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QUIZ CASES

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A patient with a papulo-nodular lesion on the shoulder

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CASE PRESENTATION

A man in his 40s presented with an asymptomatic erythematous, infiltrated plaque, topped by multiple papular and nodular lesions on the left shoulder that appeared 8 months prior (Figure 1). The patient reported no systemic symptoms, fever or weight loss. He had no significant medical history, denied any recent travels and his complete clinical examination was otherwise normal, including the lymph node areas. A complete work-up with blood test (blood cell count, C-reactive protein levels, hepatic, renal and thyroid function, electrolytes, serum protein electrophoresis, infectious serologies for HIV, hepatitis B and C and syphilis), 18F-FDG PET/CT and cranioencephalic magnetic resonance imaging (MRI) was normal. A punch biopsy was performed (Figure 2a,b).

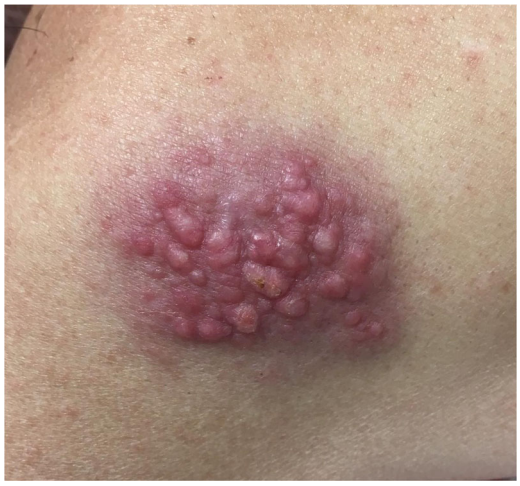

FIGURE 1 Clinical image showing an erythematous, infiltrated and inflammatory plaque, topped by multiple papular and nodular lesions on the left shoulder.

Fanny Ickx and Axel De Greef contributed equally as first authors.

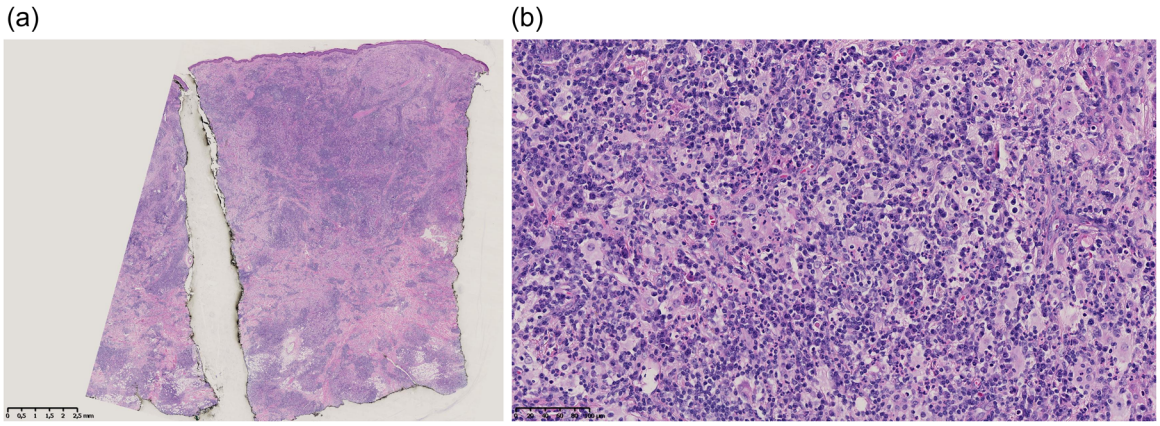

FIGURE 2

WHAT IS THE DIAGNOSIS?

Cutaneous Rosai–Dorfman disease (CRDD) (Sinus histiocytosis with massive lymphadenopathy).

DISCUSSION

Histological and immunohistochemical (S-100 protein) analysis of skin biopsy specimen showed a characteristic feature of emperipolesis (Figure 2a,b) and a strong staining of histiocytes for S-100 (Figure 3) protein which confirmed the diagnosis of RDD. An increase in IgG4-positive plasma cells was also observed (Figure 4). Due to the lack of systemic involvement, the diagnosis of CRDD was made. In this case, surgical resection was performed.

RDD, a non–Langerhans cell histiocytosis, include painless noninflammatory massive cervical node enlargement, fever, leukocytosis with neutrophilia, elevated erythrocyte sedimentation rate, anaemia and hypergammaglobulinemia.[1] Extranodal involvement is observed in 40% of cases.

CRDD is a rare and benign form of RDD characterized by histiocytic proliferation exclusively located into the skin.[2,3] We report an observation of CRDD, which is frequently misdiagnosed clinically.

Patients with CRDD have an older mean age and a female predominance compared to RDD patients.[2,4] The case herein reported concerned a young man (in his 40s), which has been rarely described.

In CRDD, patients may usually have yellow, reddish-brown or violaceous papules, nodules or plaques. Plaque or nodule topped by multiple papules was distinctive in the case reported here. Cutaneous lesions can be either single or numerous, and the most common distribution of these is head and upper part of the body.

