

# Cytological and histopathological diagnosis of a multifocal Rosai dorfman disease with involvement of Pinna– A rare case report

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## Abstract

Rosai-Dorfman disease (RDD) is a rare lymph proliferative disorder with nodal and extranodal involvements. We are presenting this case of Rosai dorfman disease with presentation in pinna of ear and with previous history of Rosai dorfman disease at multiple sites including lymph node. Cytological and histological examination of the submandibular lymph nodes and skin biopsy demonstrated evidences of RDD.

**Keywords:** Rosai Dorfman Disease, Sinus Histiocytosis, Extranodal, Multifocal

## Introduction

Rosai dorfman disease was first described by Rosai and Dorfman as sinus histiocytosis with massive lymphadenopathy in the year 1969 [1]. RDD can affect various head and neck sites, including the nasal cavity, paranasal sinuses and nasopharynx. Concomitant cervical node involvement may or may not be present [2,3]. It is an idiopathic, nodal-based histiocytic proliferative disorder that usually resolves spontaneously [4,5,6]. About 43% of cases occur in extra-nodal disease, which can be widespread and most

frequently involves the respiratory tract, paranasal sinuses, visceral organs, skin, bones, central nervous system, genitourinary tract and orbit [7]. In the absence of lymph node involvement, RDD limited to the skin is called as cutaneous Rosai-Dorfman disease (CRDD). To date, very few cases of CRDD involving the ear have been reported [8] [9] [10]. The diagnosis of Rosaidorfman disease is made on the basis of clinical presentation, histopathological examination and immunohistochemical studies.

## Case Report

We are presenting a case of 16-year old female a resident of Marthandam in Kanyakumari district who is a known case of Rosaidorfman disease of cervical lymph node and nasopharynx, now presented with swelling right external ear since 2 months in ENT OPD. Swelling was aspirated and submitted to our cytology department for cytological diagnosis. On physical examination swelling measured 1x0.8x0.5cm, and it was soft, nontender, beaded in appearance and was located on the border of right pinna. She had no significant medical and family history General examination were within normal limits. Patient had a history of swelling nasopharynx and cervical lymph node one year back, which was aspirated and then excised later and was sent for cytological study and histopathological examination respectively. It was reported as Rosaidorfman disease both in cytological study and histopathological examination.

The aspirate from pinna was sent to us after fixing in isopropyl alcohol. The smear was then pap stained and examined under microscopy. The smear was cellular with inflammatory cells composed of large histiocytes with intact neutrophil and plasma cells within the cytoplasm of histiocytes (figure1). Also noted are multinucleated giant cell, lymphocyte, histiocytes and neutrophil (figure 2). We received two specimens one excised specimen from right external ear and other right external auditory canal mass. Grossly both were tiny grey white mucosal fragments one measuring 0.7x0.5x0.5cm and other aggregate measuring 0.8x0.5x0.5cm respectively. The specimens were excised and send to our department of

