Varied manifestations of Rosai-Dorfman disease and its management – a case report and review of literature

Pradipta Kumar Parida · Naresh K Panda · Aman sharma · V. Mahesha · Ashim Das

Abstract

Rosai Dorfman disease or sinus histiocytosis is a rare, idiopathic, benign and self-limiting histiocytic proliferative disorder, usually seen in younger patients. It most commonly involves the cervical lymph nodes, with a predominant infiltration of sinusoidal histiocytes and classically presents with massive cervical lymphadenopathy. Extranodal disease occurs in about 43% of cases and produces different signs and symptoms depending upon its location. We report a case of this disorder in 22-year-old male with initial isolated involvement of bilateral nasal cavity and paranasal sinuses with subsequent involvement of cervical lymph nodes and skin. The clinical presentation, histologic characteristics, radiographic findings and treatment of the disease are discussed.

Key messages Our case demonstrated, isolated involvement of nose and paranasal sinuses with subsequent involvement of lymph nodes and skin. Most of the time, the disease process undergoes spontaneous remission indicating that conservative, expectant management is sufficient in most patients, but more aggressive treatment may be necessary in selected cases.

Introduction

Sinus Histiocytosis with massive lymphadenopathy (SHML) or, Rosai Dorfman disease (RDD) is a histiocytic proliferative disorder that affects lymph nodes. It was first described by Rosai and Dorfman in 1969 [1]. Although the cause remains unknown, the disease is thought to be a disorder of immune regulation or response to a presumed infectious agent. It is characterized by painless cervical lymphadenopathy, leukocytosis, low-grade fever, elevated ESR and polyclonal hypergammaglobulinemia. Its major manifestation is in the form of massive lymph node enlargement with the proliferation of sinusoidal histiocytes. Extranodal involvement is present in about 43% of cases, with a particular predilection for the head and neck region [2]. The extranodal sites commonly affected are skin [3], nasal cavity [4, 5], paranasal sinuses [6], orbit [7], ear [8], breast [9] and central nervous system [10]. The disease usually affects children and adolescent. Its course is usually characterized by insidious onset, protracted duration of active disease state and eventual spontaneous remission, but recurrences are also reported occasionally. Six cases of RDD involving nasal cavity and paranasal sinuses (PNS) have been reported in the world literature. Out of these six cases, three cases had involvement of both nasal cavity and paranasal sinuses. We are reporting a case RDD with initial isolated involvement of nasal cavity and PNS with subsequent involvement of lymph nodes and skin.

P. K. Parida¹ · N. K. Panda¹ · A. sharma² · V. Mahesha³ · Ashim Das³

¹Department of Otorhinolaryngology and Head and Neck Surgery

²Department of Internal Medicine

³Department of Histopathology

Post Graduate Institute of Medical Education and Research,
Chandigarh - 160 012, India

N. K. Panda (✉)

E mail: npanda59@yahoo.com

Case report

A 22-year-old man presented with 12-month history of progressive nasal obstruction, intermittent epistaxis, watering of both eyes and widening of dorsum of the nose. Examination revealed a widened nasal dorsum and bilateral firm, fleshy, polypoidal mass that bled easily with manipulation. There was no cervical lymphadenopathy at the time

of presentation. Haematological investigations were normal except raised ESR. Computed tomography (CT) scan of sinuses and neck revealed bilateral soft tissue opacification of the nasal cavity and all sinuses. On the right side there was erosion of anterior and posterolateral wall of maxillary sinus, and lamina papyracea. The mass was infiltrating into the infratemporal fossa and orbit (Fig. 1). The biopsy from the right nasal cavity showed plenty of large cells with abundant eosinophilic vesicular cytoplasm, heavily infiltrated by lymphocytes, plasma cells, eosinophils and few rosette cells. An initial diagnosis consistent with RDD was made. An excisional biopsy of the mass done by mid-facial degloving approach confirmed the diagnosis of RDD (Fig. 2). The patient made an uneventful post-operative recovery and received prednisolone for two weeks with which there was no local recurrence for four months after surgery. Subsequently the patient was lost to follow up. One year later, he presented with progressive nasal obstruction, cervical lymphadenopathy and subcutaneous nodules ranging from one to two cm in diameter all over the body (Figs. 3 and 4). Fine needle aspiration cytology of cervical lymph node and excision biopsy of subcutaneous nodule confirmed the diagnosis of RDD. The repeat CT scan showed recurrence in nose and PNS. He was started on tapering dose of prednisolone (1mg/kg/day) which he received for one year but did not show good response and the skin lesions and lymph node swelling increased in size. The patient has now been started on one gram monthly pulses of cyclophosphamide.

