

## Cutaneous Rosai Dorfman Disease



### Medical Science

**KEYWORDS :** Rosai Dorfman disease(RDD), emperipolesis, hypergammaglobulinemia, sinus histiocytes, lymphadenopathy.

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### ABSTRACT

*Rosai-Dorfman disease (RDD) also known as sinus histiocytosis with massive lymphadenopathy (SHML) is a benign disorder of histiocyte proliferation that usually affects the lymph nodes. RDD most frequently seen in children and young adults. The disease is more common in males and has 2:1 male -to-female ratio. The most frequent clinical presentation of RDD is a massive bilateral and painless cervical lymphadenopathy with fever, night sweats, weight loss, leucocytosis, an increased erythrocyte sedimentation rate (ESR) and hypergammaglobulinemia. More than 40% of patients affected by RDD have extranodal involvement. Skin involvement is one of the most common extra nodal manifestation apart from involving nasal cavity, eye, thyroid, pancreas or in other extra nodal sites. Cutaneous Rosai-Dorfman disease (C-RDD) is a distinct entity with unknown etiology, broadly different from systemic RDD, confined to the skin without lymphadenopathy. Primary CRDD without lymphadenopathy is rare. We present a rare case of extra nodal RDD in a 32 yr old female patient presented with multiple tender erythematous indurated subcutaneous plaques over abdominal wall, buttocks, lower limbs with left periorbital swelling. Histologically scattered and clusters of large histiocytes intermingled with mixed inflammatory cells along with emperipolesis or lymphophagocytosis, the hallmark feature that is diagnostic of RDD is seen.*

### INTRODUCTION

Rosai-Dorfman disease (RDD) also known as sinus histiocytosis with massive lymphadenopathy (SHML) [1] is a rare benign, idiopathic proliferative disorder of unknown etiology. First described in 1965 by Destombes [2] and later recognized as a distinct clinico-pathologic entity by Rosai and Dorfman [3] in 1969. RDD most frequently seen in children and young adults.[4] The disease is more common in males and has 2:1 male -to-female ratio.

The most frequent clinical presentation of RDD is a massive bilateral and painless cervical lymphadenopathy with fever, night sweats, weight loss, leucocytosis, an increased erythrocyte sedimentation rate (ESR) and hypergammaglobulinemia. Mediastinal, inguinal, axillary and retroperitoneal nodes may also be involved. More than 40% of patients affected by RDD have extranodal involvement.[5] The most frequent extra-nodal sites being skin, soft tissue, eye, breast, spinal cord, parotid gland, liver, pancreas, thyroid and lungs.[6] Most of the clinical manifestations in the disease are due to extra nodal involvement. Castleman disease, dermatopathic lymphadenitis, Kawasaki disease(mucocutaneous lymph node syndrome),Kikuchi disease (histiocytic necrotizing lymphadenopathy) and pseudotumor of lymph node are among the other rare causes of lymph node enlargement. The clinical course of RDD is unpredictable with episodes of exacerbations and remissions. The disease is often self limiting with a very good outcome. In patients with several extra nodal involvement, severity depends on type and number of extra nodal sites.[7]

Cutaneous Rosai-Dorfman disease (C-RDD) is a distinct entity with unknown etiology, broadly different from systemic RDD confined to the skin without lymphadenopathy. Primary CRDD without lymphadenopathy is rare. It affects older white and Asian women, unlike its systemic counterpart has a predilection for younger blacks.[8] The mean age of presentation is 47 yrs. Skin is the most frequently involved extranodal site.[9] Skin lesions are usually papules or nodules that are firm, indurated ranging in size from 6cm to 10cm. Pustular ,psoriasisform and acneiform presentations have also been documented. Common affected sites include the extremities, trunk and face. Cutaneous lesions may involve the dermis and subcutaneous tissue. The hallmark histological feature of CRDD is the presence of intact inflammatory cells within the cytoplasm of large histiocytes, a phenomenon known as emperipolesis.[10] The presence of emperipolesis and S-100 antigen positivity on histiocytes by immunohistochemistry are considered diagnostic. C-RDD has benign course usually with spontaneous regression in most cases.

Therapy may be needed for relapsed cases and for cosmetic reasons only.

### CASE REPORT

A 32 yr old female patient presented with complaints of swellings over right thigh, left leg and buttock since 2 yrs which are insidious in onset, progressive in nature associated with pain, redness and raised temperature. Swellings subsided spontaneously after few weeks and reappeared after few days. Patient had similar type of swellings over both upper limbs 1 yr ago and subsided spontaneously. Left periorbital swelling present since one month which is progressively increasing in size and associated with pain on pressure. Patient had history of on and off fever and joint pains. Her medical history was non contributory and had no personal or family history of malignancy.

### EXAMINATION

On physical examination multiple tender erythematous indurated subcutaneous plaques were noted over lateral aspects of right thigh (Fig:1), anterior aspect of left leg, anterior abdominal wall(Fig:2), left buttock and left labia majora and left periorbital swelling. The lesions were firm in consistency and size varied from 6cm to 10cm. Bilateral inguinal lymph nodes were enlarged which are firm, discrete, mobile and non tender. Systemic examination found to be normal.



