



A case of isolated cutaneous Rosai-Dorfman-Syndrome

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Abstract

Rosai-Dorfman Syndrome (RDD) is a rare, benign, self-limiting disorder which is characterized by the non-malignant proliferation of distinctive histiocytic cell within lymphatic system. RDD has been described as a dynamic entity in the spectrum of histiocytosis with non-Langerhans cell histiocytosis at one end and Langerhans cell histiocytosis at the other.

The exact etiology of this disease is uncertain despite widespread search for infectious or immunological reasons. We present a case of purely cutaneous Rosai-Dorfman Syndrome presenting as abdominal wall swelling.

Keywords

Rosai-Dorfman Disease, Lymphoma

Introduction

Rosai-Dorfman disease, also known as sinus histiocytosis with massive lymphadenopathy (SHML) was first described by Ronald Dorfman and Juan Rosai in 1969. They were also the first to use the term sinus histiocytosis. The initial description of disease specifically excluded cutaneous manifestations but it was later acknowledged in 1978 when case series of 7 patients was reported with multiple skin nodules⁽¹⁾

It is a rare and benign disorder with questionable etiology that is characterized by the overproduction of histiocytes. It typically involves the lymph nodes, though extranodal sites are simultaneously involved in 43% of cases. When extranodal disease is seen it generally involves more than one organ. Involvement of gastrointestinal tract, orbit, lower respiratory tract, oral cavity, testis, skin and soft tissue has all been reported. It is important to note that lymphadenopathy may not be initially present and might develop during the course of disease.

While exact etiology of RDD is uncertain, immunological or infectious sources have been investigated. Increased antibody titers to Measles and Epstein Barr virus has been detected in some cases. Similarly, Human Herpes Virus 6 DNA

has also been isolated in biopsy specimen of some of the patients but etiological evidence is lacking⁽²⁾

Purely cutaneous disease without lymphadenopathy or visceral involvement rarely occurs and has estimated to be seen in only 3% of cases. The clinical morphology of lesions ranges from papules, nodules, plaques, patches to pustules. The diagnosis of cutaneous RDD is hampered by its variable clinical presentation, misleading histopathological patterns, and the absence of lymphadenopathy. We report this rare case of purely cutaneous Rosai-Dorfman disease in the anterior abdominal wall.

Case History

A 56-year-old female with past medical history diabetes, asthma, and essential hypertension presented with small, solitary, painless mass (the size of a pencil tip) on her left anterior abdominal wall for approximately 10 months. It was initially 1 cm or so in size but had increased markedly over the months. On review of systems the patient reported fatigue and fever. On examination, an approximately 10 X 10 cm subcutaneous soft tissue swelling was noted. There was no redness or inflammation noticed on the skin and the only associated symptom was mild itchy. Patient had eosinophilia of 8.8% but no anemia or hypergammaglobulinemia was noticed in blood work. Also no abnormality was detected in serum chemistry and liver function test.

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Patient underwent wide local excision of the soft tissue mass due to progressive increase in size. The biopsy showed a mixed infiltrate comprising predominantly of spindle shaped histiocytes admixed with small lymphocytes and few plasma cells. There was no evidence of epidermotropism, or movement towards the dermis. The histiocytes were described as large with abundant pale or foamy cytoplasm. The specimen was tested with fungal (silver methenamine) and mycobacterial (Ziehl-Neelsen) stains and cultures which were negative. An immunohistochemical panel showed the infiltrate comprised CD68 positive histiocytes, CD20 and CD79A positive B cells, and CD3, CD4, CD8, CD20, CD43 and BCL2 positive T cells. Immunohistochemical staining showed the histiocytes were S-100 positive. This morphological and immunohistochemical analysis confirmed the diagnosis of extranodal Rosai-Dorfman disease.

Post-operatively the patient underwent CT scan of chest, abdomen and pelvis but no evidence of hepatosplenomegaly was detected. There was also no clinical or radiological evidence of lymphadenopathy. The fact that RDD is a benign condition with no significant malignant potential in majority of the cases, argues against the use of aggressive immunosuppressant therapy. The patient agreed for watchful waiting and continues to be asymptomatic at 6 months follow-up with no evidence of recurrence.

Discussion

Bilateral and painless lymphadenopathy is the most common physical complaint seen in 57 % of the patients with RDD. Associated fevers, night sweats and weight loss may also be present. Extranodal sites including intracranial, retro-orbital tissue, nasal cavity, upper respiratory tract, thyroid, breast, GIT, liver, pancreas, kidneys may be involved in up to 43% of cases, and occurs only in 23% of patients with isolated extranodal RDD.⁽³⁾

