Pure Cutaneous Rosai Dorfman Disease: An Uncommon Location for a Rare Histiocytic Proliferative Disorder

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Abstract

Rosai Dorfman disease (RDD) is a rare, self-limiting disease of uncertain etiology involving lymph nodes as well as extranodal sites. Isolated or pure cutaneous RDD (PCRDD) without lymph node involvement is very unusual accounting for only 3% of all described cases of RDD. The clinical features of PCRDD are quite different from RDD according to the literature on extranodal RDD, thereby emphasizing that PCRDD is a distinct clinical entity. Histopathology remains the gold standard for the diagnosis of both systemic and PCRDD with the presence of characteristic emperipolesis observed in histiocytes while immunohistochemistry (IHC) (S100, CD 68 positive, and CD 1a-negative) serves as a useful adjunct. We hereby report a case of a 36-year-old female who presented with a tender, indurated plaque on the left forearm with a clinical differential diagnosis of borderline tuberculoid leprosy/sarcoidosis and lupus vulgaris. However, on histopathology, a diagnosis of RDD was performed and confirmed on IHC. This case highlights the need to create awareness among young pathologists and clinicians about PCRDD to prevent overzealous treatment.

Keywords: Cutaneous rosai dorfman disease, emperipolesis, histiocytic disorder, rosai dorfman disease

Introduction

Rosai Dorfman disease (RDD) is a rare, clinically distinct entity of uncertain etiology involving lymph nodes as well as extranodal sites. Although cutaneous involvement in RDD is common, isolated pure cutaneous RDD (PCRDD) is very unusual. RDD is self-limiting, and simple excision is usually curative.[1] The clinical features of PCRDD are quite different from RDD as it occurs at an older age, more common in females compared to RDD without any significant systemic extracutaneous or serologic manifestations.[2-4] A combined clinical suspicion and histopathological examination of the lesion may enable us to impart an accurate diagnosis.

“The eyes don’t see what the mind doesn’t know.” This case highlights the need to create awareness among young pathologists and clinicians about the pure cutaneous form of RDD to prevent overzealous treatment.

Case Report

A 36-year-old female patient presented to the dermatology clinic with a lesion on the forearm since last month. There was a history of fever for 3–4 days 1 month back. On examination, there was an indurated plaque with tenderness on the left forearm measuring 7 cm × 4 cm [Figure 1]. No thickened nerve was present in the vicinity and no lymphadenopathy. Based on the clinical findings, the dermatologist made a differential diagnosis of borderline tuberculoid leprosy/sarcoidosis and lupus vulgaris.

Complete blood count revealed that hemoglobin 11.9 g%, total leukocyte count 10,920/µl with differential leukocyte count within the normal limits, platelets 1.6 lacs/µl, and mildly raised erythrocyte sedimentation rate of 22 mm/h. Biochemical investigations showed mildly elevated total proteins (8.8 g/dl) as well as globulins (3.99 g/dl), the rest of the values were in the normal reference range.

Microscopic examination of the skin biopsy revealed a mixed inflammatory infiltrate in the superficial, mid,
and deep dermis comprising histiocytes, lymphocytes, neutrophils, and plasma cells. The histiocytes were large, polygonal with abundant cytoplasm containing lymphocytes, red cells, and neutrophils-emperipolesis-a hallmark of RDD [Figures 2 and 3]. On immunohistochemistry (IHC), these histiocytes were positive for S-100 and CD68 [Figure 3] while they were negative for CD1a. RDD was considered on account of characteristic microscopy. A complete investigative work up with the help of imaging techniques (Chest X-ray, ultrasound, computed tomography of the chest, abdomen, and pelvis) was done to check for other organ system involvement, but there was no evidence of lymphadenopathy or any other lesions. Hence, finally, a diagnosis of PCRDD was rendered.

On her next visit after a period of 4–5 weeks, the patient’s lesions showed features of regression. She was kept on follow-up with no active intervention.

**Discussion**

RDD, also known as Sinus histiocytosis with massive lymphadenopathy (SHML) is characterized by benign histiocytic proliferation, which was first described in 1965 but was recognized as a distinct clinical entity in 1969. The typical clinical presentation involves painless, massive cervical lymphadenopathy (often bilateral) associated with fever, leukocytosis, raised erythrocyte sedimentation rate, and polyclonal hypergammaglobulinemia. The disease has a predilection for young adults (mean age 20.6 years), although it may occur in any age group.