Diagnosis must be supported by skin biopsies with histological and immunochemistry analysis. The most representative histologic feature is a dense dermal infiltrate of histiocytes with the characteristic images of *emperipolesis* (intact inflammatory cells in a histiocyte cytoplasm, or lymphophagocytosis) and a mixed inflammatory infiltrate. The immunohistochemistry reveals histiocytes expressing PS100, CD163 and CD68, macrophagic markers, but not CD1a.[2–4] The numbers of typical S100-positive histiocytes, the importance emperipolesis as well as the quality and quantity of the inflammatory response may be variable.[4] Although an association between RDD and IgG4-related disease remains controversial, the Histiocyte Society recommends the evaluation of all cases of RDD for IgG4-positive plasma cells. An increase in IgG4-positive plasma cells, as it was the case for our patient, should be documented but interpreted regarding the clinical, serological and radiological context.[3]

The exact pathophysiology remains unknown, but the polyclonal cellular infiltrate suggests a reactive process rather than a neoplastic one. A link with some infections has been suspected. Several cases are associated with autoimmune diseases or lymphomas.[2] A complete systemic work-up is therefore indicated with 18F-FDG PET/CT, cranioencephalic MRI and complete blood tests.

For localized disease, surgical excision remains a first choice. For refractory cases, oral steroids, dapsone, thalidomide, methotrexate, retinoids, doxycycline or imatinib can be proposed. The prognosis of CRDD is usually good with the possibility of spontaneous resolution.[5,6] Evolution into systemic involvement seems extremely rare.[4]

Differential diagnosis in this case included primary cutaneous B-cell lymphoma (pCBCL), dermatofibrosarcoma protuberans or cutaneous infection due to non-tuberculosis mycobacterium.

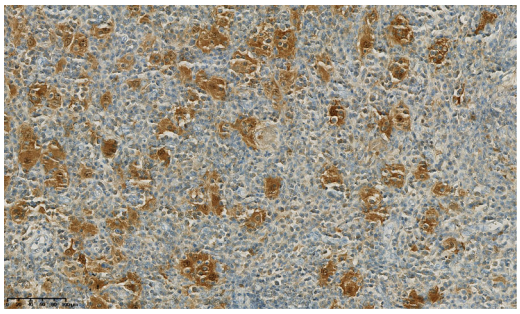

FIGURE 3

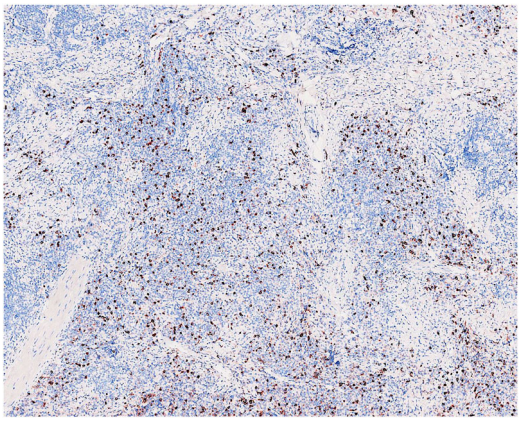

FIGURE 4

There are three main subtypes of pCBCL: primary cutaneous marginal zone lymphoma, primary cutaneous follicle centre lymphoma and primary cutaneous diffuse large B-cell lymphoma, leg type. They usually manifest as red-to-violaceous or pink asymptomatic cutaneous nodules, plaques or tumours. The diagnosis is based on specific histologic, immunohistochemical, cytogenetic and molecular features.[7]

Dermatofibrosarcoma protuberans is a low-grade slow-growing malignant sarcoma, presenting as a large, bumpy, multinodular tumour adherent to the skin surface without ulcerating it, infiltrating the dermis and hypodermis often beyond the palpable limits. The histologic diagnosis (monomorphous spindle cell proliferation in a storiform pattern) can be supported by the detection of translocation t(17;22)(q22;q13), present in 90% of cases.[8,9]

Clinical features of nontuberculosis mycobacterium skin infection are polymorphic (nodules, papules, plaques, abscesses, ulcers), single or multiple, localized to one limb or disseminated. The diagnosis should be considered in the presence of any uncharacterized eruption, especially in immunocompromised patients. Histopathological findings are often nonspecific; tissue culture and PCR assays may be necessary to identify the species.[10]

This case illustrates the clinical appearance of the cutaneous form of RDD which remains a diagnostic challenge for the clinician.

AUTHOR CONTRIBUTIONS

Fanny Ickx and Axel De Greef performed the literature search and prepared the manuscript. Diane Declaye and Léo-Paul Secco were in charge of the investigation process. Marie Baeck reviewed and approved the manuscript and decided to submit the manuscript for publication.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

ETHICS STATEMENT

The patient in this manuscript has given written informed consent for the use of deidentified, anonymized, aggregated data and the case details (including photograph) for publication. Ethical Approval: Not applicable.

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