In sinus histiocytosis, there is progressive filling up of the lymph node sinuses with histiocytes, plasma cells and lymphocytes. A constant feature on histology (emperipolesis

or lymphophagocytosis) is the presence of intact lymphocytes within the cytoplasm of histiocytes (Figures 1 and 2). This is of great diagnostic significance. Pericapsular fibrosis and inflammation are also seen. The histiocytes in RDD are S100 positive and CD1 negative. Histiocytes in RDD also lack Birbeck granules - a feature used in differentiating them from Langerhans cells of epidermis that are also S-100 positive. Other panels facilitating the diagnosis may comprise of CD68, CD163 and HAM56.⁽⁴⁾ Presence of plasma cells may explain the polyclonal hypergammaglobulinemia, a serological abnormality commonly seen in systemic RDD. The expression of IL-6, IL-1 β , TNF- α in plasma cells may have led to fever, fatigue, inflammation and other systemic symptoms. We confirmed RDD in our patient though excisional biopsy of the left anterior abdominal wall mass. Emperipolesis was pronounced in the resection specimen. Infiltrate

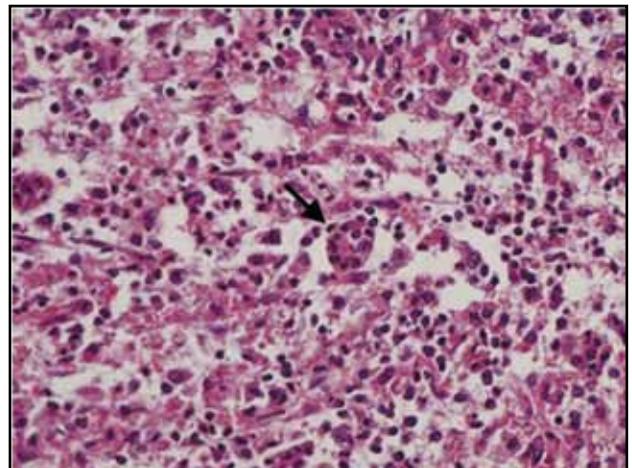


Figure 1. Emperipolesis or lymphophagocytosis suggested by the presence of intact lymphocytes within the cytoplasm of histiocytes.

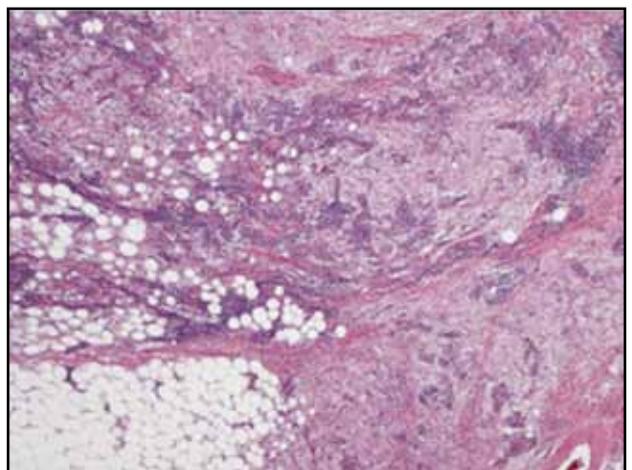


Figure 2. Slide showing prominent Histiocytosis

was comprised of CD68+ histiocytes with abundant pale foamy cytoplasm. Further staining showed S100 positivity.

Typical Rosai-Dorfman disease takes place in young male adults. However, cutaneous disease affects an older (49-year old average) and predominantly female, Asian population. This unique epidemiology and lack of systemic involvement have led some authors to view cutaneous RDD as a distinct clinical entity.⁽⁵⁾ Longitudinal follow-up shows that lesions typically began with papules or plaques and grew to form nodules with satellite lesions and resolved with fibrotic plaques before complete remission.

Patients with RDD may mimic lab findings of lymphoma as in the lymphocytosis, polyclonal gammopathy and anemia of unknown origin. Other lab findings could include elevated ESR, normocytic normochromic anemia and elevated ferritin as well.⁽⁶⁾ In the absence of lymphadenopathy and visceral involvement of Langerhans cell histiocytosis, storage disorders such as Gaucher's disease, histiocytic sarcoma should be considered in the histological differential diagnosis of purely cutaneous RDD.⁽⁵⁾ Presence of infections particularly mycobacteria and histoplasma should also be ruled out. In contrast to the usually associated findings in RDD our patient presented with an elevated eosinophil count, but did not have

increased inflammatory markers, evidence of anemia or lymphocytosis.

In general RDD is a benign disease with spontaneous resolution in majority of cases. Occasionally periods of exacerbations alternating with remissions have been noticed. Due to the rarity of this condition there is lack of randomized trials between different treatment options. No standard treatment for SHML is known and management is largely based on expert opinions. The use of chemotherapeutic agents (MTX, 6-MP, anthracyclines, Interferon α) is only partially effective and no definite role has been identified. These options can be considered in refractory cases.⁽⁷⁾ Similarly, Cladribine (2-CDA), which targets TNF- α , IL-6, has shown some efficacy in severe, refractory or recurrent cases of RDD. Cutaneous lesions have responded to radiotherapy, cryotherapy, topical and oral corticosteroids but no guidelines exist for their management. Surgery and debulking procedures may be required in extranodal RDD with vital organ compression. Watchful waiting is also a variable option particularly if patient is asymptomatic.

Our patient had no clinical or radiological evidence of visceral involvement and was asymptomatic. She had negative resection margins. She continues to do well with conservative management.

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