

CASE REPORTS / REPORTE DE CASO

Sinus histiocytosis in cervical adenopathy, case report. Histiocitosis sinusal en adenopatía cervical única, reporte de caso.

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Abstract: Rosai-Dorfman disease (RDD) is a rare histiocytosis which is typically accompanied by painless bilateral cervical lymphadenopathy. The laboratory data are non-specific and the histological characteristic which prevails is the presence of emperipolesis in large foamy histiocytes positive for CD68, S-100 and negative for CD1a. It is still difficult to determine the pathogenesis. The case of a male African-Ecuadorian young adult who made a consultation due to presenting right cervical adenopathy is presented.

Key words: Histiocytosis, adenopathy, emperipolesis.

Resumen: La enfermedad de Rosai-Dorfman (RDD) es una histiocitosis rara, que en forma típica se acompaña de linfadenopatía cervical bilateral indolora. Los datos de laboratorio son inespecíficos y la característica histológica que predomina es la presencia de emperipolesis en histiocitos grandes espumosos positivos para CD68, S-100 y negativos para CD1a. La patogénesis sigue siendo difícil de establecer. Se presenta el caso de un paciente masculino afroecuatoriano adulto joven, quien acudió a consulta por presentar adenopatía cervical derecha única.

Palabras clave: Histiocitosis, adenopatía, emperipolesis.

Introduction

The lymphadenopathy is a frequent reason for consultation in ambulatory care, being mostly benign and self-limited. Causes may include infections, autoimmune diseases and malignance, as well as iatrogenic disorders. To define the etiology, diagnosis includes laboratory tests, images, ganglionic or bone marrow biopsy, depending on the clinical condition, localization and distribution of lymph nodes and risk factors¹.

Rosai-Dorfman Disease is characterized by non-painful cervical lymphadenopathies which may compromise other lymph nodes, and in 43% of the cases it may be accompanied by extranodal condition, having an unpredictable clinical evolution with remission and exacerbation episodes. The histological characteristics are infiltration of lymph nodes sinuses due to mononuclear or multinuclear histiocytes, the cytoplasm of which is often full of lipids; there are also emperipolesis lesions of blood cells (vacuole aspect which comprises lymphocytes, plasmocytes, polymorphonuclear leucocytes or red blood cells)².

Clinical case

Male patient of 47 years of age, with personal pathological history of right groin hernioplasty ten years ago and head trauma four years ago, which caused right laminar epidural hematoma (not operated) and fracture of right petrous bone with effects of peripheral facial paralysis. The patient visits Hospital General Ibarra due to showing right cervical region mass of several months, without specifying the exact time of evolution.

During physical examination, the only thing evidenced which draw attention is right cervical adenopathy of 1.5 cm, non-painful and non adhered to deep planes; no hepatomegaly,

no splenomegaly, no petechiae, no ecchymosis.

Exams are requested, evidencing a normal hemogram, normal liver and renal tests, normal globular sedimentation velocity, normal antinuclear antibodies, rheumatoid factor; cytomegalovirus, HIV, Epstein-Barr: negative, ultrasound: left renal lithiasis without ectasia; no hepatomegaly, no splenomegaly, chest radiography: normal.

With the foregoing we have diagnosed the Rosai-Dorfman disease (sinus histiocytosis). The patient has been kept with regular controls for one year without showing new adenopathies or signs or systemic condition (by means of imaging studies), so that management of this case has not required any systemic therapy, only observation.

