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Original Research Paper

Histopathology

EXTRANODAL SOFT TISSUE ROSAI-DORFMAN DISEASE, A CHALLENGING DIAGNOSIS

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ABSTRACT Rosai-Dorfman disease (RDD) is a rare, benign histiocytic disease of unknown etiology. The characteristic presentation is lymphadenopathy due to abnormal production and accumulation of histiocytes in the lymph nodes. (1) Extranodal presentation may occur in rare instances in the soft tissue, posing a diagnostic dilemma to clinicians and radiologists alike.(2,3) Here, we report a case of a 56 year old lady of Indian descent, who presented with swelling on the left thigh which was clinically diagnosed as a soft tissue neoplasm. Histopathological examination revealed the classical features of RDD. There were large macrophages showing emperipolesis which were surrounded by dense lymphoplasmacytic infiltrate. On immunohistochemistry, the histiocytes were positive for S100 and CD68. (4)The diagnosis of extranodal soft tissue RDD was thus confirmed.

KEYWORDS : Rosai-Dorfman disease, extranodal, emperipolesis, S100, CD68

INTRODUCTION

Rosai –Dorfman disease (RDD) is a rare disorder first described in 1965 by Destombes, and later in 1969 by Rosai and Dorfman, who recognized it as a separate entity and termed it as sinus histiocytosis with massive lymphadenopathy. It is a benign histiocytic proliferative disorder characterized by massive, painless and often bilateral cervical lymphadenopathy, along with fever, neutrophilia, anemia, raised erythrocyte sedimentation rate and polyclonal hypergammaglobulinemia. [5] The etiology remains unknown. However, some studies show association between this disorder and viral infections such as human immunodeficiency virus (HIV), herpes simplex virus; and autoimmune disorders like systemic lupus erythematosus (SLE) and Crohn's disease.[6] Extranodal involvement by RDD has been reported in various sites, including the skin, soft tissue, upper respiratory tract, bone, eye and retro-orbital tissue, urogenital tract, breast and gastrointestinal tract.[7]

Case History

A 56 year old Indian lady presented with complaints of a large painless swelling in the left thigh since one year. The mass was noted on the medial aspect and was gradually increasing in size. There was no associated pain, redness or discharge and no antecedent trauma. Constitutional symptoms were absent. No weight loss was reported. The patient had a medical history of hypertension and diabetes. There was no organomegaly or lymphadenopathy on clinical examination. Systemic findings were within normal limits. CBC revealed mild normocytic normochromic anemia with normal total and differential leucocyte counts. Blood investigations showed elevated ESR (108 millimeter/ hour). The liver and renal function tests were in the normal range. Physical examination revealed a poorly defined, firm and non-tender swelling of size 7cm x 4 cm, on the medial aspect of the left thigh. The overlying skin was smooth and normal in appearance. A provisional diagnosis of lipoma/ soft tissue neoplasm was made. The ultrasonography reported a diffuse hyperechoic lesion suggestive of diffuse lipomatosis measuring 7.5 cm x 4.3 cm involving the medial aspect of the left thigh. The mass was surgically excised and sent for histopathological examination. Grossly, the specimen consisted of a tan-yellow fibrofatty mass measuring 8 cm x 4.5 cm. The cut section showed few grey white foci of fibrosis. Microscopic examination demonstrated sheets of large pale histiocytes and variable inflammatory infiltrate composed mainly of lymphocytes and plasma cells. These histiocytes had round vesicular nuclei and abundant granular eosinophilic cytoplasm and showed phagocytosis of inflammatory cells (emperipolesis). The intervening stroma showed fibrosis. On immunohistochemistry, the histiocytes gave positive staining with S100 and CD68 and stained negative for CD1a. The constellation of findings on microscopy and immunohistochemistry corroborated the diagnosis of extranodal soft tissue Rosai- Dorfman disease.

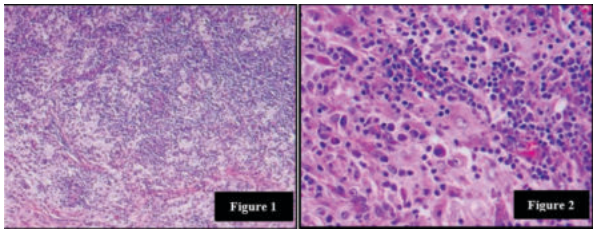

Figure 1. Photomicrograph showing many large histiocytes in a background of lymphoplasmacytic inflammatory infiltrate (H & E; 100X)

Figure 2. Photomicrograph showing histiocytes demonstrating emperipolesis of inflammatory cells (H & E; 400X)

