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Authors

Elbuluk, Nada
Egbers, Robert
Taube, Janis M
et al.

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Case presentation

Cutaneous Rosai-Dorfman Disease in a Patient with Human Immunodeficiency Virus

Nada Elbuluk MD MSc¹, Robert Egbers MD MSc², Janis M Taube MD MSc², Timothy S Wang MD²

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¹**New York University**

²**Johns Hopkins Hospital**

Correspondence:

Nada Elbuluk
New York University
nada.elbuluk@nyumc.org

Abstract

Rosai-Dorfman disease rarely presents in a solely cutaneous form. A subset of patients with skin limited disease have associated immune disorders such as lupus, autoimmune hemolytic anemia, and Crohn disease. We report an interesting case of cutaneous Rosai Dorfman disease in a patient with human immunodeficiency virus (HIV).

Introduction

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a histiocytic proliferative disorder that typically affects children and young adults [1]. Patients often present with febrile illness, painless lymphadenopathy, anemia, elevated ESR, neutrophilia, and polyclonal hypergammaglobulinemia. Approximately 43 percent of RDD patients present with extranodal involvement, with the skin being a commonly involved site [2]. Systemic RDD has been reported in patients with various diseases of the immune system, including HIV [6].

Only three percent of patients present solely with skin disease and this distinct entity is termed cutaneous Rosai-Dorfman disease (CRDD) [3]. CRDD has been described as occurring in older patients (average age 40 years old) and has an increased incidence in Asians. No gender predilection has been described [4]. CRDD can present as solitary or multiple red to red-brown macules, plaques, papules or nodules, ranging in size from 1-10 cm [5]. Fifteen percent of CRDD patients have an associated immune disorder and to our knowledge, only two cases of CRDD in HIV positive patients have been reported previously [7,8]. We report a third case of a patient with HIV presenting with cutaneous Rosai-Dorfman disease.

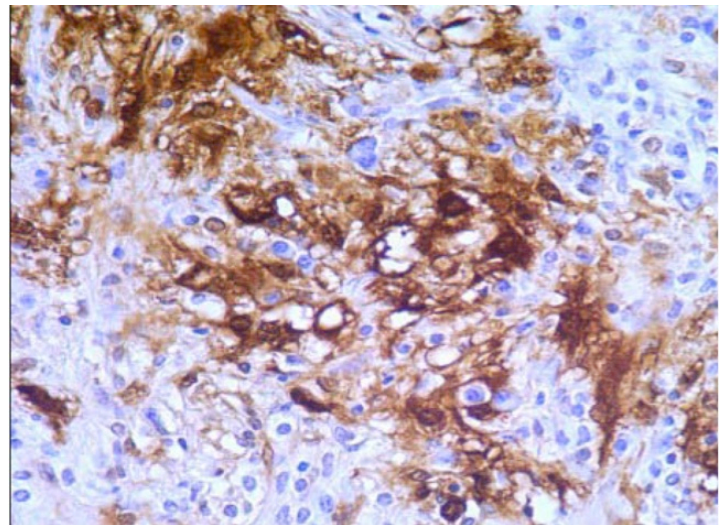
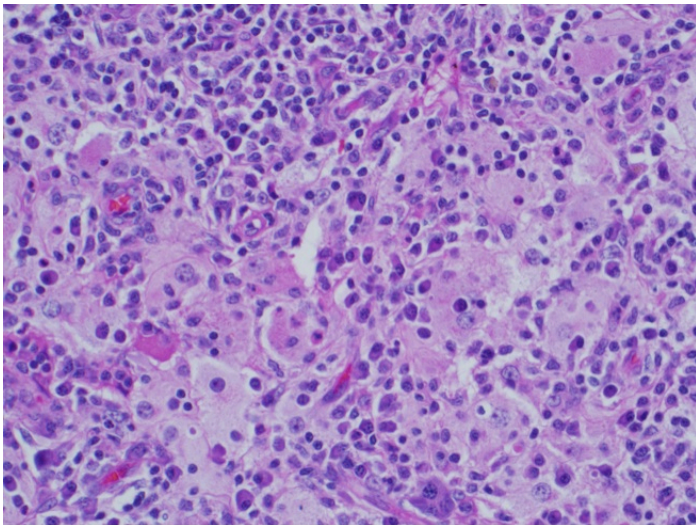
Case synopsis

A 33-year-old woman with human immunodeficiency virus (HIV) presented to our clinic with a one-year history of a slowly growing, tender nodule on her right upper extremity (Figure 1). The lesion began as a pruritic, scaly, erythematous patch and did not improve with 0.25% triamcinolone cream. Over time, the patch became indurated and developed into a larger nodule. On physical examination, the patient was well appearing and had a solitary 4 cm rubbery, firm, mildly tender, red-brown nodule with no sign of epidermal change on the right medial upper extremity. She had no other cutaneous findings and no palpable lymphadenopathy or hepatosplenomegaly. Her HIV disease was stable on emtricitabine-tenofovir and raltegravir with a CD4 count of 305 cells/ μ L. The patient also had a history of Kaposi's sarcoma diagnosed earlier in the year. She had no other past medical or recent travel history. A punch biopsy, tissue cultures, and subsequent wedge biopsy were performed.



