidus, constitutional symptoms, retroperitoneal or ureteric/renal involvement (2). However less frequently symptoms are neurologic symptoms, body cavity effusions, cutaneous xanthomas and diffuse interstitial lung involvement (2). Isolated breast involvement by ECD is exceedingly rare and has rarely been described in the literature (3, 5, 6). There are only six cases published in the English literature (7). Our case is one of the few cases in the literature.

In histological determination, there are mainly xanthomatous non-Langerhans histiocyte cells. The histiocytes in this disease do not

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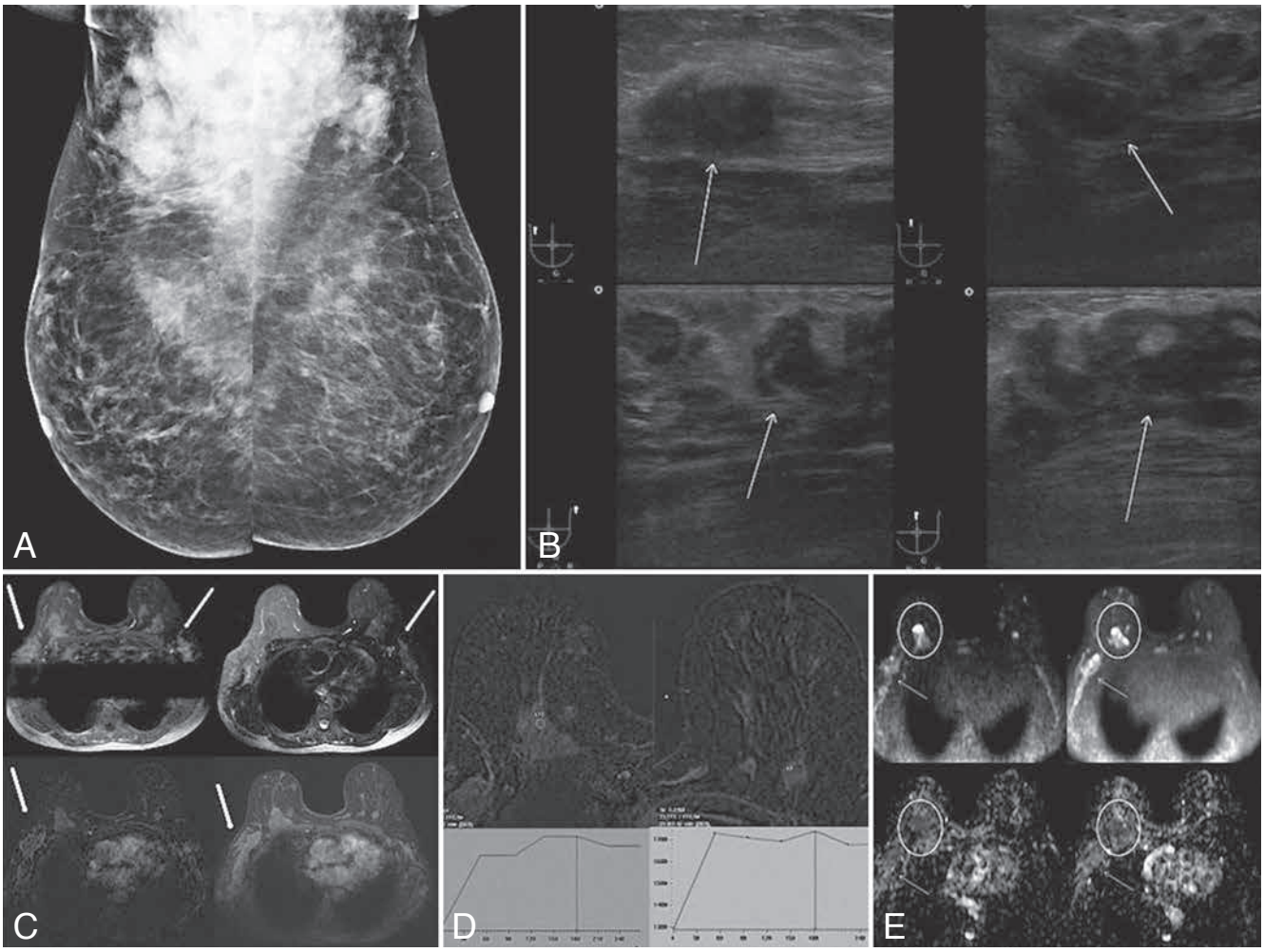

Fig. 1. — A. On mammographic examination of right and left breasts, there are irregular lesions extending from both upper outer quadrant to axillar sites. B. On ultrasonograhic examination, the images at the upper are breast lesions, and the lesions at the lower part are axillar lesions. The breast lesions are hypoechoic, solid lesions with irregular contours. There are hyperechogen areas at the center of the lesions which were thought as hilum (arrows). C. On MR views, the images at the upper part are, axial fat saturated T2 weighted and the images at the lower part are axial post-enhanced subtracted images. There are irregular, enhanced lesions at the anterior of bilateral pectoral muscles extending to both axillar parts (arrows). D. There are type 2 pharmacokinetic curves obtained from the breast lesions. E. At the upper part there are b-1000 diffusion weighted images and at the lower part apparent diffusion coefficient images. There are marked diffusion restriction at the lesions (Circles and arrows).

express CD1a or S-100 protein (but may display weak and focal positivity by immunohistochemistry for S-100 protein), and lack intra cytoplasmic Birbeck granules ultra-structurally. The cells are typically positive for CD68 and lysozyme (2, 8, 9). The xanthomatous cells are diffusely infiltrative, apparently resulting in collagenous fibrosis of tissues, and are usually associated with sparse lymphocytic infiltrates and Touton-type giant cells. All cells lack atypical cytological features in the lesion (2, 3, 8, 9). The symptoms of the disease such as bone pain, pathologic bone fractures and pancytopenia depend on replacement of the marrow space by xanthomatous histiocytes typically. The course of disease generally reflects the extend and sites of extra skeletal involvement (2, 9).

