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PURELY CUTANEOUS ROSAI-DORFMAN DISEASE: A TRUE CLINICAL DIAGNOSIS CHALLENGE

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ABSTRACT

Rosai-Dorfman disease (RDD) is a rare idiopathic benign disease, self-limited non-Langerhans cell histiocytosis, most frequently presented as a massive bilateral and painless lymphadenopathy, associated with fever and weight loss. Extranodal manifestations of RDD represents a true diagnosis challenge for clinicians and surgical pathologists. A 64-year-old female, known with arterial hypertension and type 2 diabetes, presented to our Surgery Clinic for a left arm painless cutaneous tumour, having its onset one year before, and rapidly enlarged in the last two months. Physical examination revealed a firm and elastic cutaneous nodular lesion of 4 x 2 cm in size, prominent to the skin, with central ulceration area of 10 x 5 mm, located on the posterior side of the left arm. Surgery was performed, with lymphoma as a differential diagnosis at intraoperative extemporaneous examination. The RDD disease diagnosis was considered at histopathological analysis and confirmed by immunohistochemistry. Herein, we describe a rare case of purely cutaneous RDD presenting as unique cutaneous ulcerative nodular lesion, surgical treated only, and without local relapse after one-year follow-up.

Keywords. Rosai-Dorfman disease, emperipolesis, ulcerative cutaneous tumour, sinus histiocytosis.

Introduction

Rosai-Dorfman disease is a rare, non-malignant clinical entity, initially described by Destombes in 1965 (1), and subsequent, as a distinct clinicopathological disorder by Rosai and Dorfman, in 1969 (2). Mostly, the RDD presents as a massive bilateral and painless cervical lymphadenopathy associated with fever, night sweats and weight loss. Others nodes, such as mediastinal, inguinal or retroperitoneal, can be also involved. Extranodal involvement by RDD, although considered very rare, it has been documented in 43% of cases of skin, soft tissue, upper respiratory tract, multifocal bone (3,4), eye and retro-orbital tissue (5), urogenital tract (6), breast (7), gastrointestinal tract (8), liver, pancreas (9,10), lungs, head and neck (11–14). The cutaneous-only affection of RDD is considered a clinically distinct entity form of RDD. Further, in some studies, this form of RDD may be a separate clinico-pathological entity, with different demographic features from the nodal disease (15,16). Skin and soft tissue lesions are usually present as red-brown papules or palpable masses, that can vary in dimensions, from less than 1 cm to more than 30 cm (17). Pustular, psoriasiform and acneiform appearance have also been reported (18). Herein, we describe a rare case of purely cutaneous RDD presenting

as unique cutaneous ulcerative nodular lesion, surgical treated only, and without local relapse after one-year follow-up.

Case report

A white 64-year-old female, known with arterial hypertension and type 2 diabetes, presented to our Surgery Clinic for a left arm painless cutaneous tumour, having its onset one year before, and rapidly enlarged in the last two months. Physical examination revealed a firm and elastic cutaneous nodular lesion of 4 x 2 cm in size, prominent to the skin, with central ulceration area of 10 x 5 mm, located on the posterior side of the left arm. No others lesions were observed and no lymphadenopathy was appreciated. Also, she denied any history of fever, weight loss, night sweats or local trauma. Chest radiography demonstrated no evidence of enlarged lymph nodes, and on abdominal ultrasonography, no lymphadenopathy, and neither liver nor spleen enlargement were identified. Laboratory values were in normal ranges. The skin ulcerative appendage tumour as presumptive diagnosis was made by dermatologist, and excisional tumour biopsy was recommended. Surgery was performed, with large margins excision of the skin tumour. The surgical specimen, consisting of a 6.3 x 5 cm skin fragment and 2 cm thick subcutaneous fat tissue, exhibits a tumour size of 3.8 x 3 x 1 cm, prominent on the skin surface, with central ulceration area of 10 x 5 mm, poorly delimited, whitish and fatty appearance. The intraoperative extemporaneous examination revealed a cutaneous fragment with rich inflammatory polymorphic infiltration into the dermis, and for the confirmation of the reactive nature and the differential diagnosis with a lymphoma, the histopathological diagnosis in paraffin-embedded was required. Postoperative evolution was good and the patient was discharged after three days. The RDD disease diagnosis was considered by histopathological analysis and confirmed at immunohistochemistry.

