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Rosai-Dorfman disease confined to the breast

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Abstract Rosai-Dorfman disease (also known as *sinus histiocytosis with massive lymphadenopathy*) is an uncommon, idiopathic, benign histiocytic lesion. It usually involves the cervical lymph nodes and, less commonly, extranodal sites. Involvement of the breast is rare, with only 17 cases reported in the English literature to date. Here we describe 3 new patients with extranodal Rosai-Dorfman disease in the breast. All 3 patients—aged 45, 53, and 54 years—presented with solid breast lesions that were detected on screening mammography and had no clinical history of Rosai-Dorfman disease or radiographic evidence of extramammary involvement. Initial diagnoses were accomplished by needle core biopsy in the one case and excisional biopsy in the other two. We present the histopathologic findings and follow-up of each patient and conduct a literature review of mammary Rosai-Dorfman disease with emphasis on its differential diagnosis. Because Rosai-Dorfman disease frequently mimics invasive breast carcinoma in its clinical presentation and radiographic appearance—and can mimic other benign or malignant histiocytic lesions microscopically—awareness and appropriate diagnosis of this entity are essential for proper treatment.

Keywords: Rosai-Dorfman; Extranodal; Breast; Literature review

1. Introduction

Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease [RDD]) is an uncommon idiopathic process initially described by Lampert and Lennert in 1961 but not recognized to be a distinct entity until 1969 by Rosai and Dorfman [1]. Although it usually involves lymph nodes, the disease can have extranodal manifestations; and in rare cases, only extranodal involvement is seen. Rosai-Dorfman disease is usually self-limiting or responds well to therapy, but rare fatal cases with multiorgan involvement have been reported. Simultaneous nodal and extranodal disease with visceral involvement carries a worse prognosis. Usual sites of extranodal disease include skin, soft tissue, bone, upper respiratory tract, and orbital adnexa. Mammary involvement by RDD is very uncommon, and RDD that is confined to the breast is rarer still. Here we present 3 new cases of extranodal RDD confined to the breast. All were detected by routine screening mammography and ultimately underwent surgical excision.

Given the generally benign prognosis of RDD, the main clinical significance of extranodal disease involving breast lies in its propensity to mimic invasive carcinoma, both clinically and radiographically. In addition, it needs to be differentiated histologically from other benign and malignant histiocytic and occasionally nonhistiocytic breast lesions so that appropriate management can be provided.

2. Materials and methods

The excised breast tissue was fixed in neutral-buffered formalin, then processed in a routine manner and

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embedded in paraffin. Histologic sections were stained with hematoxylin and eosin. Immunohistochemical staining was performed on the formalin-fixed, paraffin-embedded tissue using heat-induced epitope retrieval. Staining by an avidin-biotin method was performed on an automated immunostainer (Ventana Medical Systems, Tucson, AZ). Appropriate positive and negative controls were reviewed. The antibodies used are listed in Table 1.

Molecular studies for T-cell receptor β (TCR-β) and γ (TCR-γ) chain gene rearrangements and B-cell immunoglobulin heavy chain (IgH) gene rearrangements were performed using polymerase chain reaction assay on genomic DNA extracted from a paraffin-embedded tissue block containing the lesion. The primers used for TCR-β and TCR-γ were a mixture of family-specific multicolor fluorescent-labeled V primers and unlabeled J primers [2]. For the IgH gene, V primers derived from framework 1, framework 2, and framework 3 regions in combination with a mixture of fluorescent-labeled J primers were used.

3. Results

3.1. Case 1

A 53-year-old African American woman underwent screening mammography, which detected a 1.5-cm ill-defined, high-density mass at the 7-o'clock position in the left breast (the radiographic features of this case have been previously reported [3]). Although ultrasound-guided fine needle aspiration (FNA) was initially interpreted as reactive lymphoid hyperplasia, a needle core biopsy was diagnostic of RDD. Staging studies found no evidence of extramammary disease, and bone marrow biopsies were negative for RDD and other lymphoproliferative disorders. The lesion remained stable for nearly 4 years, when it was noted on chest computed tomography scan to measure 2 cm. Needle-localized excisional biopsy was then undertaken.

The excision specimen contained an ill-defined, solid, tan, fibrous-appearing lesion measuring 2.0 cm in greatest dimension. It appeared to merge imperceptibly with the adjacent breast parenchyma (Fig. 1A, B). A corresponding specimen radiogram showed an irregular, dense mass infiltrating the surrounding breast tissue (Fig. 1C). A postbiopsy radiologic marker clip was found within reexcised tissue from the inferior margin.

Histologic sections showed sheets of large histiocytes with abundant pale cytoplasm and round to oval vesicular nuclei with prominent nucleoli. A dense lymphocytic infiltrate was present with a minor plasma cell component (Fig. 2A). Occasional histiocytes showed lymphophagocytosis (emperipolesis) (Fig. 3A). The surrounding breast parenchyma showed dense fibrous bands in a vaguely radial arrangement with scattered ducts. Other than focally prominent fibrosis, the background breast parenchyma had no significant histologic abnormality.

Immunohistochemical stains showed the infiltrating histiocytes to be positive for S-100 and CD68 and negative for CD1a, a pattern characteristic of RDD (Fig. 4). Further ancillary studies were undertaken to rule out a lymphoid malignancy. CD3 and CD20 stains showed a mixed population of T- and B-cells. Stains for κ and λ light chains highlighted polytypic plasma cells and did not preferentially label the B-cells. In addition, polymerase chain reaction was performed on genomic DNA extracted from paraffin-embedded tumor tissue. There was no evidence of clonal TCR-β or TCR-γ gene rearrangements or clonal IgH gene rearrangement.

At 5 years 10 months of total clinical follow-up, there has been no disease recurrence in the breast or progression to systemic disease.

3.2. Case 2

A 45-year-old African American woman with a history of type 2 diabetes mellitus was seen after screening mammography detected an ill-defined, solid lesion in the 9-o'clock position of the left breast. Needle-localized excisional biopsy

Table 1
Antibodies used for immunohistochemical analysis

Marker	Clone	Dilution	Manufacturer	Epitope retrieval
S-100	A6	1:40	Biogenex, San Ramon, CA	No pretreatment
CD1a	O10	Prediluted	Immunotech, Marseille, France	Citrate, HIER
KP1 (CD68)	KP1	1:500	Dako, Carpenteria, CA	Citrate, HIER
CD3	F7-2.38	1:10	Dako	TRIS:EDTA
L26 (CD20)	L26	1:100	Dako	TRIS:EDTA
κ	Polyclonal	1:20,000	Dako	Protease XIV
λ	Polyclonal	1:20,000	Dako	Protease XIV
Pancytokeratin				Protease XXIV
AE1/AE3	AE1/AE3	1:50	Dako	
CAM 5.2	CAM 5.2	1:50	Becton Dickinson, San Jose, CA	
CK MNF116	MNF116	1:50	Dako	
CK 8 and 18	Zym5.2	1:25	Zymed, San Francisco, CA	

HIER indicates heat-induced epitope retrieval.