Autopsy Case Reports

Article / Clinical Case Report

# Solitary extranodal Rosai-Dorfman disease of the mandible: an exceedingly rare presentation

Ameer Hamza[a], Zhifei Zhang[a], Basim Al-Khafaji[a]

**How to cite:** Hamza A, Zhang Z, Al-Khafaji B. Solitary extranodal Rosai-Dorfman disease of the mandible: an exceedingly rare presentation. Autops Case Report [Internet]. 2018;8(3):e2018036. http://dx.doi.org/10.4322/acr.2018.036

## ABSTRACT

Sinus histiocytosis with massive lymphadenopathy, generally known by the name of Rosai-Dorfman disease is a rare benign condition principally affecting cervical lymph nodes. Concurrent extra-nodal disease frequently occurs, however, solitary extra-nodal disease involving the mandible is exceedingly rare with less than five reported cases in the English literature. We describe a case of primary involvement of the mandible in a 27-year-old female, and discuss the differential diagnosis of this disease with other histiocytic lesions.

**Keywords**
Histiocytosis, Sinus; Histiocytosis, NonLangerhan-cell; Mandible.

## INTRODUCTION

Sinus histiocytosis with massive lymphadenopathy is a rare benign disease, primarily affecting cervical lymph nodes. It is commonly known as Rosai-Dorfman disease after the physicians who first described it in 1969.[1] The disease is exceedingly rare with an estimated prevalence of 1 in 200,000.[2] Sole extranodal disease is present in about 20 to 25 percent cases,[3-5] while simultaneous nodal and extranodal disease is present in 40 to 50 percent of the patients at the time of presentation.[3,6-8] Even after five decades, the exact etiology is still unknown. The disease mainly affects adolescents and young adults and has a slight predilection for males and African Americans.[6] It is a benign, self-limiting disease; however, it can be locally destructive and fatal in rare instances.[1,6,7] The head and neck region is the most commonly involved area by nodal as well as extra-nodal disease.[1,6-9] The sinonasal tract is the most common extranodal site within the head and neck region; however, the involvement of skin, soft tissues, orbit, salivary glands, larynx, tonsils, thyroid, ear, and facial bones have all been noted.[6,8-11] Meanwhile, the mandible can also be involved; however, the solitary primary involvement of mandible is extremely rare with only a handful of cases identified in the literature.[10,12,13] Herein we describe a case of solitary primary involvement of the mandible in a 27-year-old female.

## CASE PRESENTATION

A 27-year-old morbidly obese African American, gravida 1, para 0 female presented during the first trimester of her pregnancy with swelling in the right jaw and loosening of teeth. The patient also complained of localized pain but denied fever, weight loss, and

[a] St. John Hospital and Medical Center, Department of Pathology. Detroit, MI, United States of America.

other constitutional symptoms. On examination, there was a tender swelling of the right mandible. A biopsy was performed that showed mixed inflammation with numerous foamy histiocytes suggestive of Rosai-Dorfman disease. A CT scan was subsequently performed to delineate the extent of the disease to rule out nodal disease and other possible areas of involvement. The CT scan demonstrated a lytic lesion involving much of the body of the right side of the mandible, extending into the mentum of the mandible and crossing the midline into the anterior aspect of the left body of the mandible (Figure 1 A-C). The lesion showed avid radiotracer uptake on scintigraphy (Figure 1D). Needle core biopsies were performed of the suspicious lymph nodes, which on histopathologic evaluation showed reactive hyperplasia. The patient subsequently underwent a segmental mandibulectomy.

The gross specimen received in pathology consisted of a 14.0 cm segment of the mandible with teeth number 19-27 and 31-32 (Figure 2 A-D). Teeth 17-18 and 28-30 had been removed previously. The mandible was markedly asymmetric with an enlarged and bulging right lateral portion. Sectioning revealed a gray, soft, focally cystic mass involving two-thirds of the resected segment of the bone. Histologic evaluation showed a locally destructive lesion composed of numerous foamy histiocytes, admixed with lymphocytes, neutrophils, and scattered eosinophils and plasma cells infiltrating into the peri-mandibular soft tissue (Figure 3 A-B).