Discussion

Rosai-Dorfman Disease (Destombes-Rosai-Dorfman for other authors), is a disorder of non-Langerhans cell histiocytosis characterized by intrasinusoidal proliferation of abnormal histiocytes in sinuses of lymph nodes, lymph vessels of internal organs and in other extranodal sites. It is more common in chil-

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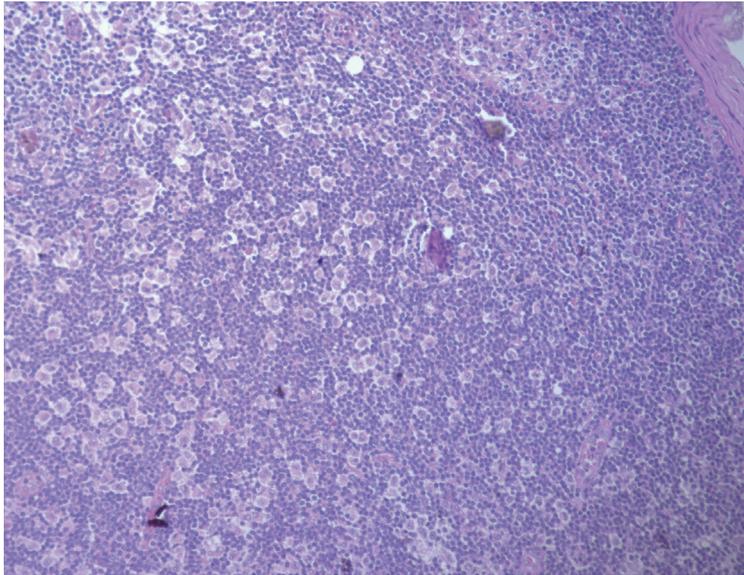
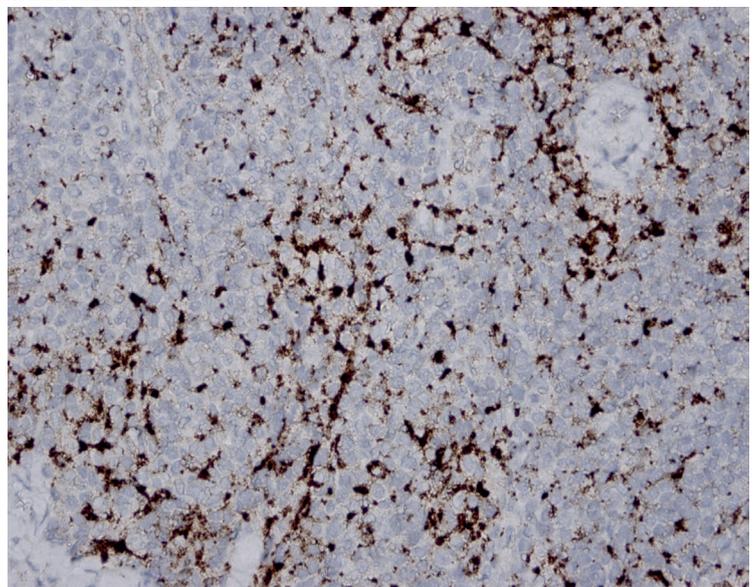


Figure 1. Emperipolesis in cervical lymph node stained with hematoxylin and eosin.

Figure 2. Immunohistochemistry of cervical lymph node, where the dark brown stained cells are Histiocytes(positive CD68 marker).



dren and young adults, with slight predominance in men over women and in African descendants in comparison with other races. This disorder was described for the first time in 1965 by Paul Destombes who reported 2 cases of adenitis with lipid deposits; then, Juan Rosai and Ronald Dorfman identified the diseases as sinus histiocytosis with massive lymphadenopathy and submitted it to a unique clinical-pathological entity with 2 studies published in 1969 and 1972. Histologically, abnormal xanthomatous histiocytes of the Rosai-Dorfman disease show abundant emperipolesis of erythrocytes, lymphocytes, polynuclear and plasmatic cells, which implies immersion of these types of cells which remain intact within cytoplasm^{3, 4}.

Abnormal histiocytes are immunoreactive for CD14, CD68, CD163 and S100 and negative for CD1a and CD207^{5, 6, 7}.