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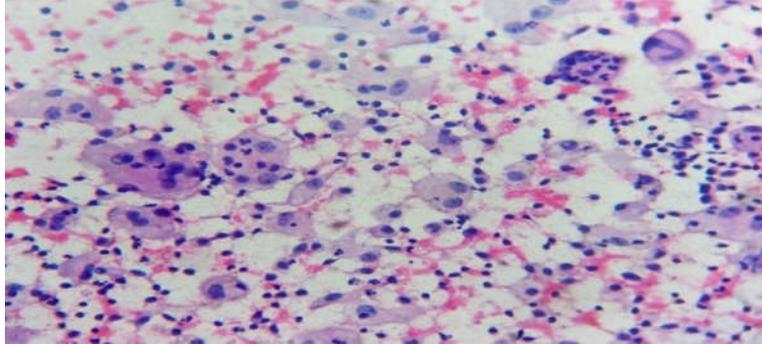
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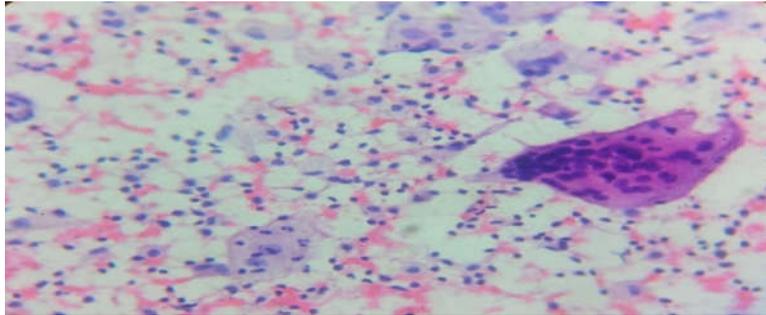
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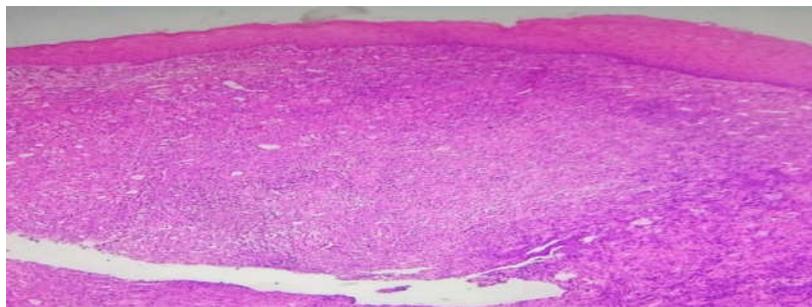
pathology for histopathological examination after fixing in 10% neutral buffered formalin. On microscopic examination, section showed tissue lined by stratified squamous epithelium, subepithelium showed dense inflammatory infiltrate composed of lymphocytes, plasma cell, foamy histiocytes and neutrophils. Also noted were large histiocytes with pale eosinophilic cytoplasm vesicular nucleus, demonstrating emperipolesis. These cells were positive for S100 and negative for CD1a which ruled out Langerhans cell histiocytosis.



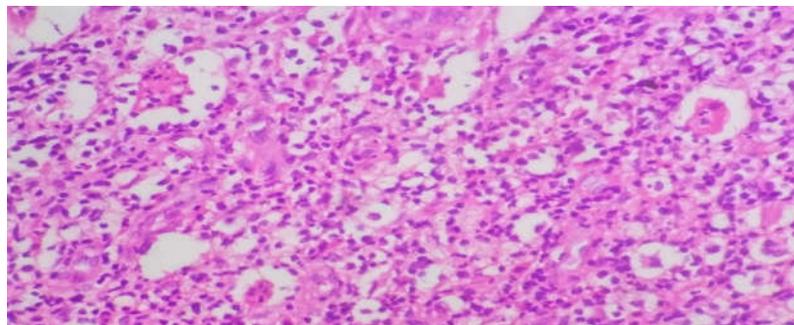
**Figure-1:** Pap stained smear showing emperipolesis with neutrophils and plasma cells in the cytoplasm of large histiocytes



**Figure-2:** Showing emperipolesis and multinucleated giant cells along with other inflammatory cells

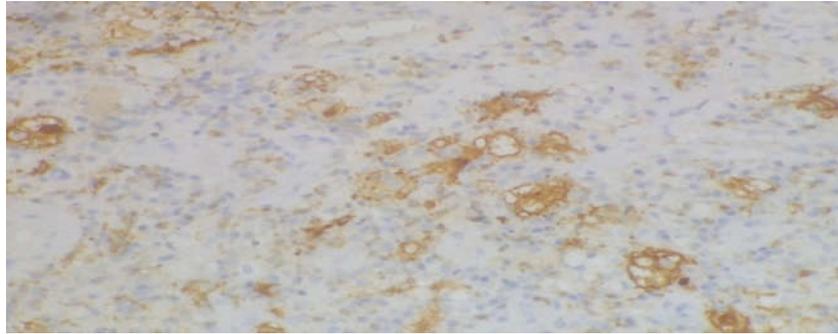


**Figure-3:** Showing stratified squamous epithelium and sub epithelium showing dense inflammation



**Figure-4:** Showing inflammatory cells along with many histiocytes demonstrating emperipolesis

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**Figure-5:** Demonstrating S100 positivity in Rosai-Dorfman disease by histiocytes