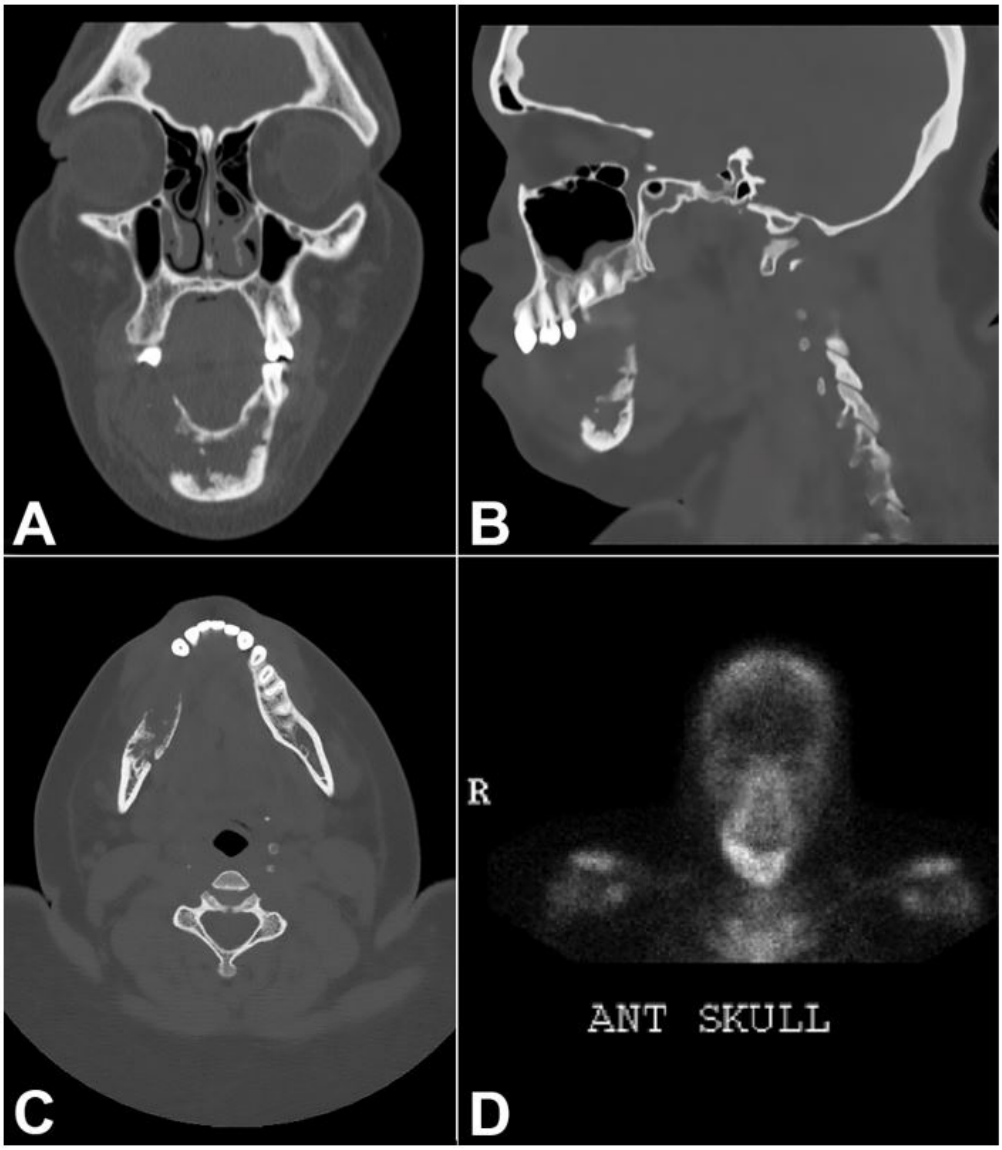


**Figure 1.** CT scan demonstrating lytic lesion involving bilateral mandible (**A –** Coronal; **B –** Sagittal and **C –** Axial plane). Avid radio tracer uptake on scintigraphy (**D**).