Emperipolesis was described in 1956 by Humble as "the active penetration of a cell by another which remains intact". In these cases, the comprised cell maintains the integrity of the normal structure inside the other cell, and both can exist without causing abnormalities for some time. On the contrary, in phagocytosis, lysosomal enzymes destroy the comprised cells. Although emperipolesis is the characteristic of RDD, it may appear in other conditions such as Hodgkin lymphoma, multiple myeloma, malign melanoma, neuroblastoma and rhabdomyosarcoma⁸.

The hypothesis of a reactive etiology with polyclonal proliferation of histiocytes prevails in the Rosai Dorfman disease. An association with immunological diseases, hematological malignance and post-infection conditions has also been described. These comorbilities could break the migration mediated by cytokines and the activation of histiocytes⁹.

As per published studies, a proposal has been made that cells may represent monocytes of intermediate recruitment with differentiation block, where both alteration of homeostasis, as well as inherent genomic alterations could contribute to the initiation of the disorder through transduction of signals, playing a vital role in the development of this pathology, different inflammatory molecules such as the stimulating factor of colonies of macrophages, IL-1 β , IL-6 and tumoral- α necrosis factor¹⁰.

In the current classification of histiocytosis, Rosai-Dorfman Disease is in the group of the R-group histiocytosis, comprised of:

Family Rosai Dorfman Disease, Classic Rosai Dorfman Disease (nodal), Extranodal Rosai Dorfman Disease, Rosai Dorfman Diseases associated with neoplasia, Rosai Dorfman Disease associated with immune pathology, other non-C non-L non-M non-H histiocytosis¹¹.

The diagnosis in the patient with the Rosai-Dorfman Di-

sease should include detection tests of EBV, cytomegalovirus, HHV-6, HHV-8 and VIH. Also, rheumatoid factor, a test of anti-nuclear antibodies, complete hemograms, liver and renal function, levels of immunoglobulins and a globular sedimentation velocity. A total of 90% of patients have been reported to have an elevated globular sedimentation velocity and polyclonal hypergammaglobulinaemia with an inversion of albumin relation: globulin. Also, leukocytosis with neutrophilia, normocytic normochromic anemia, a positive value of rheumatoid factor or of antinuclear antibodies may be found. Hemolytic anemia and eosinophilia are rare. Ideally, an excisional biopsy may be performed to obtain appropriate tissue for morphological and immunohistochemical analysis for a diagnosis¹².

The differential diagnosis of the Rosai-Dorfman Disease is wide and it is similar to other causes of non-malign lymphadenopathy, etiologies include tuberculosis, Wegener granulomatosis, sarcoidosis, disease related to IgG4, juvenile xanthogranuloma, Erdheim-Chester disease, Gaucher disease and other histiocytic disorders such as histiocytosis of Langerhans cells. Malign etiologies in differential diagnosis include Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia, melanoma, Langerhans cell sarcoma¹³.

Observation or surgical resection is sufficient in many patients. If this is not possible or in the event of relapse, the above described treatment is diverse and with the years, the best option for each specific case has been described¹⁴. Systemic treatments are necessary in the event of compressive, lithic oral-obstructing compromise, particularly in bone disorders¹⁵. At present, the current therapeutic options are: First line therapy: observation, steroids, surgery, sirolimus; second line therapy: radiotherapy, cladribine, clofarabine, imatinib, rituximab, azatioprina, 6 oral mercaptopurine, metotrexate, interferon alpha, thalidomide¹⁶. Other systemic therapies include combinations such as CVP (cyclophosphamide, vincristine, prednisone) and 6 mercaptopurine with prednisone¹⁷.

Conclusions

To conclude, the different possible diagnoses in cervical lymphadenopathy are many, and since there is no clinical or paraclinic history, biopsy is a diagnostic tool in the event of suspected malignancy and/or rare diseases. The Rosai Dorfman Disease should be considered among the possible diagnoses, reporting a self-limited case without the need of using systemic therapies.

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