Atypical Presentation and Dermoscopic Evaluation of Cutaneous Rosai-Dorfman Disease

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Accepted November 24, 2008.

Sir,

Sinus histiocytosis with massive lymphadenopathy or Rosai-Dorfman disease (RDD) is a rare benign self-limiting histiocytic disorder, which is confined mainly to cervical, but also other lymph nodes. Extranodal involvement is present in 43% of cases of RDD and the skin is the most commonly affected site (1). A purely cutaneous form of the disease, termed cutaneous RDD, is even more uncommon and has been well defined (2). Histopathological features include the presence of a dense, dermal infiltrate composed mainly of typical, large, polygonal histiocytes with feathery borders, abundant pale eosinophilic cytoplasm, vesicular nuclei and small nucleoli. Intact lymphocytes, plasma cells and neutrophils are usually seen within the cytoplasm of histiocytes, a phenomenon known as emperipolesis (3). There seem to be no differences between cutaneous RDD and the systemic form in terms of pathological findings (4). Immunohistochemistry typically shows positivity for S-100 in the histiophagocytic cells, which often highlights emperipolesis, but they are negative for CD1a.

CASE REPORT

A 25-year-old black man presented with a 5-month painful lesion on the sole of the left foot, which had been treated previously by his podiatrist as a viral wart with topical salicylic acid and curettage on different occasions over a period of 10 weeks.

The patient was a native of central Africa and there was no relevant medical history apart from previous filariasis on his right leg and a varicella infection 8 weeks previously. No fever, asthenia, weight loss or other general symptoms were reported.

Dermatological examination revealed a 1-cm ulcer with a haemorrhagic hyperkeratotic well-defined border and a clean ulcer bed, which was extremely sore on gentle pressing (Fig. 1A). Curettage of the ulcer border showed a 5-mm whitish middle-consistency tumour lesion.

Analysis using videodermoscopy at 30-fold magnification (MoleMax II, Derma Instruments, Vienna, Austria) revealed a light-red background with milky-white irregularly distributed globular structures of different sizes. A small surface ulceration was present, but neither blood vessels nor other defined dermoscopic structures could be identified (Fig. 1B).

Mild lymphoedema on the inferior lower limb corresponding to lymphatic filariasis and disseminated 2–3-mm hypopigmented scars corresponding to previous varicella infection were also observed. General physical examination was completely normal with no lymphadenopathies or hepatosplenomegaly.

An excisional biopsy was performed and histopathological examination revealed a diffuse dermal infiltrate of lymphocytes, plasma cells and many large histiocytes, which extended close to the epidermis but did not infiltrate it. The histiocytes had abundant, pale pink, cytoplasm and vesicular nuclei. They showed emperipolesis of lymphocytes and neutrophils (Fig. 2). Immunohistochemistry showed diffuse staining in the histiocytes for protein S-100 and, to a lesser degree, for CD68, while CD1a was negative.

Cell blood count, liver and kidney function test, chest X-ray and abdominal ultrasonography were all normal and a discrete polyclonal hypergammaglobulinaemia was detected. HIV and hepatitis C antibody tests were negative and Epstein Barr virus (EBV), human herpesvirus (HHV)-1 and -2 tests were positive for immunoglobulin (Ig)G but not for IgM, being consistent with past infections. Anti-hepatitis B core antigen (anti-HBc) was positive without HBsAg and anti-HBc IgM positivity. Syphilis serology showed positive treponemic and reaginic tests (fluorescent treponemal antibody absorption ++, Treponema pallidum haemagglutination assay + 1/640, Venereal Disease Research Laboratory + 1/8, rapid plasma reagin ++). Ophthalmological examination did not reveal any alterations.

On the basis of the clinical, serological, histopathological and immunohistochemical findings a diagnosis of cutaneous RDD and latent syphilis was made.

As it was not possible to perform a lumbar puncture after several attempts, the patient was treated as for neurosyphilis, with intravenous aqueous penicillin G. A 4-month follow-up showed no recurrence of the lesion and no cutaneous or systemic involvement was detected.

