CASE REPORTS / REPORTE DE CASO

Sinus histiocytosis in cervical adenopathy, case report.

Histiocitosis sinusal en adenopatia cervical unica, 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 factors[1].

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, polymorphoneuclear 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.

Without establishing a diagnosis and in addition to the persistence of adenopathy, an excisional biopsy is performed and the histopatological study of which reports: diffuse lymphoid tissue with loss of architecture where infiltration of lymphocytes, plasmatic cells and abundant atypical mononuclear histiocytic cells is observed with presence of intracytoplasmatic emperipolesis, as well as multinuclear cells, dilatation of sinusoids which do not invade the capsule (Figure 1). Immunohistochemical results: CD68: positive in histiocytoid cells; CD15: negative; CD30: negative (Figure 2).

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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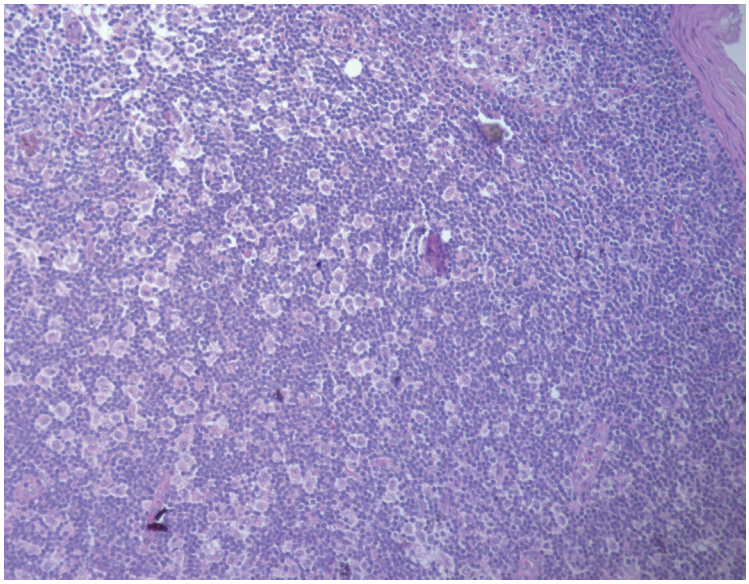

Figure 1. Emperipolesis in cervical lymph node stained with hematoxylin and eosin.

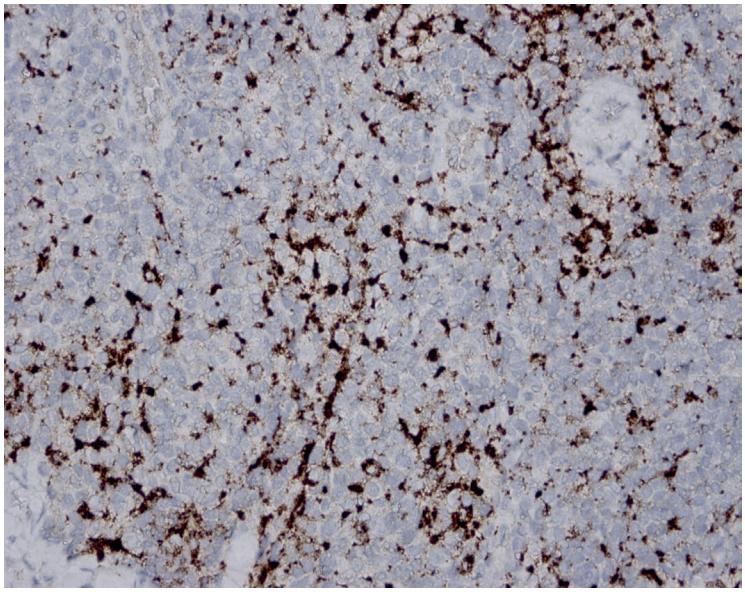

Figure 2. Immunohistochemistry of cervical lymph node, where the dark brown stained cells are Histiocytes(positive CD68 marker).

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 rhabdomyosarcoma[8].

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 cormobilities could break the migration mediated by cytokines and the activation of histiocytes[9].

As per published studies, a proposal has been made that cells may represent monocytes of intermediate recruitment with differentiation block, where both alteration of homoeostasis, 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-1β, IL-6 and tumoral-α necrosis factor[10].

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 histiocytosis[11].

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 antinuclear 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 diagnosis[12].

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 ethiologies in differential diagnosis include Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia, melanoma, Langerhans cell sarcoma[13].

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 described[14]. Systemic treatments are necessary in the event of compressive, lithic oral-obstructing compromise, particularly in bone disorders[15]. 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, thalidomide[16]. Other systemic therapies include combinations such as CVP (cyclophosphamide, vincristine, prednisone) and 6 mercaptopurine with prednisone[17].

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. TheRosai Dorfman Disease should be considered among the possible diagnoses, reporting a self-limited case without the need of using systemic therapies.

