Case Report

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An intriguing disease with unusual presentation: A Rosai-Dorfman's case report

Abstract

Rosai-Dorfman disease is a rare non-Langerhans histiocytic disease characterized by lymph node enlargement and extra-nodal involvement. Extranodal disease occurs in 40% of cases and common sites of involvement are: skin, nasal cavity, bone, orbital tissue and central nervous system. Lesions are usually plaques, nodules or papules of insidious growth and no associated symptoms. We report here an atypical case of Rosai Dorfman in an adolescent with fever of undetermined origin, without significant lymphadenopathy and diffuse facial edema.

Keywords: case reports, histiocytosis, sinus, Rosai-Dorfman

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Introduction

Rosai-Dorfman disease is a rare non-Langerhans histiocytic disease characterized by lymph node enlargement and extra-nodal involvement.[1] The most typical presentation of the classic nodal form of Rosai Dorfman's disease involves the presence of painless, massive bilateral cervical adenomagalia with fever, weight loss, and night sweats. Extranodal disease occurs in 40% of cases and common sites of involvement are: skin, nasal cavity, bone, orbital tissue and central nervous system. Cutaneous involvement is present in 10% of cases of extranodal manifestation. Lesions are usually plaques, nodules or papules of insidious growth and no associated symptoms. We report here an atypical case of Rosai Dorfman in an adolescent with fever of undetermined origin, without significant lymphadenopathy and diffuse facial edema.

Case report

Male patient 14 years old, started mild abdominal pain in association with neutropenia (2300 thousand/mm³, RV 4500-13000), mild elevation of inflammatory tests (CRP 15 mg/L VR < 5mg/L) and thrombocytopenia (62 mil, VR 150-450 K/µL). Three months later, he presented an exacerbation of the condition after a flu-like syndrome. At the time he was hospitalized with renal dysfunction, anasarca and generalized adenomegaly. To investigate oncological causes, myelogram, abdominal and chest CT scans were performed. The myelogram did not show the presence of atypical cells. CT scans showed hepatosplenomegaly and lymph nodes increased in number and size (2.5 cm in greatest diameter). In addition, infectious causes with negative serology for viral hepatitis, cytomegalovirus, EBV, leishmaniasis, toxoplasmosis, syphilis and HIV were investigated. Cultures for fungi and mycobacteria are negative. Investigation of ANA, AntiDNA, ANCA autoantibodies were negative. On admission, he received broad-spectrum antibiotics and supportive therapy with progressive improvement after 2 weeks. He presented resolution of fever, improvement of renal function, adenomegaly and anasarca. However, he maintained thrombocytopenia (83,000, VR 150-450 K/µL), mild elevation of inflammatory tests and diffuse facial edema, with no associated skin lesions. He was discharged from the hospital for an outpatient investigation (Figure 1).

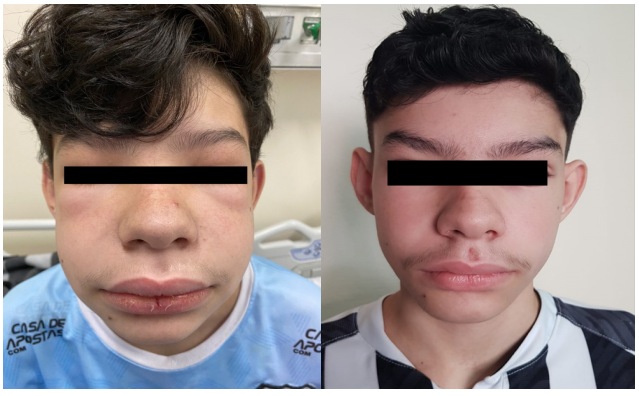

Figure 1 A – Patient at admission and B – after treatment.

Two weeks after hospital discharge, he returned due to fever, worsening facial edema, oral ulcers, dysphagia and abdominal pain related to feeding. Re-admitted for investigation, received omeprazole, cefepime and acyclovir. On examination, he had diffuse facial edema, with a predominance of lips and periorbital region; oral ulcers and palpable lymph nodes (2cm) in inguinal chains. In investigation of abdominal pain, he performed upper digestive endoscopy that showed mild gastritis. In addition, repeat abdominal and thorax tomography that showed resolution of adenomegaly. Evolved with progressive improvement of oral lesions and dysphagia, but maintained fever

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and persistent facial edema. At the time, there was no change in renal function (Cr 0.7 mg/dL – RV 0.57-0.87) or albumin (3.4 g/dL RV 3.2-4.5) to justify the edema. A hypothesis of inflammatory etiology for the condition was raised.