Sections from surgical specimen were processed and stained with haematoxylin and eosin, Giemsa and periodic acid-Schiff (PAS) stains. Histopathological examination of the lesion showed a skin fragment with ulcerative area with inflammatory cellular dermal-hypodermic infiltrate, in diffuse areas and multinodular arrangement, consisting of histiocytes with an eosinophilic abundant cytoplasm, with irregular contours (Figure 1); vesicular nuclei, some with visible nucleoli, relatively frequent multinucleated histiocytes; moderate histiocytic lympho-phagocytosis (emperipolesis) (Figure 2); numerous lymphocytes, plasmocytic, neutrophils arranged diffuse and nodular at dermal and hypodermic layers; moderate nuclear atypia; relatively rare mitosis; areas of fibrosis and dermo-hypodermic interstitial fibroblast proliferation; moderate interstitial oedema; epidermis with a area of ulceration covered by fibro-leukocyte clot. No microbial and fungal elements were identified at the special stains, Giemsa and PAS respectively.

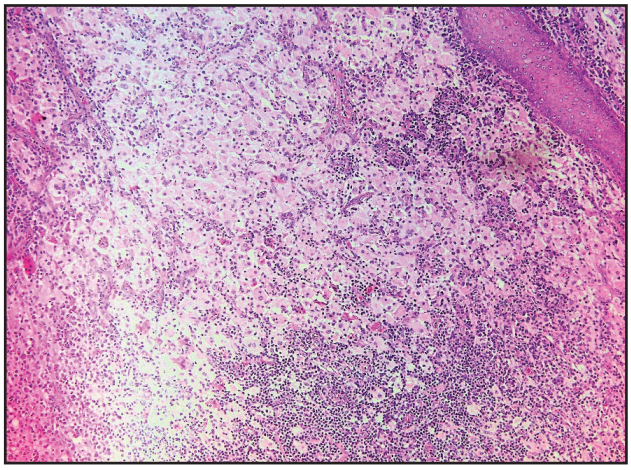

Figure 1. Diffuse dermal-hypodermic infiltrate with macrophage which present abundant eosinophils cytoplasm. HE x 100.

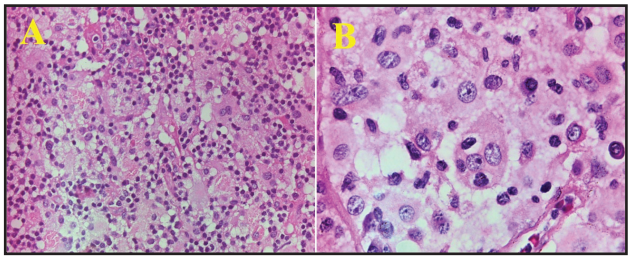

Figure 2. Macrophages with numerous intracytoplasmic phagocytic lymphocytes and/or hematite (emperipolesis). A: HE x 200; B: HE x 400.

The immunohistochemistry results revealed: CD3 positive diffuse and nodular in reactive T lymphocytes, CD20 positive diffuse and nodular in reactive B lymphocytes,

CD10 positive diffuse into dendritic cells; rare lymphocytes and polymorphonuclear neutrophils; CD15 positive in activated B and T lymphocytes and polymorphonuclear neutrophils; strongly positive CD30 in histiocytic proliferation; positive in rare B and T activated lymphocytes, and CD68 (Figure 3) and CD11c positive for histiocytosis proliferation. In addition, Ki67 index was positive in approximately 5% of lymphocytes nuclei and in 2% of histiocytes nuclei.

After one-year follow-up, the patient presents a good overall condition, healed postoperative wound, no signs of local or distant recurrences.

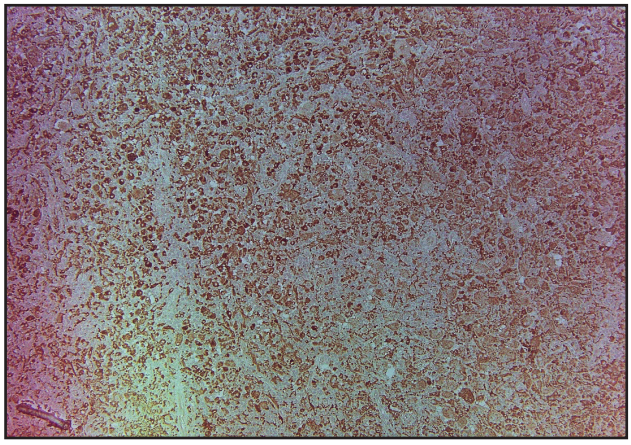

Figure 3. Intense and diffuses positive for CD68 of macrophages. CD68 x 100.