The etiopathogenesis of RDD remains uncertain, however, it may be related to a specific infection or immunodeficiency. Among the possible mechanisms, underlying immune dysfunction has been postulated. The possibility of viruses such as human herpesvirus 6, EpsteinBarr virus, cytomegalovirus, or bacteria such as Klebsiella, Brucella as a causative agent has been postulated as well. The possibility of an association between IgG4 disease and RDD has been controversial.

Extranodal manifestations of RDD involving the skin, nasal cavity and paranasal sinus, eye, and ocular adnexa, bone, central nervous system, liver, and heart, account for approximately 25% to 40% of all cases. They are diagnostically challenging for the oblivious clinician as well as a pathologist. There have been reports of extranodal RDD in virtually all organ systems often simulating neoplasms.

Although the skin is reported to be the most common site of extranodal manifestation, isolated or PCRDD without lymph node involvement is very unusual accounting for only 3% of all described cases of RDD. Foucar et al. reviewed the clinical and pathological features of 423 cases of SHML, out of which only 13 cases were PCRDD. Mantilla et al. studied the clinicopathological profile of ten patients with extranodal RDD and observed a marked female predominance (90%) and RDD was observed in the skin and superficial soft tissue in six cases, mammary glands in three cases, orbital in two cases while osseous, pancreatic, and intestinal involvement was seen in one patient each.

The clinical manifestations of PCRDD are diverse. Skin lesions usually present as dark red or yellow papules, plaques, or...
nodules most frequently involving the face, trunk, and upper and lower limbs.\textsuperscript{14-16} Kong \textit{et al.}\textsuperscript{15} (China) observed the clinical features of 39 skin lesions in 25 patients and grouped them into three main types: papulonodular type (79.5%), indurated plaque type (12.8%), and tumor type (7.7%). The present case had plaque-like lesions on the forearm.

The clinical features of PCRDD are quite different from RDD according to the literature on extranodal RDD, thereby emphasizing that PCRDD is a distinct clinical entity. Patients with PCRDD have older age at onset of disease (mean age ranging from 45 years to 47.5 years) compared to RDD (mean age 20.6 years). The male/female ratio is also reversed in PCRDD compared to RDD (1:1.4 vs. 1:4.1). There are no significant systemic extracutaneous or serologic manifestations in PRCDD. Systemic RDD is common in blacks and rare among Orientals while most of the patients with PCRDD are Asians and whites.\textsuperscript{1,5,6}

The histological hallmark of both systemic and PCRDD is the proliferation of polygonal histiocytes with characteristic emperipolesis (cytoplasm of the histiocytes appears to contain lymphocytes, red blood cells, and/or granulocytes) and a mixed inflammatory infiltrates containing histiocytes, lymphocytes, and plasma cells.\textsuperscript{1,2} Immunohistochemically, positive S-100, and CD68 with negative CD1a in histiocytes are characteristic as observed in our case.

Cutaneous RDD can clinically mimic other dermatologic diseases such as vasculitis, acne vulgaris, hidradenitis suppurativa, granuloma annulare, lupus vulgaris, sarcoidosis, and other histiocytoses.\textsuperscript{3,4} The histopathological differential diagnosis of PCRDD includes fibrous histiocytoma, juvenile xanthogranuloma, xanthoma, reticulohistiocytoma, melanoma, infections, and lymphoproliferative disease. The points in favor of PCRDD are no lymph node involvement, the presence of the typical large histiocytes displaying emperipolesis as well as positivity for S100 and CD 68 but negative for CD1a on IHC. This IHC profile helps in ruling out Langerhans cell histiocytosis and Erdheim-Chester disease. Differentiating PCRDD from reticulohistiocytoma can be particularly challenging as few cases are S100 positive and show scattered emperipolesis, but the “ground glass” histiocytic cytoplasm and lesser inflammatory infiltrate typically lacking prominent plasma cells favors reticulohistiocytoma. Sarcoidosis patients may present with characteristic reddish-brown plaques with biopsy demonstrating typical noncaseating granulomas.\textsuperscript{1,4,5}

PCRDD is a self-limiting and benign disorder; moreover, no specific treatment is available. A range of treatment options, including cryotherapy, surgery, methotrexate, and systemic or topical corticosteroids are offered to patients with clinical symptoms such as pruritus, tenderness, or for improving aesthetic appearance.\textsuperscript{1,5,6}

**Conclusion**

An appropriate clinical suspicion coupled with an accurate histopathologic diagnosis of RDD is crucial to prevent superfluous aggressive therapy. As PCRDD is extremely rare and diagnosis is difficult without associated lymphadenopathy, it is important to sensitize the budding pathologists and dermatologists regarding this entity.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts for interest**

There are no conflicts for interest.

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