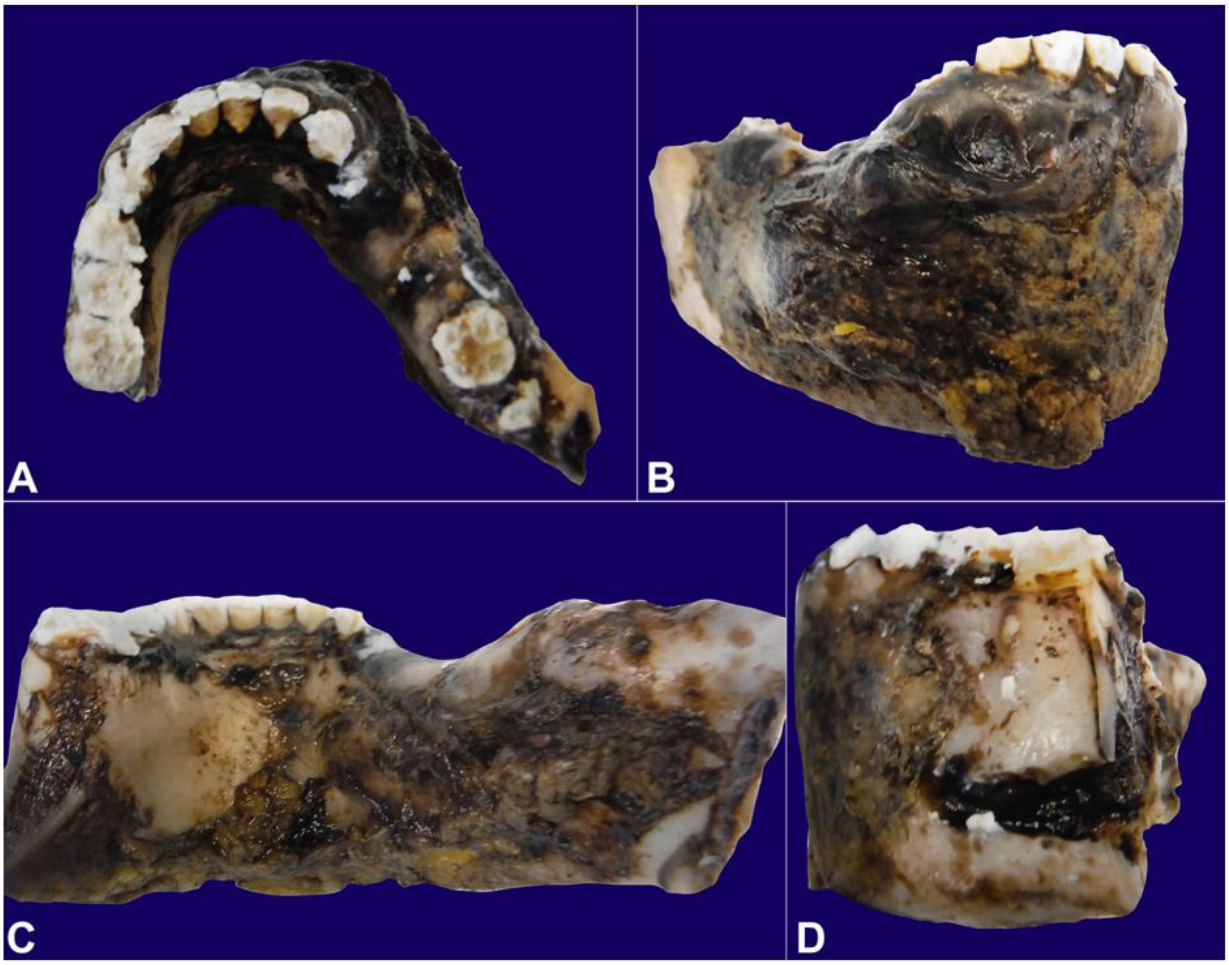


**Figure 2.** Gross images of the specimen demonstrating entire specimen – **A**; anterolateral aspect – **B**; inner aspect – **C** and cystic portion – **D**.

Some of the histiocytes also demonstrated emperipolesis (Figure 3 C-D). Immunohistochemical stains showed the histiocytes to be positive for CD68 and S100 while negative for CD1a (Figure 4). The morphology and immunohistochemical profile were consistent with Rosai-Dorfman disease. The concomitantly removed submandibular gland and suspicious lymph nodes showed no evidence of involvement by the disease. The patient underwent reconstruction with osteomycocutaneous fibular flap.

## DISCUSSION

Rosai-Dorfman disease is a benign proliferation of histiocytes that usually presents as massive but painless lymphadenopathy.[1] Adolescents and young adults are the most commonly affected age groups. Nodal disease most commonly manifests in the cervical lymph nodes, and extranodal disease also occurs most commonly in the head and neck region.[1,6-9] Primary extra-nodal disease is well documented and mainly affects the sinonasal tract.[6,8] Multiple organ systems can be involved in up to 40% of patients.[8] Bone involvement is also known, however, primary, solitary, disease of the facial bones is extremely rare.[6,10-16] Our patient presented with a solitary lesion of the mandible.