Figure 1. Erythematous nodule

The initial punch biopsy showed a mixed dermal and subcutaneous chronic inflammatory infiltrate of lymphocytes and plasma cells and was non-diagnostic. Tissue cultures were negative. The nodule continued to grow and a larger incisional biopsy was performed. This revealed enlarged, foamy histiocytes in the subcutaneous compartment demonstrating emperipolesis of lymphocytes admixed with plasma cells consistent with Rosai-Dorfman (RD) disease (Figure 2). This diagnosis was further confirmed with positive S100 staining (Figure 3). Hematologic studies revealed a normocytic anemia, mildly elevated transaminases, and mild leukopenia. Physical exam was unremarkable including being negative for any cervical, axillary, or inguinal adenopathy. CT of the abdomen and pelvis did not reveal any abnormalities. . Given that patient had no additional findings characteristic of systemic Rosai-Dorfman disease (RDD) on her history and physical exam with a Hematology-Oncology consultant and had a negative laboratory and imaging work-up, she was diagnosed with Cutaneous Rosai-Dorfman disease (CRDD). To treat the remaining area, surgical excision and radiotherapy were offered but the patient deferred further treatment. She has a residual scar with minimal nodularity, which has remained asymptomatic. She has a 3-5 mm nodule distal to the scar which has also remained stable. She has been closely followed for 38 months without local progression, new cutaneous manifestations, or symptoms of systemic involvement.



Figures 2. : Infiltrate of large foamy histiocytes exhibiting emperipolesis. **Figure 3.** Large histiocytes demonstrate positive S100 staining.

Discussion

The diagnosis of CRDD is based on characteristic histologic and immunohistochemical findings of cutaneous manifestations in the absence of systemic findings. On histopathology, there is characteristically a dermal and subcutaneous infiltrate of histiocytes with scattered lymphocytes, plasma cells, and neutrophils [2,5]. The histiocytes have large vesicular nuclei, small nucleoli, and foamy, eosinophilic cytoplasm. Lymphocytes may be encompassed (emperipolesis). In addition, occasional plasma cells, neutrophils, and red blood cells in the cytoplasm of the histiocytes may be present. The enlarged histiocytes stain positive for S100 and are negative for CD1a. The differential diagnosis includes other histiocytic disorders, sarcoidosis, infectious processes, and other infiltrative disorders [8,9].

The pathogenesis of CRDD remains unknown. However, studies have shown that the cellular infiltrate is polyclonal suggesting a reactive rather than neoplastic process [9]. Abnormal response to antigenic stimuli is thought to initiate CRDD, as some patients have been noted to have circulating antibodies to *Borrelia*, Human Herpes Virus 6, and Epstein Barr Virus. Multiple immunologic disorders have also been associated with the diagnosis of CRDD [8].

Investigation into associated immunologic disorders has been helpful in defining CRDD. Abnormal macrophage function and proliferation, particularly the immune suppressing type polarized by macrophage colony stimulating factor (M-CSF), have been identified in the pathogenesis of both Crohn disease and RDD [11]. Interestingly, CRDD has been reported to occur with Crohn disease at a significantly higher than expected rate, suggesting a possible pathogenic link [11].

Treatment of CRDD is based on clinical presentation [9]. Asymptomatic lesions can be left untreated and may persist for years or resolve spontaneously [5]. Surgically resectable lesions may be excised, although recurrences have been described after many years, necessitating long-term follow-up [12]. Alternative treatments for limited disease includes intralesional or topical steroids, cryotherapy, and radiotherapy. Widespread CRDD has been treated with systemic steroids, alkylating agents, thalidomide, dapsone, and retinoids [12]. More recently, complete response has been described with low dose methotrexate therapy [13].

Conclusion

Cutaneous Rosai-Dorfman disease is a rare dermatologic condition, previously described in association with various disorders of immune dysfunction. Although the pathogenesis of CRDD remains unknown, the occurrence of these conditions concurrently in this patient with HIV is of interest considering the proposed polarity of macrophages towards the immune suppressing type in chronic HIV infection [14]. Macrophage polarization towards this immune suppressing type may be a predisposing factor in the development of CRDD in patients with HIV.

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