ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

"ENDOSCOPIC MANAGEMENT OF ROSAI DORFMAN DISEASE OF PARANASAL SINUS AND ORBIT: A CASE SERIES"

[1]Dr. Kosha Gosalia, [2]Dr. Nishit Shah, [3]Dr. Supriya Gaware, [4*]Dr. Jay Kothari

1 Fellow in rhinology and skullbase, Department of ENT, Bombay hospital.
Email Id: kosha.gosalia@gmail.com
2 Consultant, Department of ENT, Bombay hospital. Email Id: shahentclinic@gmail.com
3 Assistant professor, Department of ENT, Bharatratna Atal bihari vajpayee medical College, Pune, Maharashtra, India. Email Id: supriyagaware2@gmail.com
4* Corresponding author: Fellow in rhinology and skullbase, Bombay hospital,
Email Id: jaykothari03@gmail.com
Corresponding Author: Dr. Jay Kothari
Email Id: jaykothari03@gmail.com

Abstract:

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a rare, benign histiocytic disorder of uncertain etiology. Initially identified in African children with lymphadenopathy, the disease was later characterized by Rosai and Dorfman in 1969. The clinical presentation typically includes painless cervical lymphadenopathy, fever, and extranodal involvement, particularly in the head and neck region. Diagnosis is confirmed histopathologically by the presence of large histiocytes exhibiting emperipolesis and positivity for S100, CD68, and CD163, with negativity for CD1a. We present five cases of extranodal RDD involving the paranasal sinuses, an uncommon site of manifestation. Patients ranged from 23 to 70 years old, presenting with symptoms such as nasal obstruction and postnasal discharge. Imaging revealed soft tissue masses in the nasal cavity and paranasal sinuses. All cases were managed successfully through endoscopic surgical excision, with subsequent symptom relief and no recurrence during follow-up. Histopathological examination confirmed RDD with characteristic histiocytic infiltration and emperipolesis. These cases underscore the importance of considering RDD in the differential diagnosis of nasal masses, particularly when typical lymphadenopathy is absent. Given the rarity of paranasal sinus involvement, management requires a tailored approach, including endoscopic debulking and regular follow-up. Our findings highlight the efficacy of surgical

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

intervention in isolated extra nodal RDD and the necessity of vigilant postoperative monitoring. Further studies with larger cohorts are needed to establish standardized treatment protocols for this rare manifestation of RDD

Introduction:

Rosai-Dorfman disease (RDD), or sinus histiocytosis with massive lymphadenopathy, is a benign condition characterized by histiocytic overgrowth and an unknown cause. Certain theories propose that immune dysregulation or infections such as HHV-6, HHV-8, parvovirus B19, EBV, CMV, VZV, brucella, and klebsiella may be the cause, but the proof is unclear. RDD was initially identified in 1965 in four African children with lymphadenopathy by Destombes, and was named "adenitis with lipid excess" due to the lipid-laden histiocytes present in the tissue sample [2]. In 1969, Rosai and Dorfman published a distinct study on four patients presenting with extensive cervical lymph node swelling and unique histopathological characteristics, identifying it as "Sinus Histiocytosis with Massive Lymphadenopathy (SHML)" [3]. Following the initial description, additional reports, such as a summary of 423 cases from a global registry in 1990, outlined both nodal and extranodal presentations of the illness [4].

Fever and painless large cervical lymph node swelling are a typical clinical presentation, but it can also affect other areas such as sinuses, brain, eyes, upper respiratory tract, and skin. The highest occurrence happens in males during their second or third decade of life [1]. Possible differential diagnoses for Destombes-Rosai-Dorfman disease encompass malignant and nonmalignant conditions like granulomatosis with polyangiitis, Langerhans cell histiocytosis, Langerhans cell sarcoma, lymphoma, sarcoidosis, IgG4-related disease, and tuberculosis [5]. Diagnosis of the disease is done through biopsy of the tissues that are affected. Examination under a microscope of stained samples will reveal histiocytes containing lymphocytes and potentially other cells confined within them, a process referred to as

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

emperipolesis [5,6]. Through immunohistochemical staining, histiocytes will show positivity for S100, CD68, and CD163, while displaying negativity for DC1a [5,6].

