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CASE REPORT

Cutaneous Rosai-Dorfman disease

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Abstract

Rosai-Dorfman disease (RDD) is a rare benign proliferative disorder of histiocytes in the lymph nodes with or without extranodal involvement. RDD limited to the skin without nodal involvement, known as cutaneous Rosai-Dorfman disease, is very rare. We describe a 34-year-old female with RDD of the skin over the chest. A large nodule with satellite lesions was excised for histopathological examination. Microscopically, there were many large histiocytes (Rosai-Dorfman cells) exhibiting emperipolesis, among many plasma cells, lymphocytes and neutrophils throughout the dermis and the subcutaneous tissue. The histiocytes were immunohistochemically positive for S-100 protein but negative for CD1a. Physical examination showed no lymphadenopathy or any extra-cutaneous lesions. Serological tests indicated a past infection with Epstein-Barr virus and cytomegalovirus. The diagnosis of cutaneous RDD may be difficult in the absence of associated lymphadenopathy or any specific features of the skin lesion. Hence, not only is histopathological examination required for definitive diagnosis but a high index of suspicion by the clinicians and pathologists is essential to help diagnose this very rare disease.

Key words: Rosai-Dorfman disease, skin, histiocytes, emperipolesis, S-100 protein

INTRODUCTION

Rosai-Dorfman disease is a rare benign proliferative disorder of histiocytes in the lymph nodes with occasional extra-nodal involvement of the skin, eyes, nasal cavity, paranasal sinuses, salivary gland, pancreas, skeletal system and central nervous system. Although skin involvement is a frequent extranodal site in this rare disease, pure cutaneous Rosai-Dorfman disease without node involvement is a very rare occurrence. We report one such case to highlight its features and emphasise awareness of this condition.

CASE REPORT

The patient was a 34-year-old Malay female who was seen at the surgical clinic with a mildly tender and pruritic chest nodule. She noticed a swelling over the sternum four months previously and had been treated by general physicians with antibiotics without improvement. She gave no significant past medical or surgical history. On examination, the patient was afebrile and there was a single large nodule over the sternum with overlying few smaller satellite lesions. It was mildly tender and warm on palpation. There was no lymphadenopathy or other abnormality detected clinically.

Laboratory investigations showed a normal complete blood count and an erythrocyte sedimentation rate of 16 mm/hr. She had positive Epstein-Barr virus (EBV) IgG titres and cytomegalovirus (CMV) IgG titres. Both the EBV and CMV IgM titres were negative. HIV, HBs Ag, HCV tests and rapid plasma reagin card test for serodiagnosis of syphilis were all non-reactive.

A chest radiogram was normal and CT scan of the thorax showed that the nodule was in the subcutaneous tissue superficial to the manubrium sternum. The bony cortex was uninvolved. The lesion was excised for histopathological examination.

Pathology

Macroscopically, the mass measured 5.5 cm in diameter with overlying multiple small raised satellite lesions (Figure 1). Microscopical examination showed a lympho-histiocytic inflammatory infiltrate in the dermis and the subcutaneous tissue in a diffuse pattern (Figure 2). Numerous large histiocytes with vesicular nuclei

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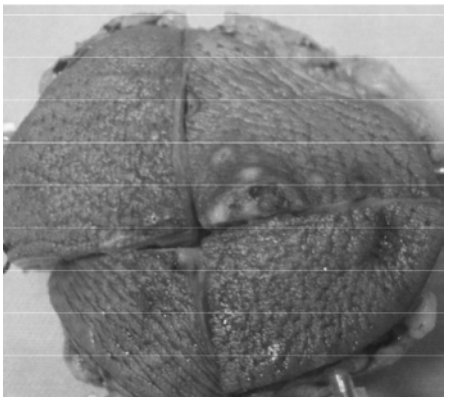

FIG.1: Skin nodule with multiple overlying small raised satellite lesions.

and indistinct cell borders were noted among many lymphocytes, plasma cells and neutrophils. Many of these large histiocytes (Rosai-Dorfman cells) exhibited emperipolesis containing lymphocytes, plasma cells and neutrophils. These large histiocytes, were strongly reactive for S-100 protein (Figure 3), weakly reactive for CD 68 but negative for CD1a. In a few foci, clusters of proliferated plasma cells were seen. Some of these plasma cells were bi- and tri- nucleated. However, the plasma cells were polyclonal in nature with positive immunostaining for either kappa or lambda chains. Occasional plasma cells contained large eosinophilic globular inclusions in the cytoplasm (Russell bodies) (Figure 4). The special histochemical stains including periodic-acid-Schiff, Grocott Mallory Silver and Ziehl-Neelsen stains for micro-organisms were all negative. The histological diagnosis was Rosai-Dorfman disease. Post-operatively, the surgical wound healed uneventfully. The patient remained asymptomatic with no signs of recurrence nor showed any other extranodal lesions or associated lymphadenopathy on the follow-up visit, six months after surgery.

