

Case Report

Cutaneous Rosai-Dorfman disease: an uncommon cause of granulomatous inflammation

羅賽—朵夫曼病案例一宗

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Rosai-Dorfman disease (RDD) is a benign idiopathic proliferative disorder. It commonly affects lymph nodes, but other organs can be involved. RDD limited to skin is rare. We report a 45-year-old Chinese man suffering from RDD. The first three skin biopsies revealed granulomatous inflammation. The diagnosis was made by the fourth skin biopsy, which showed a characteristic histology of large pale-staining histiocytes that exhibited emperipolesis and stained positive for S-100 protein.

羅賽—朵夫曼病是一種良性增生性的疾病，常見於淋巴，偶爾也會發生於其他器官。局限於皮膚者非常罕見。本文報告發生於一 45 歲之中國男性，但三次病理切片皆診斷為肉芽性發炎反應。最後一次病理切片出現典型組織球細胞而確定診斷。此典型組織球細胞為 S100 蛋白陽性並吞噬很多淋巴球及漿球細胞。

Keywords: Chinese, granulomatous inflammation, Rosai-Dorfman disease

關鍵詞：中國人，芽性發炎，羅賽—朵夫曼病

Introduction

Rosai-Dorfman disease (RDD), or sinus histiocytosis with massive lymphadenopathy (SHML), is a benign disorder that primarily

presents with lymphadenopathy. The pure cutaneous form is rare. The clinicopathological diagnosis of cutaneous Rosai-Dorfman disease (CRDD) may be difficult because of its different clinical profiles from those of the nodal form and the presence of a variable clinical and histological picture.

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Case report

A 45-year-old Chinese man presented with slowly progressive skin lesion over his right thigh over two years. The lesion started as small, erythematous papules and then coalesced to form

a confluent plaque with satellite papules. He complained of occasional itch with no systemic upset. Physical examination showed a brownish plaque measuring 10 x 11 cm over right thigh with surrounding satellite lesions (Figure 1). There was no inguinal or cervical lymph node and no organomegaly. The differential diagnoses included granulomatous inflammation, tertiary syphilis, vasculitis, cutaneous lymphoma or lymphocytic infiltration and cutaneous histiocytoses.

An incisional skin biopsy was performed on the right thigh. It revealed granulomatous inflammation. There was basket weave cornified layer with relatively intact epidermis and papillary dermis. At mid and deep dermis, there was nodular infiltration by mixed inflammatory cells with pale and dark zones in focal sclerotic stroma. The pale zone contained mainly histiocytes while the dark zone contained lymphocytes and plasma cells (Figures 2 and 3). Neutrophils and eosinophils were also apparent. Ziehl Neelsen, Wade Fite, Warthin Starry and Grocott stains did not demonstrate microorganisms. Perl and VK stain did not demonstrate Michaelis-Gutmann body. CD3 and L26 stains showed reactive pattern. Kappa and lambda stains did not show light chain restriction. S100 protein stain was positive for some large histiocytes, a few with features suggestive of emperipolesis (Figure 4). T-cell rearrangement PCR assay was negative. Tuberculosis-PCR, tuberculosis and fungal culture were negative. The findings were compatible with the diagnosis of Rosai-Dorfman disease.

Discussion

RDD is a benign proliferative disorder of histiocytes. It was first described in 1965 and recognised as a clinicopathological entity by Rosai and Dorfman in 1969 with severely enlarged cervical lymph nodes infiltrated by large histiocytes exhibiting cytophagocytosis.¹ It commonly presents as massive, painless, bilateral cervical lymphadenopathy with fever, leukocytosis,



Figure 1. Clusters of brownish papules and nodules forming a plaque of 10 x 11 cm over right thigh with surrounding satellite lesions.

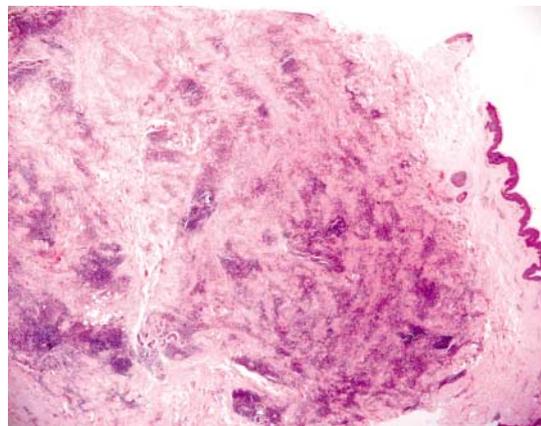


Figure 2. Low magnification showed nodular mid and deep dermal infiltration with light and dark zones (H&E x 20).

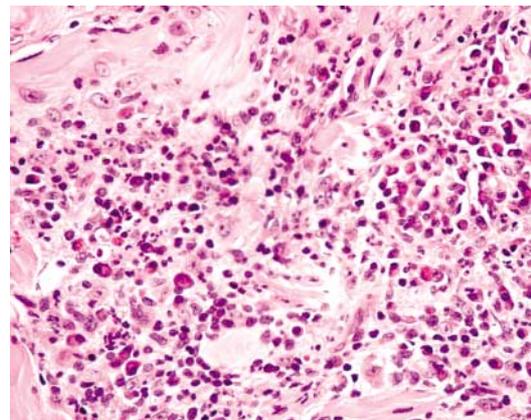


Figure 3. High magnification showed mixed inflammatory infiltrate rich in plasma cells. There were some large cells with vesicular nuclei and conspicuous nucleoli admixed with the infiltrate (H&E x 400).