We share two cases seen in our clinic to support the clinical and imaging findings of Rosai Dorfman disease and enhance understanding of this condition.

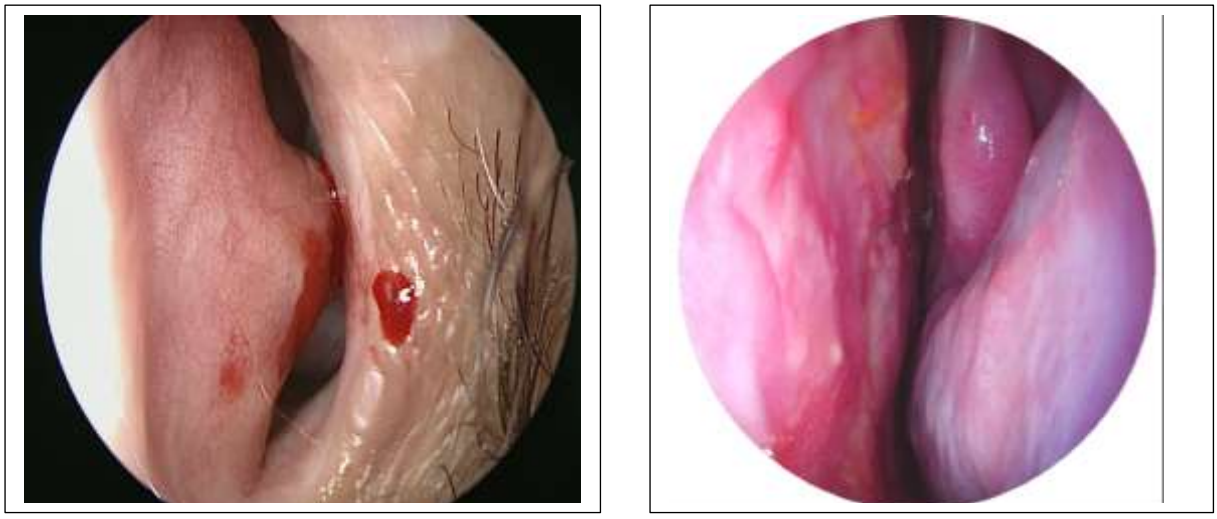
Case Presentation: Case 1:

A man who was 46 years old came to the ear, nose, and throat specialist with ongoing issues of nasal congestion. A nasal septum deviation was observed during a clinical examination and was later confirmed by a conbeam computed tomography (CT) scan of the sinuses. The scan also revealed soft tissue masses in the front part of the nasal septum, on the left side towards the back of the nostril, and at the left torus tubarius level. Suboptimal biopsy was carried out, yielding inconclusive histopathological results. A PET-CT scan revealed high uptake in the three lesions, leading to further investigations with MRI of the sinuses and a repeated biopsy. The teachings showed low signal intensity on both T1- and T2-weighted pictures and were iso- to slightly hypo-intense in comparison to grey matter. There was a uniform and mild increase in signal intensity on the T1-weighted images with fat suppression following the injection of intravenous contrast. After discovering this, the patient was diagnosed with extra nodal Rosai Dorfman disease and underwent endoscopic nasal surgery. The growth on the back of the nasal cavity septum and torus tubarius was removed, including the healthy tissue around it, and sent for examination. He experienced symptom relief after the surgery. He received oral antibiotics, oral steroids, and a local steroidal spray for two weeks after surgery. He has been having follow-up appointments every three months for the past year and has not had any symptoms return.