Patients with nodal disease usually present with painless lymphadenopathy with or without constitutional symptoms while signs and symptoms of extra-nodal disease depend on the site of involvement and invariably include localized swelling with or without pain. In the case of osseous lesions patients usually complain of swelling, which is sometimes accompanied by pain. Our patient presented in a similar fashion and since the involved bone was the mandible, the patient also reported loosening of her teeth. Alawi et al.[12] reported a case with similar presentation to our case in a 32-year-old pregnant women. As mentioned in the case presentation our patient was also pregnant at the time of presentation.

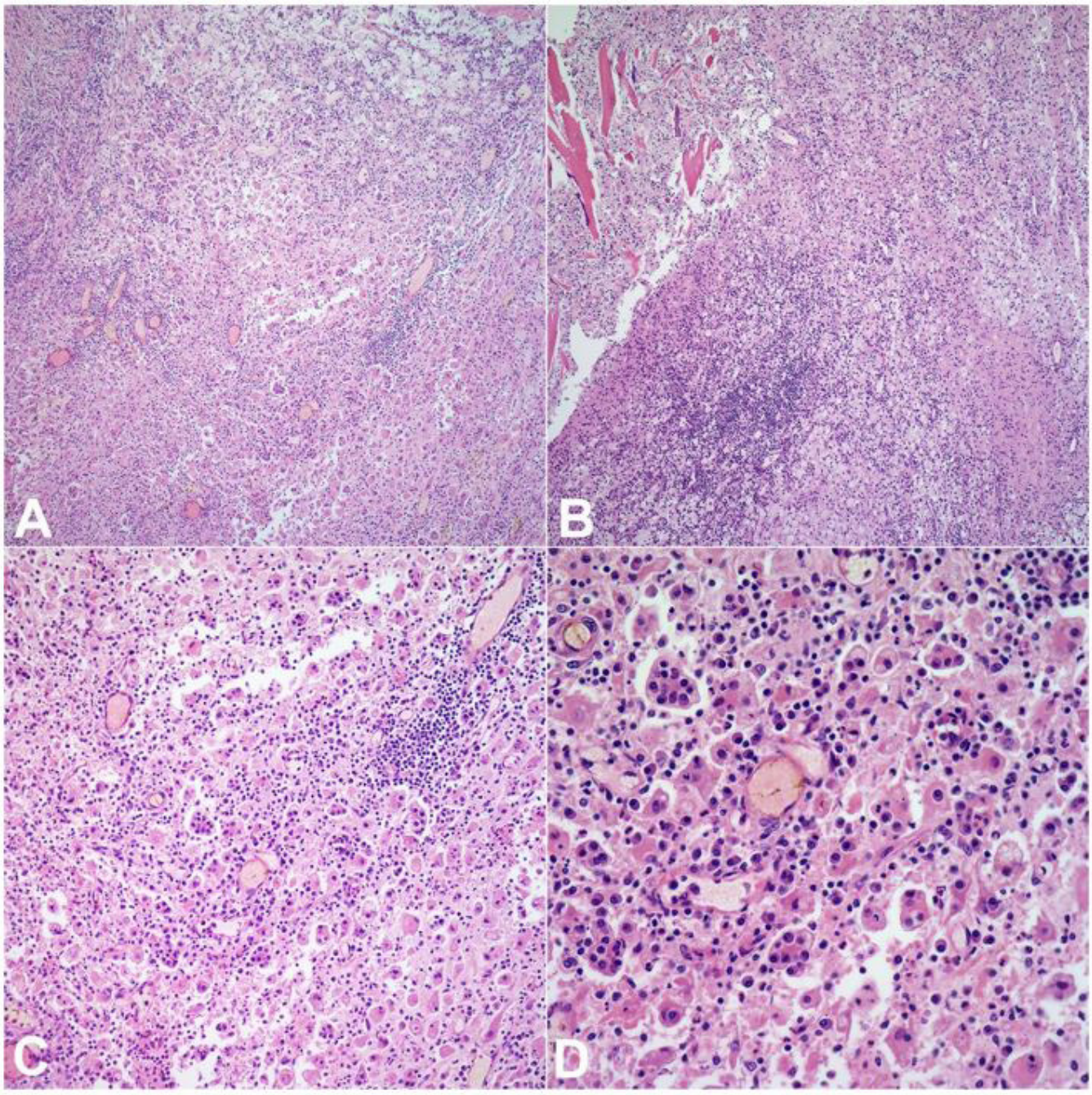


**Figure 3.** Photomicrograph demonstrating diffuse proliferation of histiocytes (**A –** H&E, 100X) causing local bone destruction (**B –** H&E, 100X). Histiocytes exhibiting emperipolesis. (**C –** H&E, 200X, **D –** H&E, 400X).