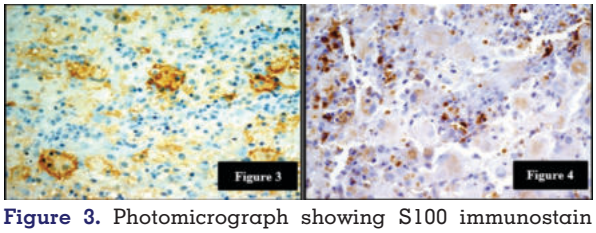

Figure 3. Photomicrograph showing S100 immunostain highlighting histiocytes in brown (H & E; 400X)

Figure 4. Photomicrograph showing CD68 immunostain highlighting histiocytes in brown (H & E; 400X)

DISCUSSION

Rosai- Dorfman disease is a rare histiocytic proliferative disorder of uncertain etiology, described by Rosai and

Dorfmann in 1969. [5]The pathogenesis remains unclear. There are studies which have linked this condition to infectious agents such as human herpes virus 6, Ebstein-Barr virus, Nocardia, Brucella and Klebsiella rhinoscleromatis. Autoimmune dysregulation or proliferation of histiocytes secondary to infection appears to be the major cause. [3, 8] A possible association between RDD and IgG4 disease has been proposed in some studies. [4] Typically, RDD manifests clinically as painless cervical lymphadenopathy, along with fever, leukocytosis and elevated erythrocyte sedimentation rate. However, affinity to lymph nodes does not prevent it from reaching other sites. Extranodal involvement by RDD has been documented in the skin, soft tissue, upper respiratory tract, bone, eye and retro-orbital tissue, urogenital tract, breast and gastrointestinal tract. [2, 9] Almost 10% cases of RDD show soft tissue involvement, with or without lymph node involvement. [4] Soft tissue RDD affects the subcutaneous adipose tissue and less commonly the deeper soft tissue. It usually presents as a slow-growing painless mass, commonly located in the extremities. Other sites of soft tissue RDD include the trunk, head and neck and retroperitoneum. The lesions are often well demarcated with the size ranging from 0.5 cm to 13.7 cm (median 2.4 cm). [10] The overlying skin has a normal appearance. Laboratory findings show anemia (65.7%), leukocytosis (59.4%), neutrophilia (68.4%) and increased ESR (88.5%). [9] Radiographs are unremarkable. [11]

The non specific findings on clinical examination, laboratory and imaging in a patient of soft tissue RDD make it imperative to rely on histopathology to ascertain the diagnosis. On microscopy, aggregates of large, pale-staining histiocytes are noted. They have smooth contoured hypochromatic nuclei, small distinct centrally placed nucleoli, and ill-defined, pale, wispy cytoplasm [5] and show emperipolesis (engulfment) of lymphocytes and other inflammatory cells. Emperipolesis is the striking feature in RDD, and it refers to the condition in which hematopoietic cells in the living and intact states are seen in the cytoplasm of the host cell without any damage. [8] Along with these sheets of histiocytes, microscopic examination also shows a mixed inflammatory infiltrate consisting of mainly lymphocytes and plasma cells and at times neutrophils. Extranodal RDD may show more prominent fibrosis than the nodal form. [4, 12] Diagnostic adjuncts include immunohistochemistry in which the histiocytes demonstrate positive staining with S100 and CD68. The pathognomic feature of emperipolesis is highlighted by S100. The histiocytes are typically negative for CD1a, thereby excluding Langerhans Cell Histiocytosis, which is a common differential diagnosis. [5]

The other diagnostic possibilities which need to be ruled out include Hodgkin lymphoma, melanoma, xanthoma, lysosomal storage diseases, some infectious and inflammatory conditions like histoplasmosis, leishmaniasis or rhinoscleroma, inflammatory myofibroblastic tumour, and IgG4-related disease. Whenever there is prominent fibrosis with a storiform pattern, extranodal RDD mimics fibrohistiocytic tumour. [13]Malignant diagnosis is usually dispelled by the lack of cytological atypia.

Extranodal soft tissue RDD is a self-limiting disease and surgical excision of the lesion is usually curative. It was observed that the patient tolerated the procedure well and had an uneventful postoperative period. The disease has a good prognosis and outcome. Local recurrences may occur in some cases. [4]

CONCLUSION

In summary, we report an exceptional case of extranodal soft tissue RDD, which can be a diagnostic conundrum for clinicians. Histopathological examination and immunostaining play a crucial role in establishing the diagnosis. Classically, they demonstrate proliferation of histiocytes, with many showing emperipolesis of lymphocytes and other inflammatory cells. The histiocytes are positive for S100 and CD68. Surgical resection is the most effective mode of treatment at present. Follow up is advised to rule out any recurrences.

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Conflict Of Interest

We declare that there is no conflict of interest among the authors.

Ethical Approval

Not applicable since it is a case report.

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