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Case Report

Isolated extra nodal soft tissue Rosai-Dorfman disease, masquerading as soft tissue neoplasm: A rare entity

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ABSTRACT

Rosai–Dorfman disease (RDD) is a rare, nonmalignant disorder of histiocyte proliferation which usually involves the cervical lymph nodes. Isolated extranodal RDD is rare which mimics other neoplastic processes thus causing diagnostic difficulties to the clinicians and radiologists. Here we report a case of 32 year old lady who presented with swelling in right thigh, clinically diagnosed as soft tissue neoplasm. Histopathology revealed pathognomonic findings of RDD showing sheets of large pale histiocytes showing emperipolesis along with dense lymphplasmacytic infiltrate. In extranodal RDD the typical histological findings of RDD are less common and there is pronounced fibrosis compared to nodal disease. The pathological diagnosis may be challenging in such cases. The surgical pathologist should have a high index of suspicion in such cases so that aggressive therapy can be avoided. The course of extranodal disease is generally less indolent and can be aggressive if vital organs are involved.

1. Introduction

Rosai–Dorfman disease (RDD) is a rare, nonmalignant disorder of histiocyte proliferation which usually involves the cervical lymph nodes.[1] It belongs to the group of primary histiocytic disorders like Langerhans cell histiocytosis and Erdheim- Chester disease.[2] It is predominantly seen in young males and commonly presents with bilateral painless cervical lymphadenopathy associated with fever, leukocytosis, elevated erythrocyte sedimentation rate (ESR) and polyclonal hypergammaglobulinemia.[3] Isolated extranodal RDD is rare which mimics other neoplastic processes thus causing diagnostic difficulties to the clinicians and radiologists. Since in extranodal RDD, the typical findings of that involving lymphnodes like emperipolesis, are less common and there is prominent fibrosis, the disease causes diagnostic challenge to the pathologists. The case is presented here for its rare presentation and clinical significance.

2. Case History

A 32 year old lady presented with a complaint of large painless swelling in right thigh since two years. On clinical examination, patient did not have any lymphadenopathy or organomegaly. Systemic examination findings were was within normal limits. Blood investigations revealed mild normocytic normochromic anemia with increased ESR (113 millimeter/1hour) and mild increase in total serum protein and serum globulin levels. Total and differential white cell counts were within normal limits. Rest of the liver and renal function parameters were within normal limits. Local examination revealed an ill defined, non tender swelling in subcutaneous plane over right thigh. Skin over the swelling was normal. Clinical diagnosis of lipoma/soft tissue neoplasm was made. Ultrasound (USG) revealed a diffuse hyperechoic lesion suggestive of diffuse lipomatosis

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measuring about 9.0 x 4.2 cm involving the medial aspect of right thigh. Chest X-ray and High resolution computed tomography (HRCT) of chest were normal. USG abdomen showed grade 1 fatty liver, otherwise no organomegaly. Patient underwent excision of right thigh lump which was sent for histopathological examination. On gross examination, the specimen consisted of a large fibrofatty mass measuring 15x8.5x5.2cm. One surface showed fascia with skeletal muscle bundles. Cut surface showed ill defined greyish white fibrous areas running between the fat lobules and partly replacing them. There was no gross evidence of haemorrhage or necrosis (Figure 1). Microscopy showed a relatively circumscribed lesion consisting of sheets and syncytia of large pale histiocytes with large round vesicular nuclei and abundant granular eosinophilic cytoplasm. Many of the histiocytes showed emperipolesis (Figures 2 and 3). Some of these cells showed mild atypia, however no mitosis or necrosis seen. Amidst this, there were foci of moderate to dense lymphoplasmacytic collections with sheets of plasma cells showing Russell bodies. The intervening stroma showed dense fibrosis with thick collagen bundles. There was no evidence of storiform type fibrosis or obliterative phlebitis. Stains for bacteria, fungus and acid-fast bacilli were negative. The diagnosis of extranodal Rosai-Dorfman disease was made on histopathology which was further confirmed by immunohistochemistry which showed sheets of CD68 and S100 immunopositive histiocytes along with negativity for CD1a(Figure 4).

