

Cutaneous Rosai Dorfman disease

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Abstract

Rosai Dorfman disease (sinus histiocytosis with massive lymphadenopathy) is a rare polyclonal histiocytic disorder of unknown origin. Extra-nodal involvement is seen in about 43% of cases. We report the occurrence of cutaneous Rosai Dorfman disease in a 32-year-old woman in the absence of demonstrable lymph node involvement. As the skin manifestation of Rosai Dorfman disease may precede systemic involvement, it is important to distinguish this disease entity from other types of histiocytic proliferations. Accurate diagnosis enables close follow up of the patient for subsequent development of local recurrence or systemic involvement.

Introduction

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy (SHML), is a polyclonal histiocytic proliferation, characterized by large histiocytes with a distinctive morphology commonly exhibiting emperipolesis (1, 2). It was first recognized as a distinct clinicopathological entity by Rosai and Dorfman in 1969(1). Although RDD typically affects lymph nodes, extra-nodal involvement has been described (1,2,3). This report describes RDD occurring in a 32-year-old woman who presented with a single subcutaneous nodule in the nape of the neck, without lymph node involvement.

Case Report

A 32-year-old woman presented with a single non-tender subcutaneous nodule in the nape of the neck of five-months duration. The nodule gradually enlarged, reaching a maximum size of 3.5cm in diameter. The lump was immobile and firm with ill-defined margins. There were no accompanying constitutional symptoms, lymphadenopathy, hepatosplenomegaly or other subcutaneous lumps. The white blood cell count was $10.5 \times 10^9/\text{mm}^3$ with a relative lymphocytosis. Her past medical history was unremarkable. The lump was excised under general anaesthesia. Convalescence was uncomplicated.

Histologic examination of the lesion under scanning magnification revealed a thin epidermis with a narrow rim of relatively well-preserved underlying dermis. The dominant pathologic process involved the lower dermis and subcutaneous tissue, which showed blue strips and nodules of lymphoid cells alternating with pale staining bands of cells displaying a vague sinusoid like pattern (Figure 1). Examination of the pale staining areas at high magnification revealed the distinctive histiocytes of Rosai-Dorfman disease. The histiocytes were three to six times larger than the conventional histiocytes with centrally placed, round, vesicular nuclei containing prominent nucleoli. The cytoplasm was watery and voluminous with an occasional foamy appearance. There were admixed plasma cells and occasional eosinophils. A striking feature of the infiltrate was the presence of lymphophagocytosis (emperipolesis) by the histiocytes (Figure 2). Occasional scattered large atypical nuclei were observed in some areas.

Immunoperoxidase stains were performed on formalin fixed paraffin embedded tissue using Streptavidin Biotin Complex method. The large histiocytic cells showed strong cytoplasmic and nuclear staining with S-100 protein. (Dako, 1:100 dilution, microwave antigen retrieval).

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This immunostain accentuated the sinusoid like pattern and the individual histiocytes were well highlighted with the emperipolesis phenomenon becoming obvious.

Discussion

Involvement of extra-nodal sites is seen in about 43% of cases of RDD. This involvement is usually seen in conjunction with lymph node involvement, although RDD occasionally affects extra-nodal tissue alone. Isolated skin involvement may be seen in about 40% of extra-nodal cases, as in the current case. For those cases without nodal disease, the lack of lymphadenopathy makes the term 'sinus histiocytosis with massive lymphadenopathy' inappropriate, and the eponym Rosai-Dorfman disease is now being applied to this disorder with increasing frequency. In about 60% of cases, more than one extra-nodal site is involved, including in order of frequency, skin (12%), the sino-nasal region (11%), soft tissue (9%), eyelid/orbit (8%), bone (8%), salivary gland (5%), and the central nervous system (5%)(4). Patients with skin involvement usually present with multiple, papular or nodular lesions, although solitary lesions are seen in about one third of cases as in our case.

The characteristic pattern of infiltrate with pale staining bands alternating with dark staining nodules and bands of lymphoid aggregates is highly suggestive of RDD in the skin. Emperipolesis though present in this case, is uncommon and is not necessary for the diagnosis.