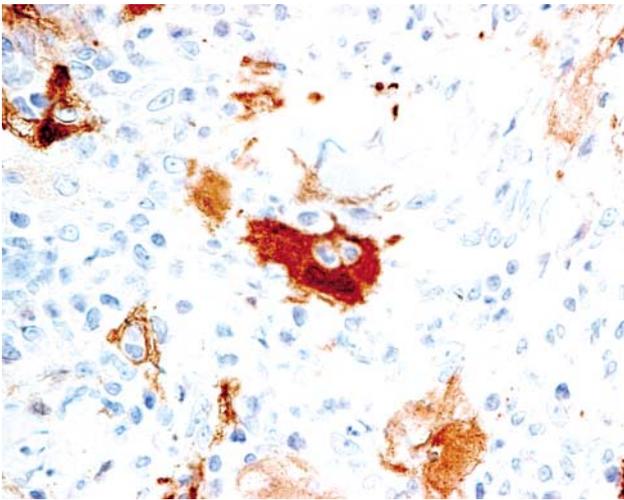


Figure 4. S100 protein stain highlighted the Rosai-Dorfman cells with emperipolesis (S100 protein x 600).

anaemia, polyclonal hyperglobulinaemia, and increased erythrocyte sedimentation rate. It is previously known as sinus histiocytosis with massive lymphadenopathy (SHML). However, it is found that lymph nodes are not always involved. Up to 15% of patients present with extranodal disease only, 57% with lymph node involvement only and 28% with both nodal and extranodal disease.² The most common extranodal sites are skin and upper respiratory tract. Rosai-Dorfman disease has marked predilection for the first and second decades of life, with slight male predominance (Male:Female = 1.4:1). It is more commonly seen in Africans.²

Cutaneous RDD is rare, accounting for 3% of reported RDD cases.³ In previous series of cutaneous RDD, the age of onset is older (mean age: 46-year-old) with a slight female preponderance (male to female ratio is 1:1.7).⁴ Brenn et al analysed the ethnic background for cutaneous RDD and found a significant white and Asian predominance (white:Asian:black = 8:7:3).⁵ In addition, systemic symptoms like fever, malaise, cervical lymphadenopathy, haematological and immunological abnormalities are commonly seen in systemic RDD but are only rarely seen in cutaneous RDD.² In systemic RDD, orbital involvement occurs in 12% of patients and it may

manifest years before lymphadenopathy.⁶ Despite uveitis was found in several reports of cutaneous RDD, it might represent systemic RDD with skin and orbital involvement rather than true cutaneous RDD.

The clinical features of cutaneous RDD are variable and non specific. The cutaneous lesion may be solitary or multiple. It may present as papules, nodules or plaques, or as a combination of these.⁷ The most common presentation is the confluence of a cluster of papules or nodules to form a verrucous plaque with surrounding satellite lesions as that shown in this case. The usual features are skin discolouration and lack of obvious epidermal change. It may mimic other skin diseases like acne conglobata, rosacea, sarcoidosis, ruptured epidermal cyst, deep fungal infection, tuberculosis cutis, other histiocytoses, vasculitis, pyogenic granuloma, dermatofibroma or dermatofibrosarcoma protuberans, inflammatory pseudotumour of soft tissues or lymphoma cutis. The face is the most commonly affected site, otherwise there is no clear predilection for other specific body areas.⁸

Histologically, a dense histiocytic infiltrate is accompanied by a background infiltrate of lymphocytes and plasma cells. The large histiocytic cells, also called Rosai-Dorfman cells (RD cells), have indistinct borders, abundant amorphous cytoplasm, and a large vesicular nucleus with prominent nucleoli. The RD cells uniquely express the monocyte/macrophage markers such as lysozyme, Mac-387 and CD68, as well as the dendritic/Langerhans cell marker S-100.⁴ The S-100 positivity allows us to exclude the possibilities of the inflammatory pseudotumour and other cutaneous histiocytoses. The cytoplasm and nuclei of the histiocytes stain strongly positive for S-100 protein but the inflammatory cells within the cytoplasm of the histiocytes remain unstained with S-100 protein and are surrounded by a clear halo. Therefore, it enhances the identification of emperipolesis and helps to confirm the diagnosis.⁸

The course of cutaneous RDD is benign but variable, but it can be associated with involvement of other organs or immune-mediated diseases, such as bilateral uveitis, antinuclear antibody-positive lupus erythematosus, rheumatoid arthritis, hypothyroidism, and lymphoma. Uveitis is the most common associated condition, which influences the morbidity but not prognosis. Cutaneous RDD tends to resolve spontaneously over months to years.⁹ Cutaneous RDD usually does not require treatment but surgical excision may be needed for cosmetic reasons or symptomatic relief. Response to oral thalidomide in high doses (300 mg/d) had been reported.¹⁰ High dose thalidomide can be considered to control the extensive cutaneous diseases, if its adverse effects can be tolerated by the patients.

In summary, the diagnosis of cutaneous RDD is difficult as it has variable and non specific features both clinically and histologically. It is distinct from the systemic RDD as it has different demographic distribution and clinical course.

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