Fig. 1 Axial section, contrast enhanced CT scan of paranasal sinuses showing homogenous mass in both nasal cavity and maxillary sinus. The mass destroying the anterior and posterolateral wall of right maxillary sinus

Discussion

RDD is a rare, idiopathic, histiocytic proliferation affecting nodal and extranodal sites with a particular predilection for cervical lymph nodes. It is predominately a disease of childhood and adolescence; with 62% of cases occurring in the first decade of life. The most common clinical finding is massive painless, bilateral cervical lymphadenopathy seen in approximately 85% of patient [11, 12]. Additional symptoms include fever, weight loss, nasal obstruction or discharge and tonsillitis. Extranodal involvement is seen

Fig. 2 Photomicrograph showing characteristic histiocytes of Rosai-Dorfman disease in a distended sinus demonstrating the phenomenon of emperipolesis (H&E stain X20)

Fig. 3 Clinical photograph showing widening of external nasal pyramid and bilateral massive cervical lymphadenopathy

Fig. 4 Clinical photograph showing multiple cutaneous nodules over the trunk

in 43% of the patient. The disease almost invariably runs a benign course with gradual resolution of the lymphadenopathy over a period of many years. A review of literature showed six cases of RDD with involvement of nose, nose and PNS, or both [4, 5, 6, 13]. In three cases there was no involvement of paranasal sinuses and in the remaining three cases, the nose and PNS were involved in addition to lymph node, skin, orbit, spine, lung, genitalia and kidney (Table 1).

Our case demonstrated the unique presentation and diagnosis of RDD in the form of initial isolated involvement of nose and PNS without nodal disease and involvement of lymph nodes and skin after 1 year with massive cervical lymphadenopathy and subcutaneous nodules with simultaneous recurrence in nose and PNS which to the best of our knowledge has not previously been reported.

The pathologist needs to be aware of the microscopic feature of this condition to be able to diagnose it accurately, especially in the absence of nodal involvement. A firm diagnosis can be made by identifying the distinctive CD68 positive histiocytes [14]. The characteristic histopathological

feature of RDD is the tendency for the infiltrates to recapitulate lymph node architecture with dilated “sinuses” (lymphatic) and reactive germinal centers [2]. The sinusoids are distended by pale staining histiocytes intermixed with variable numbers of plasma cells. Current evidence suggests that these characteristic foamy histiocytes are functionally activated histiocytes derived from monocytes containing one or more viable lymphocytes in the cytoplasm [14]. The lymphocytes are thought to have penetrated the cytoplasm in a process known as emperipolesis. Because lymphocyte emperipolesis is thought to relate to antigen presentation, RDD may present a derangement of the method by which histiocytes contact lymphocytes for antigen delivery [15].

The differential diagnosis of RDD includes a wide variety of reactive and malignant lymphadenopathies. Among these lesions are infectious (granulomatous) diseases, midline destructive diseases (Wegener’s granulomatosis, midline malignant reticulosis), and eosinophilic granuloma, Hodgkin’s disease and fibroinflammatory lesions.

There is no ideal protocol for treating RDD as it is uncommon; the disease is usually self limiting and seldom life threatening, rendering therapy unnecessary in most cases. For those who require therapy because of persistent or worsening symptoms, the treatment modalities include surgery, chemotherapy, and radiotherapy. However, none of these are reported to consistently achieve sustained remission. Various reports in the literature indicate the surgery is the best choice for the local disease and it often results in long-term remission of disease. RDD in nose and paranasal sinuses can be treated by endoscopic approach [4, 3] or by external approach (craniofacial resection [5]). In our case in view of bilateral, extensive involvement of all sinuses with infratemporal fossa and intraorbital extension and for cosmetic purpose a midfacial degloving approach was chosen to remove the lesion. Drug therapy for RDD includes corticosteroids, cytotoxic agents or a combination of both. However the most effective regimens would be a combination of corticosteroid (prednisolone) and vinca alkaloid (vincristine and vinblastin) with an alkylating agent (cyclophosphamide) achieving a complete and partial response rate of 44 percent according to Komp’s series [16]. In the same series, the response rate of RDD to radiotherapy alone was 29 percent. Jabali et al [17] has