While it could be a mere coincidence, we suggest that extranodal Rosai-Dorfman disease with osseous involvement may have a predilection for pregnant females. This speculation is further strengthened by a case reported by Butler et al.[17] Their patient had nodal disease that was exacerbated during two pregnancies and went into remission during the time in between the two pregnancies. Some authors have suggested autoimmunity as underlying basis for Rosai-Dorfman disease. This hypothesis is strengthened by presence of IgG4 positive plasma cells in the lesion.[18-21] This suggests that the exacerbation during pregnancy may very well be associated with autoimmunity.

Radiologic appearance of Rosai-Dorfman disease can vary from a well-defined radiolucent lesion to a poorly defined mixed lesion with areas of sclerosis.[14,15] The disease is locally destructive, and it is not uncommon to see the lesion extending into the surrounding soft tissue. In our patient, the CT scan demonstrated a lytic lesion involving much of the

body of the mandible with no soft tissue extension, however, microscopically the lesion extended into the peri-mandibular soft tissue.

Other histiocytic diseases such as Langerhans cell histiocytosis and Erdheim-Chester disease can have a similar clinical and radiologic presentation.[22-24] Additionally, even the morphology of these diseases can be quite similar.[1,6,22-26] Subtle microscopic clues and immunohistochemistry aid in the differential diagnosis. The morphologic and immunohistochemical differences that may help in routine practice are summarized in Table 1. Recently Graces et al.[27] demonstrated *KRAS* and *MAP2K1* gene mutations in one-third Rosai-Dorfman disease cases of their study cohort. This mutation is in comparison to *BRAF V600E* mutation in Langerhans cell histiocytosis and Erdheim-Chester disease.[28] In our patient, the lesion comprised of numerous foamy histiocytes, admixed with lymphocytes, neutrophils, and scattered eosinophils and plasma cells with some histiocytes exhibiting emperipolesis. The histiocytes were immunoreactive to CD68 and S100 while negative for CD1a confirming the diagnosis of Rosai-Dorfman disease. We did not perform a gene mutation analysis.

Other disease processes that may mimic Rosai-Dorfman disease include xanthomatous lesions including soft tissue xanthoma and juvenile

