Rosai-Dorfman Disease With Pure and Multifocal Cutaneous Lesions: A Case Report

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Abstract- A 52- year- old woman developed progressive infiltrated purple and hyperpigmented cutaneous lesions in the face, thighs, armpits, chest, and abdomen evolving forone year. Histopathological examination showed large histiocytes exhibiting intact inflammatory cells in their cytoplasm (emperipolesis). Immunohistochemical analyses showed that the histiocyte population was positive for S100 and CD68, but negative for CD1a. Based on the clinical, histopathological, and immunohistochemical findings, we made the diagnosis of Rosai Dorfman disease (RDD). Our patient didn't manifest any other extra-cutaneous involvement and all the biological and radiological investigations were normal. This form of pure cutaneous RDD (P-CRDD) with multifocal lesions has been rarely reported. RDD is very rare and hardly recognized in the absence of lymphadenopathy. The diagnosis of this entity involves a combination of histology and immunohistochemistry. To date, there is no standard treatment.
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Keywords: Rasai-dorfman disease; Emperipolesis; Corticosterois; Methotrexate

Introduction

Rosai Dorfman disease (RDD) is a rare benign histiocytosis, individualized as a clinicopathological entity from two publications reporting 4 then 34 observations by Rosai and Dorfman in 1969 and 1972 under the term of sinus histiocytosis with massive lymphadenopathy (SHML) (1,2).

Lymphadenopathy is the main clinical manifestation. However, multi-organ disease including extranodal manifestations occurs in almost half of the cases (3,4). The skin is among the most frequently involved extranodal organs (16%) (5) but pure cutaneous RDD (P-CRDD) without lymph nodes is a very rare situation (6). Herein, we report a case of RDD with pure and multifocal cutaneous damage.

Case Report

We report the case of a 52-year-old Tunisian woman, without a particular medical history. She presented to our department with progressive infiltrated cutaneous lesions evolving forone year. In the skin exam, she had multiple indurated purple to hyperpigmented plaques ofdifferent sizes. They were located on her face, thighs, armpits, chest, and abdomen. Some of them were painful (Figures 1 and 2).

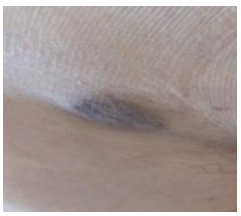

Figure 1. Pigmented infiltrated plaque in the inguinal region

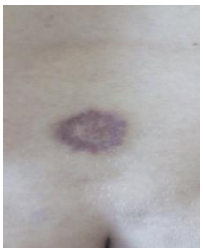

Figure 2. Purple plaque in the lower back

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Moreover, our patient did not report systemic symptoms in association with these lesions. She had no history of fever, malaise, or weight loss. Physical examination did not reveal any lymphadenopathy or hepatosplenomegaly.

Laboratory tests were all within normal ranges, including Erythrocyte Sedimentation Rate (ESR), complete blood count, liver enzymes, antinuclear antibodies, and rheumatoid factors.

A CT scan of the facial bones, abdomen, and pelvis was performed, as well as a brain MRI. All investigations were normal.

Two skin biopsy specimens were taken from the thigh, and complete surgical resection of the plaques in the face was performed. Histological examination revealed large histiocytes exhibiting intact inflammatory cells in their cytoplasm: lymphocytes, plasma cells, and even neutrophils (emperipolesis). Immunohistochemical analyses showed that the histiocyte population was positive for S100 and CD68, but negative for CD1a, confirming the diagnosis of RDD.

RDD with pure and multifocal cutaneous manifestations was diagnosed (P-CRDD).

Since the lesions were multiple, involved the face, and were very embarrassing to our patient, we started high-dose intravenous corticosteroid therapy (1 mg/kg daily). The lesions continued to grow and new ones appeared despite the good adherence to treatment. The treatment was intensified using methotrexate (15 mg weekly). It was a partially effective treatment. After 6 months of follow-up, the size of some lesions decreased and no other lesions were noted.

Discussion

Typically, RDD shows itself clinically inthe form of massive painless cervical lymphadenopathy and fever (4). However, the lymph node affinity of RDD doesn't prevent this disease from reaching other extranodal sites. The most commonly affected sites are skin and subcutaneous tissues, eyes and ocular adnexa, head and neck region, upper respiratory tract, and central nervous system (4).

Although the skin is the most frequently affected extranodal site, P-CRDD is rare (3%) (7).