Case 2:

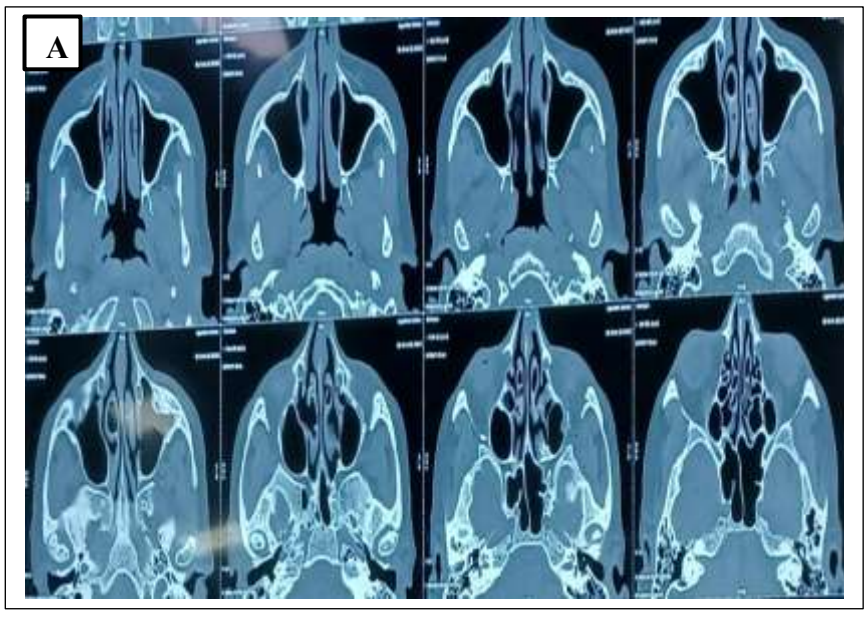
ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

A 70-year-old female patient complained of left-sided nasal blockage and postnasal discharge during clinical examination, a deviation of the nasal septum to the left and soft tissue hypertrophy on the left anterior septum were observed. Diagnostic nasal endoscopy and computed tomography confirmed the findings of soft tissue hypertrophy. The patient underwent endoscopic nasal surgery on the left septum to remove the hypertrophy along with surrounding healthy mucosa for biopsy. The histopathological examination revealed a nasal polyp on the left side. A strip of cartilage was also removed from the septum. A nasal splint was placed and removed three weeks post-surgery. The patient was treated with oral antibiotics and steroids for two weeks. Monthly follow-ups over the past six months have shown no recurrence of symptoms.



Before the surgical treatment RDD **After the surgical Treatment**

Figure 1. Showing the endoscopic images before and after the surgical treatment of RDD.



ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

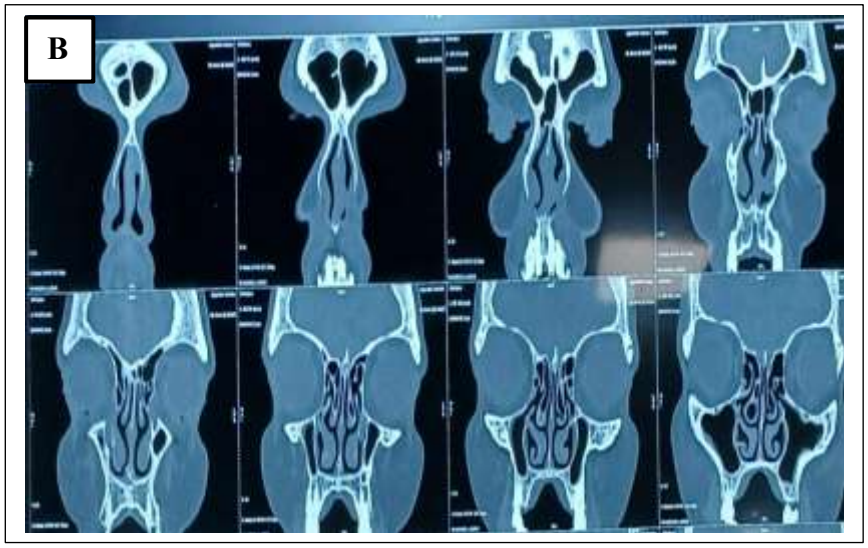


Figure 2: Radiological Investigation A: Axial scan of Paranasal Sius showing RDD, B: Coronal scan showing RDD

Case 3.

A 52-year-old woman, known case of Rosai-Dorfman Disease and, who had surgery for a paranasal mass three years ago, reported experiencing off and on nasal blockage in both nostrils for the last six months. A CT scan of the paranasal sinuses showed a sphenoid mass with uniform enhancement in the clival area. The patient had endoscopic surgery involving turbinates lateralization, Hadad flap harvesting, posterior septectomy, sphenoid widening, U-shaped pharyngeal flap creation, clivus and pterygoid drilling, and mass excision for biopsy. Next, the Hadad and pharyngeal flaps were inserted. After surgery, the patient felt better. She has been consistently following up for six months each year for the past two years, amounting to a total of five years of follow-up, with no signs of the previous issue returning or any new issues mentioned.