Bibliographic references

1. Gaddey HL, Riegel AM. Unexplained lymphadenopathy: evaluation and differential diagnosis. Am Fam Physician. 2016 [quoted Jun 12 2018]; 94(11):896-903. Available at:https://www.aafp.org/afp/2016/1201/p896.pdf
2. Haroche J, Emile JF. Systemic histiocytosis. EMC - Tratado de Medicina. 2017 [quoted Jun 2 2018]; 21(2):[Approx 4 p.]. Available at: https://www.sciencedirect.com/science/article/pii/S1636541017842501
3. Durham BH. Molecular characterization of the histiocytoses: Neoplasia of dendritic cells and macrophages. Semin Cell Dev Biol. 2018 [quoted Apr 6 2018]; [Approx 15 p.]. Available at:https://www.sciencedirect.com/science/article/pii/S1084952117303646?via%3Dihub
4. Zoungrana-Ouattara C, Ouédraogo F, Toguyéni L, Kalmogho A, Yonaba C, Bouda CG, et al. The Destombes-Rosai-Dorfman Disease or sinus histiocytosis with massive lymphadenopathy: a rare case described in the Paediatrics Department of Yalgado Ouedraogo University Hospital. Open Journal of Pediatrics. 2017 [quoted Apr 25 2018]; 7:345-52. Available at: http://file.scirp.org/pdf/OJPed_2017122016222405.pdf
5. Vokuhl C, Oschlies I, Klapper W, Leuschner I. Histiocytic diseases in childhood and adolescence. Pathologe. 2015 [quoted Apr 7 2018]; 36:443-50. Available at: https://link.springer.com/article/10.1007%2Fs00292-015-0043-x
6. Emile JF, Charlotte F, Chassagne-Clement C, Copin MC, Fraitag S, Mokhtari K, et al. Histiocytoses: general classification and molecular criteria. La Presse Médicale. 2017 [quoted Apr 7 2018]; 46(1):46-54. Available at:https://www.sciencedirect.com/science/article/pii/S0755498216000476?via%3Dihub
7. Egan C, Jaffe ES. Non-neoplastic histiocytic and dendritic cell disorders in lymph nodes. Seminars in Diagnostic Pathology. 2018 [quoted Apr 6 2018]; 35(1): 20-33. Available at: https://ac.els-cdn.com/S0740257017301247/1-s2.0-S0740257017301247-main.pdf?_tid=49a0038f-e079-4e74-be87-69e624cd6530&acdnat=1523071678_5bfc28bc70d49a0605d6c15767960cd9
8. Piris MA, Aguirregoicoa E, Montes-Moreno S, Celeiro-Muñoz C. Castleman Disease and Rosai-Dorfman Disease. Seminars in Diagnostic Pathology. 2018 [quoted Apr 5 2018]; 35(1), 44-53. Available at: https://ac.els-cdn.com/S074025701730148X/1-s2.0-S074025701730148X-main.pdf?_tid=38141e47-771c-4599-abad-ff6bb1033ead&acdnat=1522985835_e16f-4ba49e375d4c9f4f6a2e2a8f1390
9. Luder C, Nordmann T, Ramelyte E, Mühleisen B, Kerl K, Guenova E, et al. Histiocytosis – cutaneous manifestations of hematopoietic neoplasm and non neoplastic histiocytic proliferations. J Eur Acad Dermatol Venereol, 2018 [quoted Apr 5 2018]; 32: 926-34. Available at:https://onlinelibrary.wiley.com/doi/abs/10.1111/jdv.14794
10. Cai Y, Shi Z, Bai Y. Review of Rosai-Dorfman Disease: New insights into the pathogenesis of this rare disorder. Acta Haematol. 2017 [quoted Apr 5 2018]; 138:14-23. Available at:https://www.karger.com/Article/Abstract/475588
11. Emile J, Abla O, Fraitag S, Horne A, Haroche J, Donadieu J, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood. 2016 [quoted Apr 6 2018]; 127(22):2672-81. Available at: http://www.bloodjournal.org/content/bloodjournal/127/22/2672.full.pdf
12. Bösmüller H, Nann D, Horger M, Fend F. Erdheim-Chester disease and Rosai-Dorfman disease. Pathological, radiological and clinical features of adult non-Langerhans cell histiocytosis. Pathologe. 2015 [quoted Apr 5 2018]; 36:458-65. Available at: https://link.springer.com/article/10.1007%2Fs00292-015-0057-4
13. Dalia S, Sagatys E, Sokol L, Kubal T. Rosai-Dorfman Disease: tumor biology, clinical features, pathology, and treatment. Cancer Control 2014 [quoted Apr 5 2018]; 21(4):322-7. Available at:http://journals.sagepub.com/doi/10.1177/107327481402100408
14. Classen CF, Minkov M, Lehrnbecher T. The non-Langerhans cell histiocytoses (rare histiocytoses) – Clinical aspects and therapeutic approaches. Klin Padiatr. 2016 [quoted Apr 7 2018]; 228:294-306. Available at:https://www.thieme-connect.de/DOI/DOI?10.1055/s-0042-109713
15. Cohen Aubart F, Haroche J, Emile JF, Charlotte F, Barete S, Schleinitz N, et al. Rosai-Dorfman disease: diagnosis and therapeutic challenges. La Revue de Médecine Interne. 2018 [quoted Apr 4 2018]; [Approx 6 p.]. Available at: https://www.sciencedirect.com/science/article/pii/S024886631830047X?via%3Dihub
16. Haroche J, Cohen-Aubart F, Rollins BJ, Donadieu J, Charlotte F, Idbaih A, et al. The Lancet Oncology. 2017 (quoted 6 abril 2018); 18 (2): e 113-e125.
17. Goyal G, Ravindran A, Patnaik MM, Nowakowski GS, Thanarajasingam G, Habermann TM, et al. Clinical features and treatment approaches in patients with Rosai-Dorfman Disease: The Mayo Clinic experience. Blood. 2017 [quoted Apr 4 2018]; 130(Suppl 1):3573. [Approx. 6 p.]. Available at:http://www.bloodjournal.org/content/130/Suppl_1/3573

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