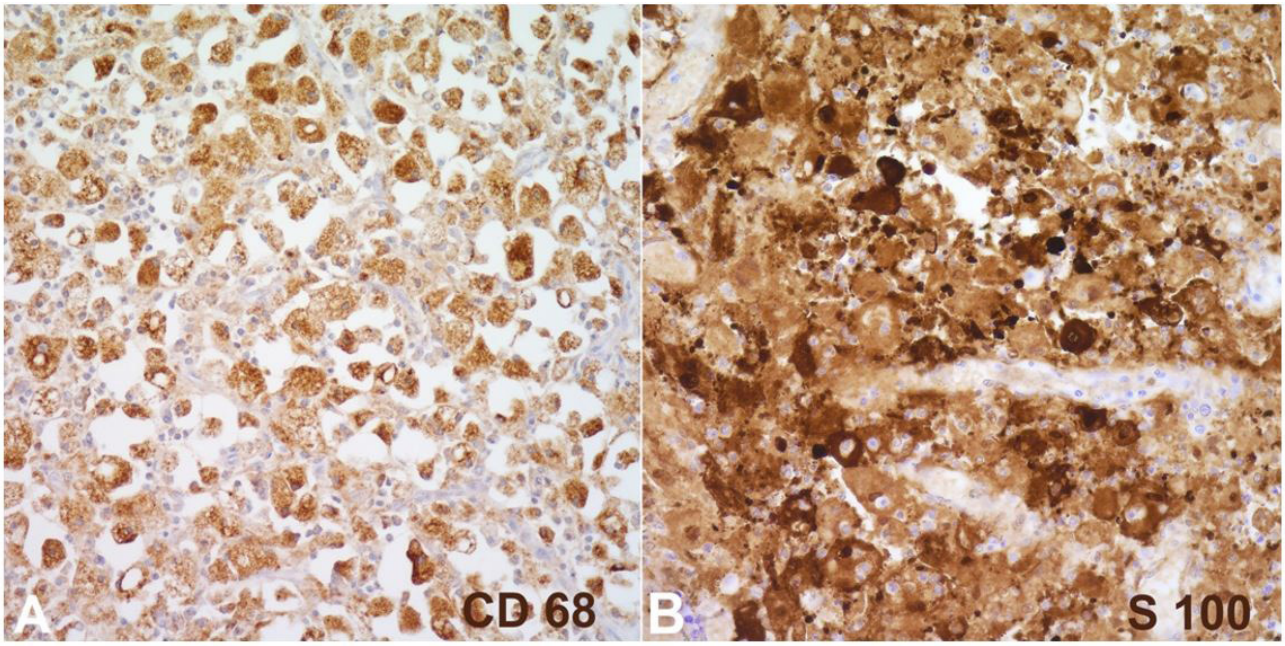


**Figure 4.** Histiocytes exhibiting diffuse immunoreactivity in with CD68 (**A –** 200X) and S100 (**B –** 200X).

**Table 1.** Morphology and immunohistochemical profile of Rosai-Dorfman disease, Langerhans cell histiocytosis and Erdheim-Chester disease[18-20]

| | Rosai-Dorfman disease | Langerhans cell histiocytosis | Erdheim-Chester disease |
|---|---|---|---|
| Morphology | Diffuse proliferation of large foamy histiocytes with vesicular nuclei and eosinophilic cytoplasm.<br>Mixed inflammatory infiltrate composed of neutrophils, lymphocytes, plasma cells and **rare eosinophils**.<br>Rare or no mitosis.<br>**Emperipolesis.** | Diffuse proliferation of slightly smaller foamy histiocytes with **grooved nuclei** and eosinophilic cytoplasm.<br>Mixed inflammatory infiltrate **typically containing eosinophils.**<br>Rare mitosis.<br>Rare or no emperipolesis. | Diffuse proliferation of small histiocytes with moderate amount of cytoplasm in a fibrotic background.<br>Multinucleated giant cells.<br>**Hemophagocytosis**<br>No emperipolesis. |
| Immunohisto-chemical profile | CD68 and S100 positive.<br>**CD1a negative.** | CD68, S100, CD1a and langerin (CD207) positive. | CD68 positive.<br>S100 focally positive.<br>**CD1a negative.** |

xanthogranuloma; infectious processes such as lepromatous leprosy; and lysosomal storage disorders such as Gaucher disease.[29-34] Histiocytes in all these lesions except leprosy are usually S100 negative which can immensely aid the differential diagnosis. In lepromatous leprosy the macrophages loaded with mycobacteria are S100 positive, however, clinical presentation and fite staining for mycobacterial organism can aid the diagnosis.[33,34]

Treatment depends upon the extent of disease and varies with each individual patient. About 70% to 80% of patients have spontaneous improvement of symptoms without any treatment; however, there can be episodic exacerbations and remissions that may last for years.[1,6,16,17,35-37] Severe, locally destructive and persistent disease may require treatment with surgery, and corticosteroids. Chemotherapy and rarely radiotherapy have also been tried with limited success.[1,6,16,35-37] While there is no "ideal" treatment, the goal of treatment is to keep the disease under control and preserve the quality of life. In our patient, the disease presented as a solitary lesion which was locally destructive. Therefore, surgery was considered the treatment of choice.

Rosai-Dorfman disease has a protracted and indolent course. While the disease is usually self-limiting with an excellent prognosis, it can be persistent and even fatal in rare instances.[3] More recent data shows that mortality rate can be up to 7%.[21] Foucar et al's.[7] analysis of 14 fatal cases of the disease showed that the mean age the patients was 33 years. Autopsy was performed in eight of these patients which showed the Rosai-Dorfman disease to be culprit in only two cases while the cause of death in other cases was either some immunologic abnormality or unusual infections.[7] The prognosis of solitary osseous lesions is generally excellent with rare recurrences.[6,12,13,15] Thus far for our patient, her post-operative recovery has been without complications, and her prognosis appears to be excellent.