DISCUSSION

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy (SHML), was first described in 1969.[1] It is a rare benign clinicopathological entity characterized by massive painless lymphadenopathy, anaemia, fever, raised erythrocyte sedimentation rate (ESR), leucocytosis and hypergammaglobulinaemia. Although the disease was originally thought to involve only the lymph nodes, it is now known to include many extranodal sites as well. RDD with extranodal involvement occurred in 43% of the cases, with skin being the commonest extranodal site.[2] However, pure cutaneous

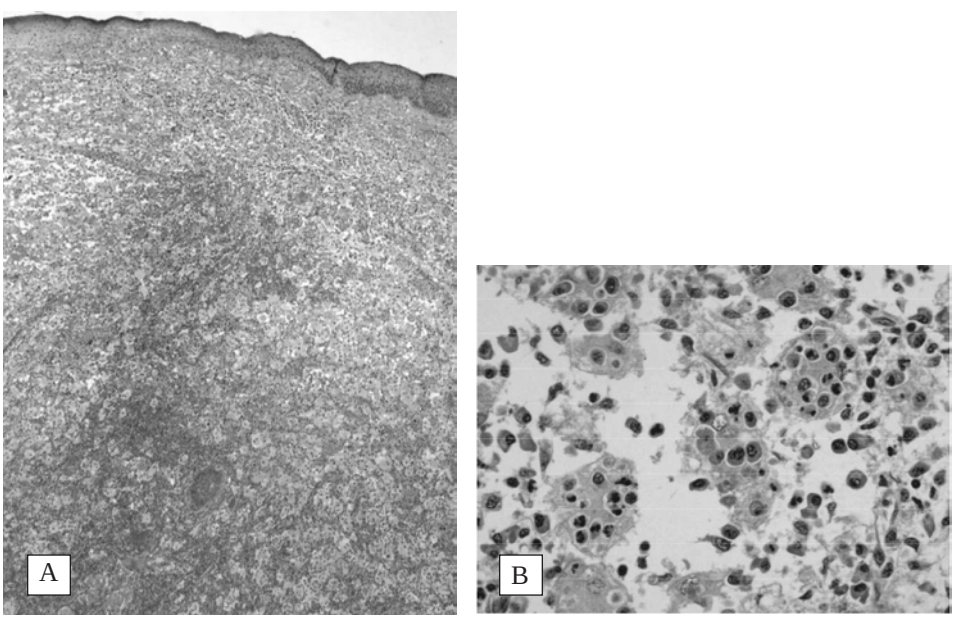

FIG. 2: A. Photomicrograph shows a lympho-histiocytic inflammatory infiltrate in the dermis and the subcutaneous tissue in a diffuse pattern. Large pale histiocytes are seen with a starry-sky appearance (Haematoxylin and eosin stain, original magnification x 40).
B shows large pale staining histiocytes (Rosai-Dorfman cells) contain many intra-cytoplasmic plasma cells, lymphocytes and neutrophils (emperipolesis).