DISCUSSION

Only a few cases of purely cutaneous RDD have been reported since the first description of the systemic disease

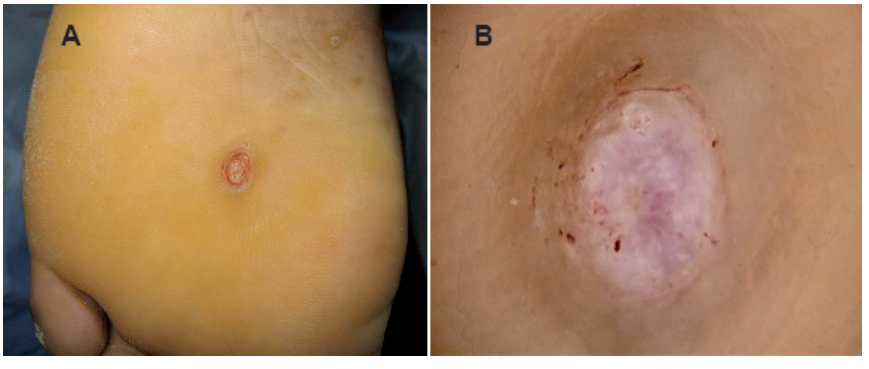

Fig. 1. (A) A 10-mm ulcerated skin lesion located on the central anterior part of the left sole with a clean bed and a hemorrhagic hyperkeratotic border. (B) Videodermoscopy of the lesion at 30-fold magnification showed cotton-like white irregularly distributed globular structures over a light-red background and a small ulceration.

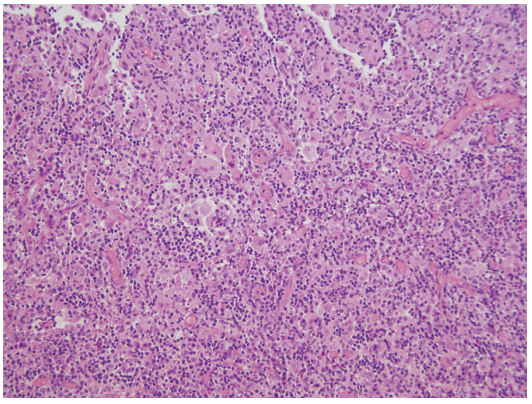

Fig. 2. Centrally-located histiocytes exhibiting emperipolesis. H&E staining, original magnification ×200.

by Destombes in 1965 (5) and the subsequent definition as a distinct clinicopathological entity by Rosai & Dorfman in 1969 (6). The epidemiological distribution of cutaneous RDD is different from the systemic form, meaning a predilection for young adults (mean age 20.6 years), males (1.4:1) and blacks and whites in the latter (1), and a predominance of Asian or white middle-aged (fifth decade of life) females in the former (2). Interestingly, the epidemiological characteristics of our patient match the profile of the systemic disease.

The clinical features of cutaneous RDD are heterogeneous and include single or, more commonly, multiple, indurated papules, plaques or nodules of different sizes with no anatomical predilection site. A 3-type classification based on the clinical morphology of 39 skin lesions has been made, the "papulonodular" type being the most common (79.5%), followed by the "indurated plaque" type (12.5%) and the "tumour" type (7.7%) in which our patient can be included (7). Other reported clinical cutaneous manifestations are erythema, fistulas, ulcers, bilateral cauliflower ear deformity and lesions resembling granuloma annulare, xanthomas, Peyronie's disease, exfoliative dermatitis or rosacea. Histopathological diagnosis rests on the identification of large histiocytes with emperipolesis, which stain immunohistochemically for protein S-100 but not for CD1a.

The aetiology of RDD remains unclear. The polyclonal nature of the cell infiltrate led to speculation of a reactive rather than neoplastic origin of the disease (8). Different theories have been proposed, such an alteration in the cell-mediated immunity (9) or a correlation with infectious agents, mainly HHV-6 or EBV (10–12). Serological studies in our patient revealed EBV, hepatitis B virus (HBV), HHV-1 and -2 past infection and latent syphilis. A possible aetiopathogenic role of these infections could be speculated. As far as we know, a plantar location of a solitary lesion of RDD has not been reported previously, and an abnormal activation of histiocytes after local trauma or past local infection cannot be ruled out.

Milky-white ovoid structures with a cotton-like appearance over a light-red background were observed with dermoscopy. This image is similar to those observed in xanthogranulomas, with yellowish cloud-like structures over an orange-yellow background, being the "clouds" identified as the xanthogranulomatous dermal infiltrate (13) and resembling the yellow nodules present in sebaceous hyperplasias (14), also named "cumulus sign" (15). Similarly to xanthogranulomas, the milky-white globules in our patient would correspond to the dermal histiocytic infiltrate. Hence we can speculate that three types of lesions with common white-yellow globular structures but distinctive features can be recognized with dermoscopy: sebaceous hyperplasia with typical crown vessels, xanthogranulomas with orange background and yellowish hue of globules and cutaneous RDD with red background and whitish hue of globules, lacking the last two entities in blood vessels.

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