## REFERENCES


1. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. Arch Pathol. 1969;87(1):63-70. PMid:5782438.
2. Mahzoni P, Zavareh MH, Bagheri M, Hani N, Moqtader B. Intracranial Rosai-Dorfman disease. J Res Med Sci. 2012;17(3):304-7. PMid:23267385.
3. Zhu F, Zhang JT, Xing XW, et al. Rosai-Dorfman disease: a retrospective analysis of 13 cases. Am J Med Sci. 2013;345(3):200-10. http://dx.doi.org/10.1097/MAJ.0b013e3182553e2d. PMid:22652821.
4. Setareh M, Zahra M, Vahid M, Farah S. Generalized lymphadenopathy in infancy; a case report. Iran J Pediatr. 2013;23(1):105-8. PMid:23548976.
5. Igrutinovic Z, Medovic R, Markovic S, et al. Rosai-Dorfman disease of vertebra: case report and literature review. Turk J Pediatr. 2016;58(5):566-71. http://dx.doi.org/10.24953/turkjped.2016.05.020. PMid:28621104.
6. Foucar E, Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): review of the entity. Semin Diagn Pathol. 1990;7(1):19-73. PMid:2180012.
7. Foucar E, Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. An analysis of 14 deaths occurring in a patient registry. Cancer. 1984;54(9):1834-40. http://dx.doi.org/10.1002/1097-0142(19841101)54:9<1834::AID-CNCR2820540911>3.0.CO;2-F. PMid:6478418.
8. Duan HG, Zheng CQ, Wang DH, et al. Extranodal sinonasal Rosai-Dorfman disease: a clinical study of 10 cases. Eur Arch Otorhinolaryngol. 2015;272(9):2313-8. http://dx.doi.org/10.1007/s00405-014-3297-7. PMid:25318688.
9. Goodnight JW, Wang MB, Sercarz JA, Fu YS. Extranodal Rosai-Dorfman disease of the head and neck. Laryngoscope. 1996;106(3 Pt 1):253-6. http://dx.doi.org/10.1097/00005537-199603000-00002. PMid:8614184.
10. Wenig BM, Abbondanzo SL, Childers EL, Kapadia SB, Heffner DR. Extranodal sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) of the head and neck. Hum Pathol. 1993;24(5):483-92. http://dx.doi.org/10.1016/0046-8177(93)90160-I. PMid:8491488.
11. Carbone A, Devaney KO, Passannante A, Rinaldo A, Gloghini A, Ferlito A. Review of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) of head and neck. Ann Otol Rhinol Laryngol. 1999;108(11 Pt 1):1095-104. http://dx.doi.org/10.1177/000348949910801113. PMid:10579239.
12. Alawi F, Robinson BT, Carrasco L. Rosai-Dorfman disease of the mandible. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;102(4):506-12. http://dx.doi.org/10.1016/j.tripleo.2005.10.071. PMid:16997119.
13. Kademani D, Patel SG, Prasad ML, Huvos AG, Shah JP. Intraoral presentation of Rosai-Dorfman disease: a case report and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2002;93(6):699-

704. http://dx.doi.org/10.1067/moe.2002.123495. PMid:12142877.

14. Walker PD, Rosai J, Dorfman RF. The osseous manifestations of sinus histiocytosis with massive lymphadenopathy. Am J Clin Pathol. 1981;75(2):131-9. http://dx.doi.org/10.1093/ajcp/75.2.131. PMid:7468520.

15. Lehnert M, Eisenschenk A, Dienemann D, Linnarz M. Sinus histiocytosis with massive lymphadenopathy: skeletal involvement. Arch Orthop Trauma Surg. 1993;113(1):53-6. http://dx.doi.org/10.1007/BF00440596. PMid:8117513.

16. Günhan O, Finci R, Günaydin Y, Somuncu I. Sinus histiocytosis with massive lymphadenopathy: a case with facial bones involvement. J Oral Maxillofac Surg. 1991;49(2):205-9. PMid:1990100.

17. Butler WM, Armstrong WA. Pregnancy and sinus histiocytosis with massive lymphadenopathy. Ann Intern Med. 1985;102(2):278. http://dx.doi.org/10.7326/0003-4819-102-2-278. PMid:3966775.

18. Swerdlow SH, Campo E, Harris NL, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. 4th ed. Geneva: WHO; 2017.

19. Jaffe ES, Harris NL, Vardiman J, Arber DA, Campo E. Hematopathology e-book. Philadelphia: Elsevier Health Sciences.

20. Ranganathan S. Histiocytic proliferations. Semin Diagn Pathol. 2016;33(6):396-409. http://dx.doi.org/10.1053/j.semdp.2016.08.009. PMid:27720561.

21. Emile JF, Abla O, Fraitag S, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood. 2016;127(22):2672-81. http://dx.doi.org/10.1182/blood-2016-01-690636. PMid:26966089.

22. Eckardt A, Schultze A. Maxillofacial manifestations of Langerhans cell histiocytosis: a clinical and therapeutic analysis of 10 patients. Oral Oncol. 2003;39(7):687-94. http://dx.doi.org/10.1016/S1368-8375(03)00080-0. PMid:12907208.