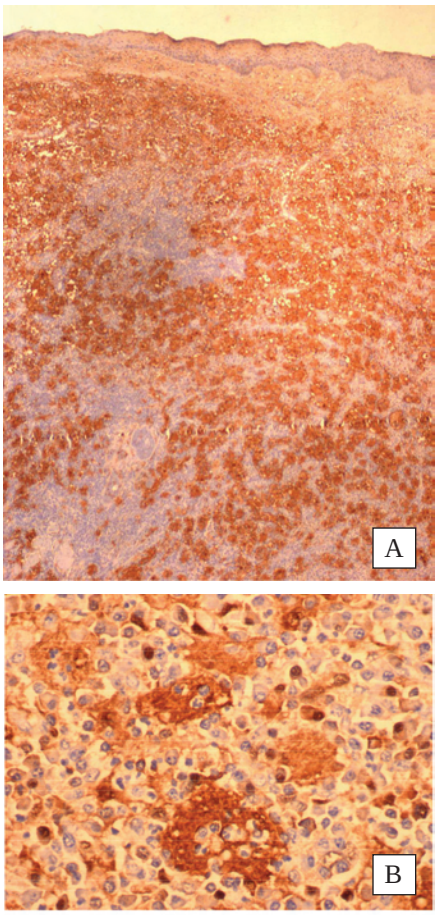

FIG. 3: A. The large histiocytes among the lymphoplasmacytic infiltrates show strong positivity to S100 protein (Immunohistochemical stain x 400). B. The emperipolesis is highlighted as the engulfed inflammatory cells within the histiocytes, remain unstained and are surrounded by a clear halo.

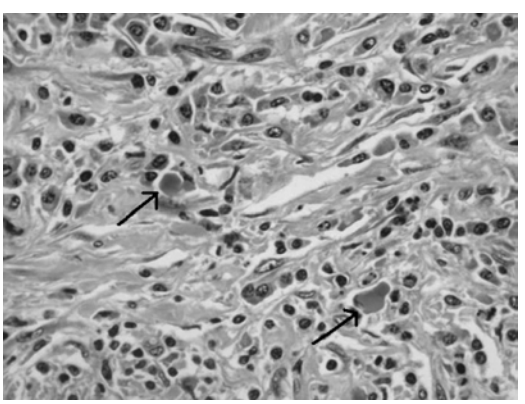

FIG. 4: A few plasma cells with Russell bodies (arrow) present among lymphoplasmacytic infiltrates (Haematoxylin and eosin stain, original magnification x 400).

Rosai-Dorfman disease with no evidence of lymph node involvement is very rare and only over 30 cases have been reported to date. In our case, the disease is limited to the skin nodule over the chest with no nodal or other extra-cutaneous lesions evident. Systemic symptoms (fever, malaise), anaemia, raised ESR and immunological abnormalities commonly seen in systemic Rosai-Dorman disease may not be seen in pure cutaneous RDD. The definitive diagnosis of pure cutaneous RDD requires histopathological examination. This is characterized by dense histiocytic infiltrates with plasma cells and lymphocytes. The large histiocytes (Rosai-Dorfman cells) have vesicular nuclei with indistinct cell borders. They exhibit the phenomenon of emperipolesis. These histiocytes are strongly reactive for S-100 protein and variably positive for CD68 but are negative for CD1a. Clusters of plasma cells are usually found in the lesion, but are polyclonal in nature. Lymphoid follicles with germinal centres may occur in cutaneous Rosai-Dorfman disease. The histological differential diagnoses for cutaneous RDD are many. They include fibrous histiocytoma, xanthoma, juvenile xanthogranuloma, infections and other histiocytic disorders showing emperipolesis viz. malignant histiocytosis, histiocytic lymphoma, reticulohistiocytoma cutis, hemophagocytic syndrome, Langerhans' cell histiocytosis and T cell lymphomas.

The exact aetiology of systemic and cutaneous Rosai-Dorfman disease is unknown, but in many case reports and small studies, the laboratory findings suggest an immune dysfunction to an antigen or infectious organism. In our patient both the IgG titres for EBV and CMV were positive indicating past EBV and CMV infections. Although serological tests are not conclusive for an aetiological role, many cases of cutaneous Rosai-Dorfman disease have been associated with human herpes virus (HHV) 6[3,4,5,6] infection, Epstein-Barr virus[6,7,8] infection, HIV positivity[6] , varicella[9] and herpes zoster[10] to suggest that RDD is an exaggerated immune response to an infective agent. Rosai-Dorfman disease has also been associated with immune abnormalities including uveitis[11,12], systemic lupus erythematosus[11] and autoimmune haemolytic anaemia[13] in some patients.

Rosai-Dorfman disease is a benign disorder with good prognosis when the disease is limited to the skin. Spontaneous regression and recovery often occur over months to years[14] and most

cutaneous lesions do not require treatment unless cosmetically unacceptable to the patients.

Purely cutaneous Rosai-Dorfman disease is very rare and diagnosis is difficult without any lymphadenopathy or any distinguishing features of the skin lesion. However, a high index of suspicion by clinicians and pathologists with histopathological examination of the lesion may enable a correct diagnosis be made.

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