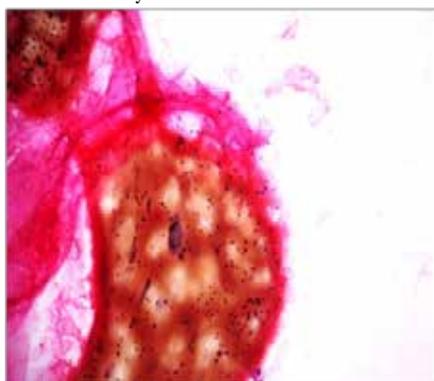
**Fig:1** Indurated erythematous lesions



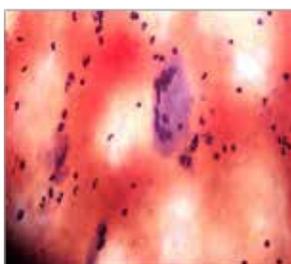
**Fig:2 Indurated erythematous lesions** over lateral aspect of right thigh over anterior abdominal wall

### INVESTIGATIONS

Laboratory findings showed leucopenia (2,500 cells/cumm), microcytic hypochromic anemia and elevated erythrocytic sedimentation rate (ESR) 75 mm/ 1st hr. Chest X-ray was normal. Cutaneous lesions may involve the dermis and subcutaneous tissue. Fine needle aspiration cytology (FNAC) from lesions at different sites showed the pathognomonic cell histiocyte with foamy eosinophilic cytoplasm and a larger vesicular nucleus containing prominent nucleoli seen in small clusters and scattered individually in these lesions (**Fig:3**) along with lymphocytes and plasma cells. The presence of intact inflammatory cells like lymphocytes and plasma cells within the cytoplasm of large histiocytes known as emperipolesis(**Fig:4**), the hallmark of RDD also demonstrated in these lesions. Immunohistochemical staining for S-100 positive histiocytes could not be done due to non-availability in our institute.



**Fig:3 Low power view showing emperipolesis**



**Fig:4 High power view showing emperipolesis**

(H and E staining) (H and E staining x 400)

### MANAGEMENT

In majority of cases, RDD has benign course and treatment is not necessary. In extranodal RDD with vital organ involvement and causing life threatening complications therapy may be needed. Surgical excision, systemic steroids, immunosuppressive agents, chemotherapeutic agents and radiotherapy are some of the treatment modalities available. In CRDD, therapy may be needed for relapsed cases and for cosmetic reasons. The ultimate goal of an overall treatment plan is to use as little treatment as possible to keep the disease under control and preserve quality of life.

### PROGNOSIS

The clinical course of RDD is unpredictable with episodes of exacerbations and remissions. The disease is often self limiting with a very good outcome. C-RDD has benign course usually with spontaneous regression in most cases.

### DISCUSSION

Rosai-Dorfman disease (RDD) also known as sinus histiocytosis with massive lymphadenopathy (SHML) [1] is a rare benign, idiopathic proliferative disorder of unknown etiology. More than 40% of patients affected have extranodal involvement.[5] RDD occurs in any age group, but most frequently seen in children and young adults[4] with a male predominance. Black and white are more affected than Asian.[7] Etiology of the disease is unclear but different stimuli are known to reactivate the disease process. The potential causative factors include coexistence of RDD with autoimmune diseases or with post infectious conditions due to human herpes virus 6 (HHV-6),[11] Epstein Barr Virus (EBV) [12] and parvo virus.[13] A cytokine mediated migration of monocytes may be involved in histiocytes accumulation and activation. Systemic symptoms in RDD may be related to enhanced production of cytokines like IL-6, IL-1 $\beta$  and TNF- $\alpha$ .

Cutaneous Rosai-Dorfman disease (C-RDD) is a distinct entity with unknown etiology, broadly different from systemic RDD, confined to the skin without lymphadenopathy. Primary CRDD without lymphadenopathy is rare. Skin involvement is one of the most common extra nodal manifestation. However, strictly cutaneous disease devoid of systemic involvement has been reported in only 3% of cases. Patients with RDD usually present with fever, night sweats and weight loss where as pure CRDD patients generally are afebrile and have no systemic symptoms. Laboratory features in RDD are often non specific with leucocytosis, elevated ESR, hypergammaglobulinemia and anemia are reported in many patients[14] where as in pure CRDD such laboratory abnormalities were usually not observed.[15] In the present case leucopenia, elevated ESR, microcytic hypochromic anemia were observed.

The most common clinical manifestation in RDD is painless, bilateral cervical lymphadenopathy in (86%) and fever in 30% of cases. In extranodal RDD most common site involved is skin (28%) followed by nasal cavity in 27%, orbit and eyelids in 20% and bone in 18%. Various reports revealed anemia in 66%, leucocytosis (60%),neutrophilia (69%), elevated ESR in (89%) and hypergammaglobulinemia in 90% of cases. The cutaneous lesions in this case were seen over both lower limbs, buttocks, right thigh, anterior abdominal wall and over face as periorbital swelling. Histologically, these lesions showed histiocytes with large vesicular nucleus containing prominent nucleoli with a phenomenon known as emperipolesis.[16] which is the hallmark feature of RDD. The disease is often self limiting with a very good outcome. The severity of disease depends on the type and the number of extranodal sites.[7] C-RDD has benign course usually with spontaneous regression in most cases. The present case was diagnosed as cutaneous RDD based on involvement of skin along with inguinal lymphadenopathy, microcytic hypochromic anemia, raised ESR, leucopenia and characteristic feature emperipolesis on histopathological examination.

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