23. Kenn W, Eck M, Allolio B, et al. Erdheim-Chester disease: evidence for a disease entity different from Langerhans cell histiocytosis? Three cases with detailed radiological and immunohistochemical analysis. Hum Pathol. 2000;31(6):734-9. http://dx.doi.org/10.1053/hupa.2000.8229. PMid:10872668.

24. Petrikowski CG, McGaw WT. Erdheim-Chester disease of the jaws: literature review and case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000;90(3):389-98. http://dx.doi.org/10.1067/moe.2000.107537. PMid:10982964.

25. Goldblum J, Lamps L, McKenney J, Myers J. Rosai and ackerman's surgical pathology. 11th ed. Philadelphia: Elsevier; 2017.

26. El-Naggar AK, Chan JKC, Grandis JR, et al. WHO classification of tumours. Lyon: IARC Press; 2017. p. 130-131. WHO classification of head and neck tumours.

27. Garces S, Medeiros LJ, Patel KP, et al. Mutually exclusive recurrent KRAS and MAP2K1 mutations in Rosai-Dorfman disease. Mod Pathol. 2017;30(10):1367-77. http://dx.doi.org/10.1038/modpathol.2017.55. PMid:28664935.

28. Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F. WHO classification of tumours. 4th ed. Lyon: IARC Press; 2013. p. 348-349. WHO classification of tumours of soft tissue and bone.

29. Bertoni F, Unni KK, McLeod RA, Sim FH. Xanthoma of bone. Am J Clin Pathol. 1988;90(4):377-84. http://dx.doi.org/10.1093/ajcp/90.4.377. PMid:3140652.

30. Lustmann J, Ben-Yehuda D, Somer M, Ulmansky M. Gaucher's disease affecting the mandible and maxilla (Report of a case). Int J Oral Maxillofac Surg. 1991;20(1):7-8. http://dx.doi.org/10.1016/S0901-5027(05)80685-X. PMid:2019785.

31. Weiss SW, Goldblum JR. Benign fibrohistiocytic tumors. In: Weiss SW, Goldblum JR, editors. Enzinger and weiss's soft tissue tumors. 4th ed. St. Louis: Mosby Inc; 2001. p. 441–490.

32. Kasper HU, Hegenbarth V, Buhtz P. Rhinoscleroma associated with Rosai-Dorfman reaction of regional lymph nodes. Pathol Int. 2004;54(2):101-4. http://dx.doi.org/10.1111/j.1440-1827.2004.01597.x. PMid:14720140.

33. Cuevas-Santos J, Contreras F, McNutt NS. Multibacillary leprosy: lesions with macrophages positive for S100 protein and dendritic cells positive for Factor 13a. J Cutan Pathol. 1998;25(10):530-7. http://dx.doi.org/10.1111/j.1600-0560.1998.tb01736.x. PMid:9870671.

34. Dave S, Nori AV, Thappa DM, Siddaraju N. Leprous osteitis presenting as bone cyst and erosions. Dermatol Online J. 2004;10(1):17. PMid:15347499.

35. Shemen L, D'Anton M, Toth I, Klijian A, Galantich P. Rosai-Dorfman disease involving the premaxilla. Ann Otol Rhinol Laryngol. 1991;100(10):845-51. http://dx.doi.org/10.1177/000348949110001011. PMid:1952653.

36. Dodson KM, Powers CN, Reiter ER. Rosai-Dorfman disease presenting as synchronous nasal and intracranial masses. Am J Otolaryngol. 2003;24(6):426-30. http://dx.doi.org/10.1016/S0196-0709(03)00090-5. PMid:14608579.

37. Histiocytosis Association. Rosai-Dorfman disease: diagnosis and treatment [Internet]. New Jersey: Histiocytosis Association Inc; 2018 [cited 2018 Feb 17]. Available from: https://www.histio.org/page.aspx?pid=401#.WoiD5qjwbIU

**Authors contributions:** All the authors made significant contribution to the manuscript. Hamza A designed and wrote the manuscript after gathering all the information. Zhang Z did the literature search and wrote initial draft of the manuscript. Al-Khafaji B was the staff pathologist. All authors contributed significantly and are in agreement with the content of the manuscript.

**Conflict of interest:** None

**Financial support:** None

**Submitted on:** June 4th, 2018
**Accepted on:** June 19th, 2018

**Correspondence**
Ameer Hamza
Department of Pathology, St John Hospital and Medical Center, 22101 Moross Road – Detroit/MI – USA
PO Box: 48236
Phone: +1 (313) 613-7511
ameerhamza7@hotmail.com