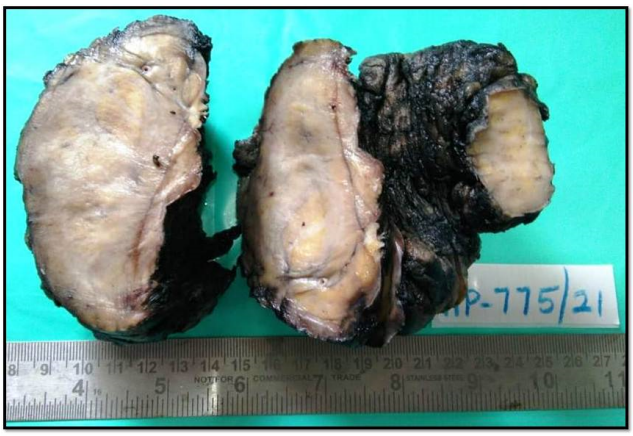

Fig. 1: Gross photograph showing fairly circumscribed mass with ill defined greyish white fibrous areas running between the fat lobules

3. Discussion

Rosai Dorfman disease was first described by Rosai and Dorfman in 1969.[1] It is a polyclonal histiocytic disorder, which was originally described as a lymph node disease. It occurs in various extranodal locations, including soft tissue.[4] About 23–40% of patients with RDD show

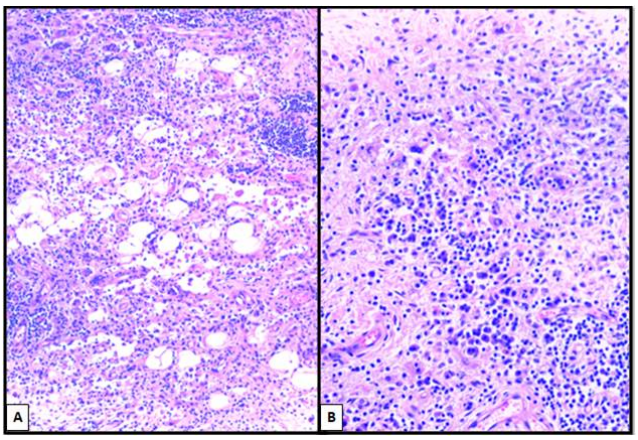

Fig. 2: A & B: Moderate to dense lymphoplasmacytic collections with sheets of pale histiocytes and plasma cells, H &E, 100x & 400X

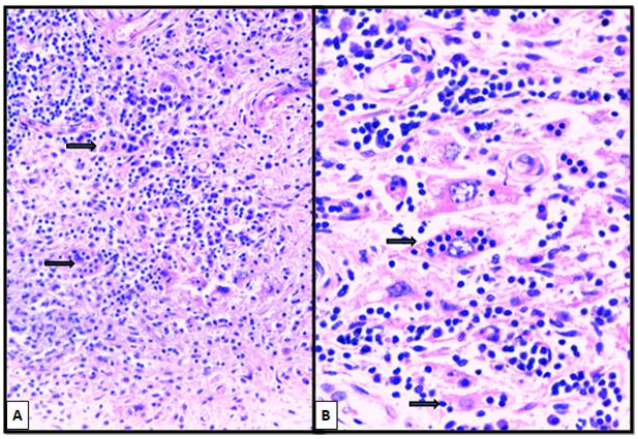

Fig. 3: A &B: Sheets histiocytes with emperipolesis (arrows), H & E, 100x & 400X

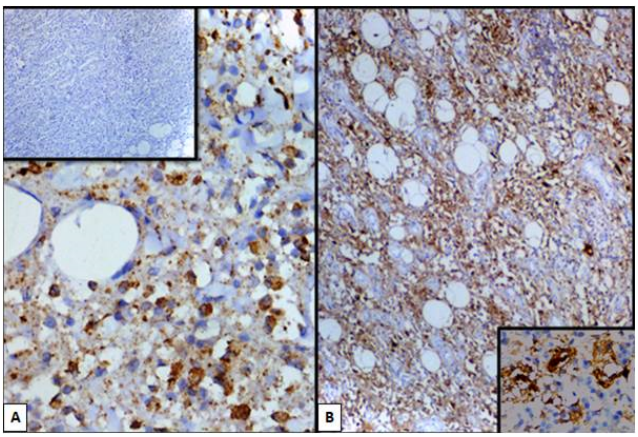

Fig. 4: (A): Histiocytes positive for CD68 and negative for CD1a (Inset), 100X Immunopositivity; **(B):** Shows histiocytes positive for S100, 100X (Inset- S100, 400X)