Further, some authors even consider the P-CRDD as a separate clinicopathological entity, with different demographic characteristics from the nodal form of the disease (8,9).

Aadil studied a comprehensive review of 220 cases of P-CRDD and compared them to 43 cases of CRDD with other systemic manifestations (CRDD-S). These cases were identified in 152 published studies. More than half of the P-CRDD group patients were Asians, while CRDD-S affected almost equally Caucasians, Asians, and Africans. Moreover, in the P-CRDD group, the mean age at the time of presentation was 47 years, there was a slight female preponderance and face was the most common site involved. In contrast to the systemic form where there is a male predominance and no site predilection (10).

As expected, CRDD-S is characterized by a higher proportion of multifocal cutaneous disease and is often accompanied by increased ESR, leukocytosis, anemia, and polyclonal hypergammaglobulinemia (4,10).

Kong *et al*., (11) described 39 skin lesions in 25 patients with cutaneous RDD. These lesions were divided into 3 main types: papulonodular (79.5%), indurated plaques (12.8%), and tumoral lesions (7.7%).

In our case, the disease was limited to the skin without lymphadenopathy or other extra-cutaneous lesions, and laboratory findings were normal.

The skin lesions observed in our patient were infiltrated purple to hyperpigmented plaques with different sizes and different localizations.

In the absence of other systemic signs and biological abnormalities, and given the non-specificity of the skin lesions, the clinical diagnosis of P-CRDD is not easy to establish. A biopsy is critical in this case. It reveals a hallmark feature of RDD which is "emperipolesis": histiocytes with intracytoplasmic inclusion of inflammatory cells, formed by lymphocytes, plasma cells, and neutrophils.

The histiocytes stain positive for S-100 and CD68 and negative for CD1a and Langerin. Compared with nodal RDD, extranodal RDD shows more fibrosis, infrequent typical histiocytes, and a lesser degree of emperipolesis (8,9).

There are several histological differential diagnoses for CRDD. They include fibrous histiocytoma, xanthoma, juvenile xanthogranuloma, infections, other histiocytic disorders showing emperipolesis, malignant histiocytosis, histiocytic lymphoma, reticulohistiocytoma cutis, hemophagocytic syndrome, Langerhans' cell histiocytosis, and T cell lymphomas (3).

To date, the pathogenesis of RDD remains unknown.A viral etiology has long been suggested. Human herpesvirus 6 (HHV-6) DNA and associated antigens have been more frequently detected in the lesions of systemic RDD than those of P-CRDD (12-14). This may suggest that HHV-6 plays a bigger pathogenic

role in systemic RDD than in P-CRDD (15). The other infectious agents incriminated include Epstein-Barr virus, parvovirus B19, Brucella, Klebsiella rhinoscleromatis, and Nocardia (9).

The suggested basic pathological mechanism for RDD is the role of M-CDF in the stimulation of macrophages to phagocyte lymphocytes, giving the emperipolesisA strong expression of M-CSF transcripts in early immigrating monocytes and the presence of M-CSF receptor transcripts in Rosai–Dorfman cellsare observed (15,16).

A genetic component has also been suggested in front of the presence of rare familial cases, and some reported associations between RDD and some genetic disorders (15). Biallelic germline mutations in SLC29A3 have been identified in Faisalabad Histiocytosis (which is an autosomal recessive inherited form of histiocytosis with similarities to RDD), and familial RDD (17). Moreover, an association between RDD and autoimmune lymphoproliferative syndrome (ALPS), a rare, inherited disorder, has been reported. Further, Maric (18) *et al*., showed that 41% of patients with confirmed ALPS 1a had histiocytic proliferation in lymph nodes, resembling RDD histologically.

The clinical course in most cases of P-CRDD is benign and self-limiting. It can spontaneously regress without treatment and generally does not relapse (19). However, several treatments are described for cutaneous and extensive involvement or if the patient is significantly embarrassed by the disease (12).

At present, various therapeutic strategies have been employed with different outcomes. However, there is no standard treatment for RDD. Surgery remains the most effective modality of treatment, especially for the management of solitary or localized lesions (11).

Other options, including high or low-dose of thalidomide, steroids, chemotherapy, and radiotherapy have been reported with various results (20-24).

Purely cutaneous RDD is very rare and hardly recognized in the absence of lymphadenopathy. The diagnosis of this entity involves a combination of histology and immunohistochemistry. To date, there is no standard treatment.

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