In our case, the breast lesions were radiological intermediate especially with axillary involvements. After all the radiologic evaluations, the lesions were accepted as BIRADS 4 lesions. In breast lesions, the differential diagnosis on histology includes fat necrosis, panniculitis such as lupus profundus mastitis, other histiocytic lesions including Langerhans cell histiocytosis and Rosai-Dorfman disease, and infection. Other lesions that can mimic histiocytes, particularly the histiocytoid variant of invasive lobular carcinoma, must be excluded (10). In fat necrosis, there should be a trauma history and architectural skin distortion of the breast. Rosai-Dorfman disease is a rare histiocytic proliferation, primarily nodal-based but with extra-nodal involvement, including the breast (11). It is represented by a histiocytic proliferation with pale acidophilic cytoplasm, mildly atypical round vesicular nuclei and so-called lymphocytophagocytosis. The histiocytes are strongly positive for S100-protein as just the opposite of ECD. The most important differential diagnosis is the histiocytoid variant of invasive lobular carcinoma (12, 13). In this pathology, additionally there can be cutaneous metastasis such as eyelids mimicking xanthelasmas of ECD. Helpful diagnostic features favouring ECD versus histiocytoid carcinoma both in the primary and metastatic depositories are the lack of nuclear atypical in the former as well as absence of the immune reactive for cytokeratin (13).

Immune suppressive drugs, prednisolone can be the first option in

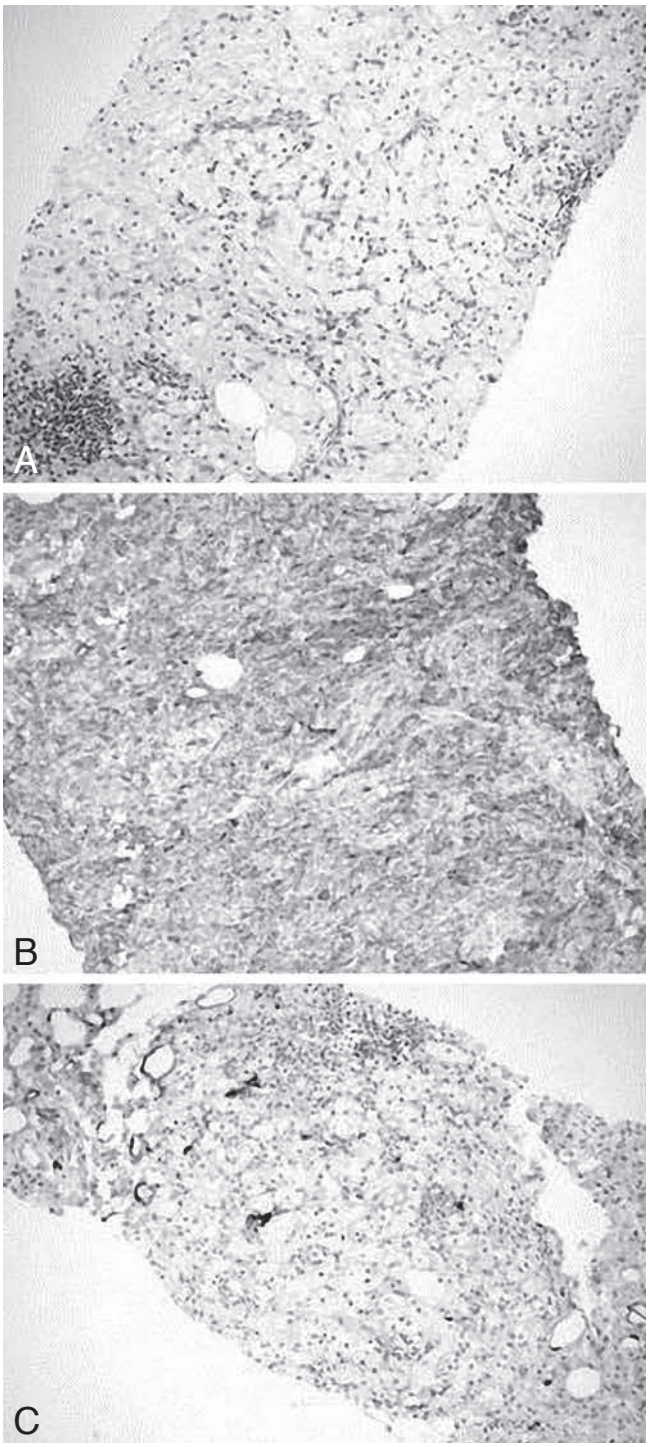

Fig. 2. — A. Core biopsies show extensive infiltration by foamy histiocytes with no nuclear atypical, and a patchy mature lymphoid infiltrate (H&E x20). B. The histiocytes are strongly positive for CD68, and C. negative for S100.

medical treatment. Furuta et al reported tyrosine kinase inhibitors for cases with BRAF V600E mutation (7). However, our patient receipt immune suppressive medical treatment, the lesions regressed and is followed-up period at our department.

In atypical breast lesions, a high grade of suspicion is needed to establish the correct diagnosis. It is important to keep in mind that patients harbouring systemic illness and breast lumps should be carefully investigated to exclude a breast involvement by the generalized disease. Although, radiological evaluations are helpful in diagnosis, histopathology evaluation should be applied for correct diagnosis.

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