Case 4.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

A man, 44 years old, presenting with masses in both nostrils, along with blocked nasal passages and headaches lasting for half a year. His CT scans revealed a mass in the right nasal passage extending from the floor to the choana, originating from the posterior ethmoids. On the left side, a mass was found in the floor originating from the maxillary sinus and attached to the floor and inferior turbinate. The PET CT Scan showed polypoidal masses on both sides in the right maxillary middle and lower turbinates extending to the choana, and on the left side in the maxillary, frontal, sphenoid, and ethmoid sinuses. The patient underwent endoscopic surgery to remove a mass from the right nasal cavity floor, as well as a right inferior turbinectomy. Additionally, masses originating from the posterior ethmoids/max ant and post-ethmoids were removed, and the frontal sinus was opened. On the left side, a mass from the maxillary sinus floor was excised and another inferior turbinectomy was performed, with the frontal, maxillary antrum, and posterior ethmoids also being opened. Patients experienced symptom relief after surgery. He has been coming for follow-up every three months for the past year and has been under observation for a total of three years without any signs of a relapse or any issues.

Case 5.

A 23-year-old man presenting with reoccurring swelling above his left eye for a period of 8 months. One year ago, he underwent surgery for the same issues involving sphenoid sinusitis, and a CT scan was performed on his paranasal sinuses. Additionally, the left side of the sphenoid sinus was cleared using an endoscope. The most recent CT Paranasal Sinuses and MRI scans revealed unusual soft tissue in the left sphenoid sinus that stretches consistently into the orbital apex and infraorbital extraconal compartment, wrapping around and moving the intraorbital segment of the left optic nerve all the way to the lower eyelid, with slight axial displacement of the left globe. Endoscopic septoplasty was performed during the surgery, the posterior wall of the maxilla was expanded, the sphenopalatine artery was located and

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

cauterized, the vidian nerve was fully exposed, the lateral recess of the sphenoid was uncovered and cleared of tissue, optic nerve was decompressed, and the patients experienced symptom relief after the operation. He has been receiving monthly check-ups for the past 6 months and has not experienced any reoccurrence or issues.

All five individuals showed infiltration of lymphocytes, histiocytes, and plasma cells in the sub mucosa. Histopathology shows positivity for Emperipolesis, S100, CD 20, CD 3, and IGG4.

Discussion:

In 1965, Pierre-Paul Louis Lucien Destombes provided a French description of four patients with "adenitis with lipid excess," considered the first documented account of the condition [2,5,7]. Hence, the condition is also known as "Destombes-Rosai-Dorfman disease" [7]. In 1969, four years later, pathologists Juan Rosai and Ronald Dorfman released a study on "sinus histiocytosis with massive lymphadenopathy" [3,8]. Later findings showed that the ailment could manifest in areas beyond the head and neck, and not just in lymph nodes, hence it is now referred to as "Rosai-Dorfman disease" [3]. Lesional histiocytes displaying specific characteristics are positive for S100, CD68, and negative for CD1a, and show varying levels of emperipolesis [5,6].

The cause of the condition is still not known. Potential but unconfirmed infectious factors may involve Klebsiella, polyomaviridae, Epstein-Barr virus, parvovirus B19, and human herpesvirus 6 [5, 6]. In 2017, experts from Jilin University suggested that monocytes brought to inflamed areas could generate macrophage colony-stimulating factor, initiating a intricate signal transduction pathway leading to the histiocytosis seen in Destombes-Rosai-Dorfman disease [6].

Throughout history, Rosai-Dorfman Disease (RDD) has been seen as a condition with no known cause that usually resolves on its own, although a small number of patients might

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

have negative outcomes. 43% of patients show extranodal disease, despite the typical presentation of RDD with bilateral cervical lymphadenopathy. RDD can appear alone or with autoimmune, hereditary, or malignant conditions as a diverse entity. The disease is not common, occurring in 1 out of every 200,000 people. It is most commonly seen in children and young adults, with an average age of 20.6 years, although there have been instances in individuals as old as 74 years. RDD is seen more frequently in men and people of African descent, whereas the skin form is more common in Asian women [6].