Despite the improvement of the adenomegaly and in view of the diagnostic uncertainty, it was decided to perform a biopsy of the inguinal lymph node. Histology showed outlines of granulomas. Investigation of EBV, fungi and mycobacteria in the sample were all negative. Lymph node immunohistochemical study showed: CD3, CD20, PAX-5, CD 15, IgG4, CD138, CD25, BRAF V600E negative; Ki67, CD68, CD1A, CD 163, s-100 positive protein, markers compatible with Rosai-Dorfman disease. After diagnosis, presnisone 40 mg daily and methotrexate 20 mg weekly were introduced with resolution of fever and facial edema.

Review and discussion

Rosai-Dorfman disease was described in 1969 and is a rare non-Langerhans histiocytic disease characterized by lymph node enlargement and extra-nodal involvement.[1] This disease spectrum varies from enlargement lymph nodes, non-pruritic skin lesion, involvement of the nasal and paranasal sinuses, central nervous system (CNS), ocular, renal and other visceral involvement. Rosai-Dorfman disease can occur as an isolated disorder or in association with autoimmune and neoplastic diseases.

As other rare diseases, the physiopathology and etiology are not well understood, but some kinase mutations are associated with disease occurrence. The most described genetic alterations are mutations in MAP2K1and KRAS, condition that was identified in 33% in a previous study.[2] Other genes associated are ARAF, NRAS and epigenetics such as viral triggering are candidates on the development of the disease phenotype.

The clinical presentation is variable: most commonly, enlargement of lymph nodes are seen, especially cervical, but almost half of patients have extranodal disease. Fever and night sweats are also frequent. The cited extranodal involvement includes, central nervous system, sclerotic bone lesions, nasal and eye alterations and rarely skin (less than 10%). The gold standard for diagnosis is biopsy that shows low power appearance of extensive sinusoidal expansion and infiltration of histicites, but cell markers such as CD1 e CD207 auxiliate differentiation with lymph neoplasms.

The presentation of the disease is usually in young masculine adults and adolescents and estimated prevalence is 1:200,000. To date, we have about 1,000 published cases. The variable presentation opens a large list of differential diagnosis, such as bacterial, mycobacterial, fungal and viral infections, neoplasms (specially hematologic) and a broad spectrum of autoimmune diseases varying from sarcoidosis and IgG4 related disease, demanding suspicion and vigilance in atypical cases.

Interestingly, in this case, the patient presented as main symptom a picture of fever of undetermined origin. During the investigation, the adenomegalies resolved, but the inflammatory markers remained high and the facial edema had no identifiable etiology. In the second hospitalization, a hypothesis of lymphoma was raised, however, the adenomegalies regressed and the only palpable lymph nodes did not present any characteristics of malignancy. This case illustrates the importance of lymph node biopsy in cases of persistent inflammation and fever of undetermined origin.

Another interesting aspect of the case is the facial edema. Despite the improvement of the acute renal dysfunction, the patient persisted with facial edema predominantly in the lips and periorbital region, without swelling of other parts of the body. Reduction in oncotic pressure or increase in hydrostatic pressure was ruled out. In addition, studies of the cervical vessels did not show obstruction to justify superior vena cava syndrome. In this context, inflammatory causes for the edema were suggested: orofacial granulomatosis and sarcoidosis.[3-7] At first, the diagnosis of Rosai Dorfman was not considered as this is not a finding typically found in this disease. The response to treatment and the concomitant resolution of additional symptoms suggests that facial edema may be a manifestation associated with Rosai Dorfman's condition.

Rosai-Dorfman disease is a relatively new disease with a broad spectrum of presentations. We reported an adolescent with Rosai-Dorfman disease whose first presentation was characterized by fever of undetermined origin and important facial edema, a previously undescribed feature of this disease. The lymph node biopsy was fundamental in establishing the diagnosis and the treatment could be introduced changing the disease's natural history.

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None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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