extranodal involvement, either isolated or secondary to lymphnode involvement which most commonly presents as a painless, palpable mass.[2] In the largest review of extranodal RDD, the most frequent extranodal sites were skin and soft tissue, nasal cavity and paranasal sinuses, eye, orbit, and ocular adnexa, bone, salivary gland, central nervous system, oral cavity, kidney and genitourinary tract, respiratory tract, liver, tonsil and breast.[5] Approximately 10% of all cases of RDD are associated with soft tissue involvement either isolated or secondary to lymphnode involvement.[6] It is most commonly located in the extremities, but it can also occur in the trunk and head and neck region.[7] In a report of 423 cases of RDD, 182 patients had extranodal disease and 13 patients had isolated soft-tissue RDD without detectable lymphadenopathy.[3] In our case also patient had isolated soft tissue involvement without any lymphadenopathy/organomegaly. The exact etiology of RDD is still unclear. Some studies,[8–10] have suggested the role of viral agents in the pathologenesis of RDD. Levine et al in their study, detected human herpes virus-6 in 7 out of 9 cases and Epstein–Barr virus DNA in one of nine by in situ hybridization.[8,9] Luppi et al demonstrated human herpes virus-6 antigen expression by abnormal histiocytes.[10] Another theory suggests the possible role of an abnormal immunologic response in the disease causation.[6] A possible association between RDD and IgG4 disease has been proposed in some studies.[11,12] Kuo et al[11] and Zhang et al[12] have shown a significant increase in the ratio of IgG4-positive plasma cells in these lesions. However, Liu et al[13] studied 32 cases of RDD and failed to demonstrate this association.

Histologically, RDD classically shows an inflammatory infiltrate predominantly showing lymphocytes, plasma cells and large histiocytes. The histiocytes show emperipolesis which is pathognomonic of the disease.[1] In Extranodal RDD the typical histological finding of RDD is less common and there is prominent fibrosis compared to nodal disease. Hence the diagnosis may be challenging in such cases.[2] However our case showed typical findings of RDD. On immunohistochemistry, the histiocytes express both CD68 and S-100 protein while negative for CD1a, thus differentiating from Langerhans cell histiocytosis and Erdheim-Chester disease.[14]

The differential diagnoses may include Hodgkin lymphoma, melanoma, xanthomas, lysosomal storage diseases, and several infectious and inflammatory conditions, such as histoplasmosis, leishmaniasis or rhinoscleroma, inflammatory myofibroblastic tumor, and IgG4-related disease.[14] Extranodal RDD may mimic a fibrohistiocytic tumour when there is prominent fibrosis giving a storiform pattern distorting the sheet like pattern.[4]

The clinical course of extranodal RDD is self-limiting, and simple excision is usually curative. When not accessible to surgery, some lesions have shown a favorable response to treatment with steroids, cytotoxic chemotherapy, and/or local radiation.[14] Prognosis of soft tissue Rosai-Dorfman disease is excellent, although some may develop recurrence. A significant number of patients with isolated cutaneous disease resolve spontaneously.[4] The nodal disease often spontaneously regresses, the course of extranodal disease is generally less indolent and can be aggressive if vital organs are involved.

4. Conclusion

Due to the absence of pathognomonic clinical and radiological features, diagnosis of extranodal RDD depends on histopathological examination with the aid of immunohistochemistry. The pathological diagnosis may be challenging in cases which lack typical histological features like emperipolesis and show fibrosis. The surgical pathologist should have a high index of suspicion in such cases so that aggressive therapy can be avoided.

5. Source of Funding

None.

6. Conflict of Interest

The authors declare no conflict of interest.

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