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Case Report

Granulomatous rosacea-like skin rash: extranodal Rosai-Dorfman disease

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Abstract: We report a 38-year-old man who presented with bilateral conjunctival congestion, hoarseness, and progressively growing pruritic, infiltrated skin lesions that had first begun over the face and neck, and later spread to the trunk and the limbs in 4 months. The clinical appearance of the lesions mimics granulomatous rosacea, acne vulgaris, or pityrosporum folliculitis. Histopathologic examination of the lesions from the face and chest both revealed dense dermal nodular lymphohistiocytic infiltrates which were positive for CD68 and S-100, but negative for CD1a. A systemic work-up for him detected no lymphadenopathy or other systemic involvement. A diagnosis of extranodal Rosai-Dorfman disease was made, and the patient received systemic glucocorticoids, with considerable improvement after 4 months of therapy.

Keywords: Rosai-Dorfman disease, extranodal

Introduction

Rosai-Dorfman disease (RDD), or sinus histiocytosis with massive lymphadenopathy, is a rare, acquired, idiopathic, benign systemic proliferative disorder of histiocytes. The typical clinical features of the disease include fever, bilateral painless massive lymphadenopathy, and polyclonal hypergammaglobulinemia. Skin lesions are the most common form of extranodal involvement in about 43% cases [1]. However, purely cutaneous variant of RDD is very rare and occurs without lymphadenopathy or internal organ involvement. Herein, we report a case with extranodal RDD who presented with skin lesions that mimic granulomatous rosacea.

Case report

A 38-year-old man with an otherwise unremarkable medical history had developed bilateral conjunctival congestion, hoarseness, and progressively growing pruritic, infiltrated skin lesions that had first begun over the face and neck, and later spread to the trunk and the limbs in the past 4 months. Previous treatments including oral antihistamines and a short course of mezlocillin resulted in minimal improvement. Physical examination revealed numerous firm, reddish papules and dome-shaped nodules, diffusely and symmetrically distributed mainly on the cheeks, chin, auricles, neck, trunk and axillae, presenting clinically as granulomatous rosacea, acne vulgaris, or pityrosporum folliculitis, as well as bilateral bulbar conjunctival congestion (**Figure 1**). He denied fever, night sweats, weight loss, lymphadenopathy, or joint pain. Aside from high serum triglyceride and uric acid levels, his laboratory examinations were negative. Histopathologic examination of the lesions from the face and chest both revealed dense dermal nodular lymphohistiocytic infiltrates with occasional eosinophils, plasma cells, and neutrophils. Emperipolesis was also observed within histiocytes, which were positive for CD68 and S-100, but negative for CD1a (**Figure 2**). The patient underwent a systemic work-up, but no lymphadenopathy or systemic involvement was detected. These findings were interpreted as being consistent with extranodal Rosai-Dorfman disea-

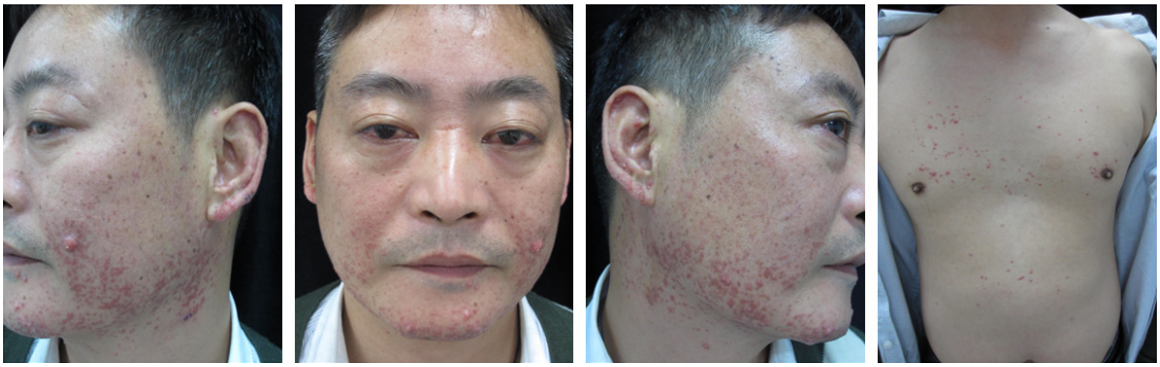

Figure 1. Numerous firm, reddish papules and dome-shaped nodules, diffusely and symmetrically distributed mainly on the face, neck, and trunk, as well as bilateral bulbar conjunctival congestion.