Discussions

The cutaneous form of RDD (CRDD) is very rare, first described in 1978, by Thawerani et al. (19). The cutaneous involvement is the most frequently extra nodal manifestation, comprises 11% of RDD, but in only 3% is presented as purely cutaneous disease (20, 21, 22). This last form of cutaneous RDD is a clinically distinct entity, about which, in some reports, it is suggested that this condition could be a separate clinico-pathological entity from nodal RDD (15). While the systemic form RDD manifests in children and young adults, in the first or second decades of life (mean age of 20.6 years old) (5, 15, 16, 23), CRDD tends to occur predominantly in women (F:M=2:1), having age distribution ranges from 6 to 68 years old, with a mean age of 45 years (22, 24). Furthermore, in contrast to the systemic form, which commonly presents as bilateral, painless cervical lymphadenopathy with fever, often accompanied by leucocytosis, anaemia, an elevated erythrocyte sedimentation rate and polyclonal hypergammaglobulinemia (25, 26, 27), CRDD usually has no systemic manifestations or laboratory abnormalities (23). Starting from the above, the clinical diagnosis of purely cutaneous RDD is not easy to establish, given its nonspecific clinical appearance.

Clinically the cutaneous lesions are identical in both systemic and cutaneous forms. In some of the first reports on cutaneous manifestations of RDD, was presented a large pallet of clinical presentations, such as exfoliate dermatitis, scaly erythematous lesions mimicking psoriasis or pinhead-sized papules (19,28). In further reports, cutaneous lesions are often slow-growing, characterized by asymptomatic yellow-brown papules (26) or red nodules that can be solitary, in groups or disseminated, frequently with purple-brown discoloration, erythema or hyperpigmentation (29). Skin lesions described in these reported cases were often divided into three main types: papulonodular (79.5%), indurated plaque (12.8%) and tumours (7.7%) [30]. These cutaneous lesions can occur in any part of body, but frequently are involved the limbs, the trunk and face (22, 30, 31). Our case, completes the clinical manifestations of purely cutaneous RDD with a new clinical presentation that we have not seen before in other reports: cutaneous nodular lesion, prominent to the skin, with central ulceration area. In this case, nodular basal cell carcinoma and skin ulcerative appendage tumour, as clinically differential diagnosis, and cutaneous lymphoma by intraoperative extemporaneous examination were considered. In addition, as a differential diagnosis of CRDD can be considered affections such as histiocytosis, dermatofibrosarcoma protuberans, sarcoidosis, infectious processes or other infiltrating neoplasms (32). Therefore, given these various clinical presentations that the CRDD manifests, the diagnosis of this type of lesion is made on the histopathological findings and the results of immunohistochemical studies.

Histopathology typically reveals a dermal or dermo-hypodermic infiltrate of histiocytes with emperipolesis, which represent

an intracytoplasmic inclusion of inflammatory cells, formed by lymphocytes, plasma cells, and neutrophils within vacuoles. Epidermal changes are usually absent or mild (15, 16, 25, 28). In our case, the epidermis showed ulceration covered by fibro-leukocyte clot. Immunohistochemical stains of RDD cells, are positive for S100, CD11c, CD14, CD163, α1-antichymotrypsin, α1-antitrypsin, fascin and HAM-56 while CD1a is typically negative (12) and CD68 (KP-1) is variable-positive. In presented case, CD68 and CD11c were intense and diffuse positive. Langerhans-cell histiocytosis, a very rare and lethal disease (20), shows a different immunohistochemical pattern, expressing CD1a, CD207 and S100, while CD68 is negative. More, the differential diagnosis of CRDD may include other affections, like histiocytic lymphoma, melanoma, xanthomas, Erdheim-Chester disease, lysosomal storage diseases, sarcoidosis or infectious and inflammatory conditions such as histoplasmosis, leishmaniasis, rhinoscleroma, inflammatory myofibroblastic tumour and IgG4-related disease (33, 34, 35). In these cases, the diagnosis assumes a good correlation between the clinical appearance, the characteristics presented in the histopathological examination and, of course, the immunohistochemical analysis for confirmation. Although our case had an atypical presentation for RDD, the histopathological examination established the diagnosis of CRDD. Furthermore, the microbial and fungal elements were excluded by special stains, Giemsa and PAS respectively.

Usually, purely cutaneous RDD does not require a specific treatment. It has a benign course, frequently self-limited. These lesions are surgically excised for aesthetic reasons or in those cases in which malignancies can not be excluded. While others treatments of RDD were reported, such as glucocorticoids, antibiotics, radiotherapy, cryotherapy, thalidomide, isotretinoin, acitretin, interferon-alpha, methotrexate, dapsone, and pulsed dye laser, the surgery remains the procedure with highest success rates (15). In our case, ulcerative lesion and suspicion of a skin neoplasm, led to surgical excision with intraoperative extemporaneous examination.

Conclusions

Purely cutaneous RDD diagnosis is difficult to establish only of its clinical presentation. It requires further examinations, particularly histopathological examination and immunohistochemical analysis, moreover if a cutaneous neoplasia is suspected.

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Declarations.

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Conflict of Interest: None declared

Ethical approval: Not required

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