In 2016, a classification system was suggested by the Histiocyte Society for histiocytosis, categorizing them into five groups labelled with the letters "C", "H", "L", "M", and "R" [9]. The Rosai-Dorfman Disease (RDD) and other unrelated noncutaneous, non-Langerhans cell histiocytosis are classified under Group "R". Various subtypes of RDD include "Familial," "Classical (nodal)," "Extra nodal," "Neoplasia-associated," and "Immune disease-associated" [8].

Since Foucar ET al [4] published the RDD registry (423 cases) in 1990, over 1000 reports detailing different aspects of the disease have been published. Due to the infrequency of the diagnosis, the wide range of differential considerations, the vague imaging findings, and the involvement of multiple sites, the diagnosis of RDD is frequently overlooked, resulting in incorrect treatment of this benign yet sometimes advancing condition. Adding to the complexity of the diagnosis, as many as 85% of patients are in overall good health and do not show any major symptoms of their illness; patients may display extra nodal disease even without lymph node enlargement.

About 75% of patients with diseases not originating in the lymph nodes have the disease located in the head and neck area. Identifying these cases with extra nodal involvement is challenging, and typically a diagnosis is only possible through the presence of specific histopathological characteristics, such as the presence of large histiocytes with round to oval

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

vesicular nuclei and ample pale vacuolated cytoplasm. Histiocytes contain lymphocytes that appear intact, as well as occasional plasma cells, neutrophils, and red blood cells. The presence of lymphocytes within the cytoplasm of histiocytes is labelled as emperipolesis.

Our cases also showed the distinctive histopathological characteristics, in line with the usual histology of Rosai Dorfman disease, with positive Emperipolesis, s100, and Ig G markers. The unusual aspect of these cases was that the patient only been involved of the paranasal sinuses, with no nodal or extra-nodal involvement.

Possible management interventions include monitoring for minor symptoms without any impact on appearance or function, removing or reducing the size of growths in surgically reachable areas, using corticosteroids systemically, administering chemotherapy (such as vincristine, 6MP, methotrexate, alkylating agents), or utilizing radiotherapy for patients with serious symptoms or compromised organ function [9]. The objective of treating orbital symptoms of Rosai-Dorfman disease is to manage both the functional and cosmetic irregularities. Surgery, systemic corticosteroids, chemotherapy, or radiotherapy may be part of the treatment for large or recurring orbital disease or a substantial residual lesion after surgery.

Goldberg and colleagues [10] effectively managed a patient suffering from Rosai-Dorfman disease and experiencing compressive optic neuropathy by utilizing a combination of cyclophosphamide, vincristine, and prednisolone, achieving outstanding outcomes after 6 months of treatment. Komp[11] also demonstrated that CVP is better than other chemotherapy treatments. Horneff et al [12] showed that methotrexate and 6-mercaptopurine (6-MP) were effective in treating cervical lymphadenopathy in a 3-year-old girl. On the other hand, Pulsoni ET al [13] did not support the use of chemotherapy. Jubran et al [14] used rituximab to treat a child who had not responded well to steroids, methotrexate, and 6MP, and observed total disappearance of lymphadenopathy. After 5.5 years, the patient treated by Jabali [15] with chemotherapy showed no signs of the disease coming back.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

All of our cases were effectively treated using only one method, which is Endoscopic excision/removing the paranasal sinus and orbital lesions, followed closely with endoscopy and imaging as needed. During the follow-up period, the patients did not report any issues indicating a return of the condition at the original location or elsewhere.