Due to the presence of large numbers of foamy macrophages, plasma cells and eosinophils, the differential diagnosis should include non-specific or specific chronic inflammatory reactions. Mycobacterial spindle cell pseudotumour and histioid leprosy were considered in this regard, and excluded due to negative Ziehl-Neelson and Wade Fite stains respectively. Xanthogranulomatous inflammation which is usually caused by chronic bacterial infection only rarely occurs in soft tissue; the most common sites being kidney and gall bladder(1).

The histiocytes of xanthogranulomatous inflammation are much more smaller than those of Rosai Dorfman disease. Inflammatory pseudotumour is composed of an admixture of spindle or polygonal cells and lymphocytes in varying proportions. The spindle cells may show a dense storiform or fascicular arrangement with relatively few inflammatory cells in-between, or there may be extensive inflammatory infiltration. Large histiocytes with emperipolesis are not seen in inflammatory pseudotumour.

The presence of scattered large atypical nuclei as seen in our case, does not exclude the diagnosis of Rosai-Dorfman disease. Histiocytic sarcoma could contain a variable admixture of lymphocytes, plasma cells, neutrophils, and eosinophils, some times to the extent that neoplastic cells can be masked, but the degree of atypia would be more severe than RDD(1). Other cutaneous histiocytic proliferation such as Langerhans cell histiocytosis, various types of xanthomas, juvenile xanthogranuloma, reticulohistiocytoma and lipidized form of benign fibrous histiocytoma were readily excluded based on the clinical features, histological and immunohistochemical findings.

In Rosai Dorfman disease, abnormal laboratory studies may include a normochromic normocytic anaemia, red cell autoantibodies, a rapid erythrocyte sedimentation rate and a polyclonal elevation of immunoglobulin(6). The white blood cell count is usually normal, although there may be a reversal of CD4:CD8 ratio(4).

Immunohistochemical studies show reactivity for CD68 and S-100 protein, and some cases have been reported to be positive for CD30. The cells are consistently negative for CD1a and markers for follicular dendritic cells such as CD35 and CD 21. Ultra structural studies typically reveal complex cytoplasmic filopodia. Birbeck granules and desmosomes are not seen. A germ line configuration of the B- and T- cell antigen receptor genes is present(4). Thus, there is no known normal counterpart for the proliferating cells in RDD. The cases are consistently negative for Epstein-Bar virus, and the finding of HHV-6 (Human Herpes Virus-6) in RDD is in need of confirmation(4).

The outcome of RDD is usually benign and lesions frequently undergo spontaneous regression(4,5). Only occasionally complications or particular sites of extra-nodal involvement (kidney, lower respiratory tract and liver) lead to severe morbidity and some times mortality. In cases with other sites of involvement, the presence of skin involvement does not affect the prognosis. In many cases the skin lesions undergo spontaneous regression, in keeping with regression seen at other sites (4,5,7).

Extra-nodal manifestation of RDD, particularly in the skin, may occasionally represent the predominant manifestation of the disease and may precede in some cases the development of the lymphadenopathy(7). While lymphadenopathy was not evident on careful physical examination in our patient, the possibility of microscopic involvement of lymph nodes or of future development of the disease in other organs cannot be discounted. The intra-lesional excision of the lesion renders the patient susceptible for local recurrence. Therefore close observation of the patient for the development of local recurrence, lymphadenopathy and systemic involvement is crucial in the subsequent management of the patient.

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Figure 1.
The characteristic low magnification appearance of blue strips and nodules (lymphocytes) alternating with whitish/pinkish strips (histiocytes)(H&E x100)

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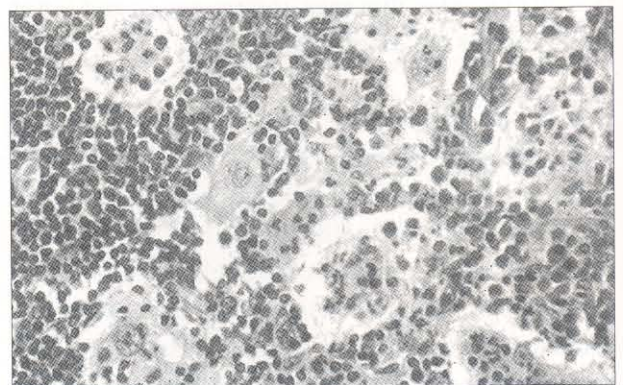


Figure 2.
Large histiocytes, some containing intracytoplasmic lymphocytes or plasma cells(H&E x 400)