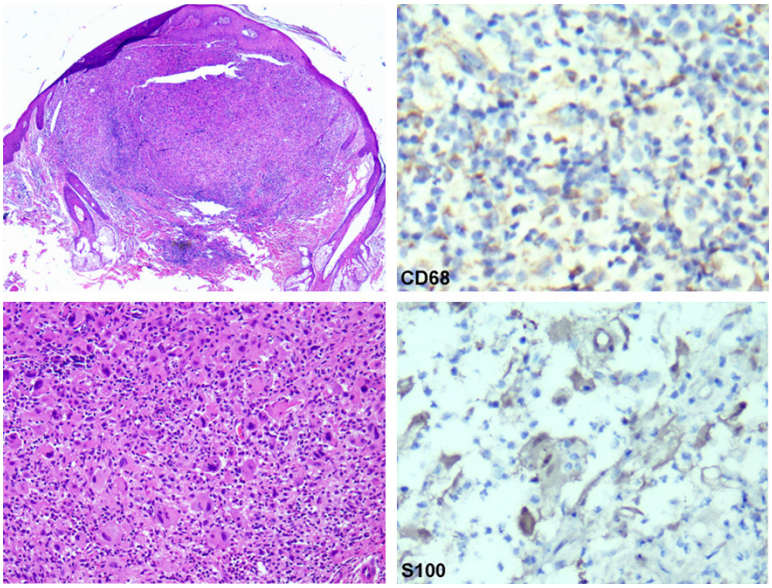

Figure 2. Histopathologic findings from a skin biopsy taken from the face showed mixed inflammatory infiltrate composed of histiocytes, lymphocytes, and plasma cells as well as characteristic lymphocytophagocytosis (well preserved lymphocytes and plasma cells within the cytoplasm of histiocytes) (hematoxylin-eosin staining, ×40 for upper panel, ×200 for down panel). The immunohistochemistry staining of histiocytes was positive for CD68 and S-100 (×200).

se, a benign, non-Langerhans cell histiocytosis with simultaneous cutaneous and ocular involvement. The patient was then given systemic glucocorticoids, with considerable improvement after 4 months of therapy as his skin lesions gradually cleared, and he is currently free of disease 2 years after their onset.

Discussion

RDD, or sinus histiocytosis with massive lymphadenopathy, is a proliferative disorder of non-Langerhans cell histiocytosis, mainly manifested as cervical lymphadenopathy [2]. As the most common extranodal site, cutaneous RDD clinically can range from single papules to multiple nodules, plaques, and patches. Most lesions are located on the face, followed by the back, chest, thigh, flank and shoulder, with rare granulomatous rosacea-like lesions and simultaneous ophthalmic involvement [3, 4]. Histologically, RDD is characterized by histiocytes with large vesicular nuclei and abundant cytoplasm. These cells are positive for markers typical for monocytes and macrophages (e.g., CD68) and in dendritic and Langerhans cells (S-100), while being negative for CD1a. Despite the clear histologic features, timely diagnosis of extranodal RDD is difficult because of variable clinical manifestations without lymphadenopathy and the non-specific histopathologic patterns of extranodal biopsy (less lymphocytophagocytosis and more stromal fibrosis) [5]. The histopathologic differential diagnosis includes multicentric reticulo-histiocytosis (MRH) and granulomatous dermatitis (GD), both of which have lack of lymphocytophagocytosis. MRH histopathologically features a diffuse inflammatory cell infiltrate and histiocytes with abundant ground glass eosinophilic cytoplasm. Histiocytes in GD stain negative for S-100, in contrast to S100-positive staining in RDD [6].

The etiology of cutaneous RDD remains unknown, although a viral pathogenesis involving an abnormal response of histiocytes to a viral stimulus (Epstein-Barr virus, human herpes virus-6) has been postulated; however, such viruses have been found in many reactive and infectious disorders of lymphoid tissues, and their presence in RDD might be non-specific [7, 8]. Clonality studies of affected tissue have demonstrated that the cell infiltrate is polyclonal, which suggests a reactive rather than a neoplastic process [9]. It has been suggested that cutaneous RDD and systemic RDD variants of the disease are distinct clinical entities. Cutaneous RDD has a median age at onset of 43.5 years, shows a female preponderance (2:1), and predominantly affects persons of Asian and white race/ethnicity. In contrast, the median age at onset of systemic RDD is 20.6 years; it occurs slightly more often in men (1.4:1), and patients are rarely of Asian race/ethnicity [10]. Involvement of multiple extranodal organ systems has been considered as unfavorable prognostic factors, and long-term follow-up is essential in light of other visceral metastasis.

Treatment of cutaneous RDD should be based on clinical manifestations. Because it is characterized as a benign, self-limiting disease, therapeutic approaches tend to be less aggressive. For example, the use of systemic glucocorticosteroids or thalidomide and antibiotic regimens, as well as cryotherapy, surgical excision, and radiation therapy for localized lesions, has been described [1]. Our case responded well to glucocorticosteroids and the lesions gradually disappeared after 4 months of therapy.

Disclosure of conflict of interest

None.

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