Conclusion:

Rosai-Dorfman disease typically appears as significant swelling in both sides of the neck and is usually a harmless condition that resolves on its own. Nevertheless, Extra nodal involvement, as well as the involvement of critical structures like the orbit and brain, and recurrences are possible. The occurrence of paranasal sinus involvement as seen by us is a very uncommon presentation. The primary method of diagnosis is histopathological, and confirmation is achieved through measuring gamma globulin levels and testing positive for S-100. Given the diverse nature of the presentation and potential for recurrences, endoscopic debulking and regular follow-up with diagnostic nasal endoscopy and imaging as needed can be essential for managing the situation. Nevertheless, a thorough examination of a significant number of patients is needed to establish a consensus and protocol for treating individuals with Rosai Dorfman syndrome affecting the paranasal sinuses and orbit.

References:

1. Amiji I, Mohammed U, Salum H, et al. Rosai Dorfman Disease —A rare case of cervical lymphadenopathy. Clin Case Rep. 2020;8:2712–2715. https://doi.org/10.1002/ccr3.3255
2. Destombes P. [Adenitis with lipid excess, in children or young adults, seen in the Antilles and in Mali. (4 cases)]. Bull Soc Pathol Exot Filiales. 1965;58(6):1169-1175.
3. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. Arch Pathol. 1969;87(1):63-70.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

4. Foucar E, Rosai J, Dorfman R. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): review of the entity. Semin Diagn Pathol. 1990;7(1):19-73.
5. Dalia S, Sagatys E, Sokol L, Kubal T. Rosai-Dorfman disease: tumor biology, clinical features, pathology, and treatment. Cancer Control. 2014 Oct;21(4):322-7.
6. Cai Y, Shi Z, Bai Y. Review of Rosai-Dorfman disease: new insights into the pathogenesis of this rare disorder. Acta haematologica. 2017 Aug 25;138(1):14-23.
7. Becker MR, Gaiser T, Middel P, Rompel R (2008). "Clinicopathological challenge. Destombes-Rosai-Dorfman disease (DRDD) (sinus histiocytosis with massive lymphadenopathy)". Int J Dermatol. 47 (2): 125–127. Doi: 10.1111/j.1365-4632.2008.03376.x. PMID 18211480. S2CID 41243620. Retrieved 2017-09-10.
8. Riyaz N, Khader A, Sarita S (2005). "Rosai Dorfman syndrome". Indian J Dermatol Venereol Leprol. 71 (5): 342–344. Doi: 10.4103/0378-6323.16786. PMID 16394460.
9. Emile JF, Abla O, Fraitag S, Horne A, Haroche J, Donadieu J, Requena-Caballero L, Jordan MB, Abdel-Wahab O, Allen CE, Charlotte F, Diamond EL, Egeler RM, Fischer A, Herrera JG, Henter JI, Janku F, Merad M, Picarsic J, Rodriguez-Galindo C, Rollins BJ, Tazi A, Vassallo R, Weiss LM (2016). "Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages". Blood. 127 (22): 2672–2681. Doi: 10.1182/blood-2016-01-690636. PMC 5161007. PMID 26966089
10. Goldberg S, Mahadevia P, Lipton M, Rosenbaum PS. Sinus histiocytosis with massive lymphaden nopathy involving the orbit: reversal of compress sive optic neuropathy after chemotherapy. J Neur roophthalmol. 1998 ;18:270-5
11. Komp DM. The treatment of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). Semin Diagn Pathol 1990;7:83-6.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

12. Horneff G, Jurgens H, Hort W, Karitzky D, Gobel U. Sinus histiocytosis with massive lymphaden nopathy (Rosai-Dorfman disease): response to methotrexate and mercaptopurine. Med Pediatr Oncol. 1996;27:187-92.
13. Pulsoni A, Anghel G, Falcucci P, Matera R, Pescarmona E, Ribersani M, Villiva' N, Mandelli F. Treatment of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): report of a case and literature review. American journal of hematology. 2002 Jan;69(1):67-71.
14. Alqanatish JT, Houghton K, Bond M, Senger C, Tucker LB. Rituximab treatment in a child with rosai-dorfman disease and systemic lupus erythem matosus. J Rheumatol. 2010;37:1783-4.
15. Jabali Y, Smrcka V, Pradna J. Rosai-Dorfman disease: successful long-term results by combinat tion chemotherapy with prednisone, 6-mercapt topurine, methotrexate, and vinblastine: a case report. Int J Surg Pathol. 2005;13:285-9.