Table 1 No of cases of RDD with nose and paranasal sinuses involvement

Authors	Site(s)	No. of cases
Peter KM et al [5]	Nose	2
James Et al [4]	Nose, PNS, L.N	1
	Nose, Skin, Eye, Larynx	1
Gregor RT et al [6]	Nose PNS, Spine, Genitalia, Lung	1
	Retroperitoneal tissue, Kidney, L.N.	
White DH et al [13]	Nose, PNS, L.N.	1
Our case	Nose, PNS, Skin, L.N.	1

PNS=paranasal sinuses, LN=lymph node

reported successful long-term results by combination chemotherapy with prednisone, 6-mercaptopurine, methotrexate, and vinblastine showing no evidence of recurrence after a follow-up of 5.5 years. In general, RDD appeared less responsive to the both modalities of treatment than hematological malignancies. These therapies should not be the initial modality, especially in the younger age group because of the potential for the long-term morbidity and complication. It is pertinent to mention that a regular follow up is required for early detection of recurrence.

Conclusion

Our case demonstrated, isolated involvement of nose and paranasal sinuses with subsequent involvement of lymph nodes and skin. The pathologist needs to be aware of the microscopic feature of this condition to be able to diagnose it accurately, especially in the absence of nodal involvement. Most of the time, the disease process undergoes spontaneous remission indicating that conservative, expectant management is sufficient in most patients, but more aggressive treatment may be necessary in selected cases. Our case also highlights the role of steroids and chemotherapy for treatment of RDD.

References

1. Rosai J, Dorfman RF (1969) Sinus histiocytosis with massive lymphadenopathy: a newly recognized benign clinicopathologic entity. *Arch Pathol* 87:63–70
2. Wenig BM, Abbondnzo SL, Childer EL et al (1993) Extranodal sinus histiocytosis with massive lymphadenopathy (Rosai Dorfman disease) of the head and neck. *Hum Pathol* 24:483–492
3. Annesi G, Gianneti A (1996) Purely cutaneous Rosai Dorfman disease. *Br J Dermatol* 134:749–753
4. Goodnight JW, Wang MB, Secarz JA et al (1996) Extranodal Rosai Dorfman disease of head neck. *Laryngoscope* 106: 253–256
5. Peter KKM, Michael TCF, Leung CY et al (1999) Nasal manifestation of extranodal Rosai-Dorfman disease-diagnosis and management. *J. Laryngol Otol* 113:275–280
6. Gregor RT, Ninnin D (1994) Rosai Dorfman disease of the paranasal sinuses. *J Laryngol Otol* 108:152–155
7. Foucar E, Rosai J, Dorfman RF (1979) The ophthalmologic manifestations of sinus histiocytosis with massive lymphadenopathy. *Am J Ophthalmol* 87:354–367
8. Foucar E, Rosai J, Dorfman RF (1978) Sinus histiocytosis with massive lymphadenopathy: Ear, nose and throat manifestations. *Arch Otolaryngol Head Neck Surg* 104: 687–693
9. Green I, Dorfman RF, Rosai J (1997) Breast involvement by extranodal Rosai-Dorfman disease: report of seven cases. *Am. J. Surg Pathol* 21:664–668
10. Resnick DK, John BL, Lovely TJ (1996) Rosai Dorfman disease presenting with multiple orbital and intracranial masses. *Acta Neuropathologica* 91:554–557
11. Paulli M, RossoR, Kindl S, et al (1992) Immunophenotypic characterization of the cell infiltrate in five cases of sinus histiocytosis with massive lymphadenopathy (Rosai Dorfman disease). *Hum Pathol* 23:647–654
12. Sacchi S, Artusi T, Torelli U et al (1992) Sinus histiocytosis with massive lymphadenopathy. *Leuk Lymphoma* 23: 647–654
13. Wright DH, Richards DB (1981) Sinus histiocytosis with massive lymphadenopathy (Rosai Dorfman disease): Report of a case with widespread nodal and extranodal dissemination. *Histopathology* 5(6):697–709
14. Eisen RN, Backley PJ, Howard DJ (1990) Immunophenotypic characterization of sinus histiocytosis with massive lymphadenopathy(Rosai-Dorfman disease). *Semin Diagn Pathol* 7:74–82
15. McAlister WH, Herman T, Dehner LP (1990) Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). *Pediatr Radiol* 20:425–432
16. Komp DM (1990) The treatment of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). *Semin Diagn Pathol* 7:83–86
17. Jabali Y, Smrcka V, Pradna J (2005) Rosai-Dorfman disease: successful long-term results by combination chemotherapy with prednisone, 6-mercaptopurine, methotrexate, and vinblastine: a case report. *Int J Surg Pathol* 13:285–9