## Discussion

Emperipolesis is derived from the Greek (em – inside; peri – around; polemai – wander about) and was defined as “The active penetration of one cell by another which remains intact.” It differs from phagocytosis in that an engulfed cell exists temporarily within another cell and with an intact normal structure while in phagocytosis, the engulfed cell is destroyed by the protective action of lysosomal enzymes. The cells involved in Emperipolesis are mainly histiocytes and megakaryocytes but can also be seen in association with tumour cells and Reed Sternberg cells. It is a hallmark feature of Rosai – Dorfman disease (RDD) but can also be part of other malignant conditions such as hematolymphoid disorders (Hodgkin’s disease, leukaemia, acute and chronic myeloid leukaemia, Non – Hodgkin’s lymphoma, myeloproliferative disorders, myelodysplastic syndrome) and Non haematological malignancies (multiple myeloma, neuroblastoma, Rhabdomyosarcoma) [11].

From review of literature, only 5 cases of CRDD involving the ear have been reported [8,9,10]. In each of those cases, the ear was the only location on the skin involved. Cervical lymph nodes are typically involved, leading to painless bilateral cervical lymphadenopathy. Associated findings often include fever, leukocytosis, elevated erythrocyte sedimentation rate, and polyclonal hypergammaglobulinemia.

The classic form of the RDD typically presents in young adults with lymphadenopathy in the neck. Approximately 20–40% of patients experience disease remission, sometimes spontaneous. Extranodal RDD has a higher tendency for a chronic relapsing course and affects older individuals.

The cause of RDD is unknown; but the source have been postulated as autoimmune diseases and viruses such as human herpes virus 6, Epstein-Barr virus, parvovirus B19, lymphoma, Langerhans cell disease, autoimmune lymphoproliferative syndrome-1, joint

disease, asthma, juvenile-onset diabetes, HIV, and red blood cell auto antibodies [11,12]. The pathogenesis involves recruitment of marrow monocytes from the peripheral blood into lymph node sinuses or extra nodal sites with subsequent transformation into the immunophenotypically distinct RDD histiocytes [13]. Histiocytes with abundant pale, vacuolated, or eosinophilic cytoplasm are typically seen within a field of lymphocytes and plasma cells [14]. Emperipolesis, the process by which histiocytes phagocytize intact lymphocytes or plasma cells, is characteristic of but is not pathognomonic for RD [6,12]. These histiocytes can release cytokines, such as tumor necrosis factor- $\alpha$ , which result in fever and other systemic symptoms [13].

RDD histiocytes share a common monocyte-macrophage lineage with other S-100 immunostain-positive antigen presenting cells such as Langerhans cell histiocytosis (LCH). In contrast to LCH, CD1a is negative in RDD [13] [15]. In addition, RDD shows CD68 positivity and factor XIII a negativity. Extranodal RDD sites often show more fibrosis, fewer histiocytes, and less emperipolesis. Thus, a more thorough evaluation of the sample and additional immunohistochemical stains may be needed to confirm the diagnosis [16]. The cytological findings in sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) were described by Van Heerde and others [17]. In this condition, smears contain many large histiocytes showing lymphophagocytosis.

Although there is no specific imaging characteristics that allow differentiation of lymphadenopathy in Rosai-Dorfman disease from other disease processes, massive painless bilateral cervical lymph node enlargement, particularly when occurring in children and adolescents, should promote consideration of Rosai-Dorfman disease in the differential diagnosis [18]. Of extranodal sites affected, the skin is the most common, followed by the paranasal sinuses and nasal cavity, subcutaneous tissue, orbit, eyelids, and bone Multiple additional sites of

extranodal involvement in the head and neck have been described, including the salivary glands, oral cavity, pharynx, tonsils, and trachea [12] [19]. Okada et al. [20] reported a case of tracheal involvement confined to the mucosa, without involvement of the tracheal cartilage. Additional lesions in the carina and left main bronchus were also present, as well as enlarged mediastinal lymph nodes [20]. Juskevicius and Finley [21] described a case of parotid gland involvement without significant lymphadenopathy in a 48-year-old patient with systemic lupus erythematosus. The orbit, globe, and eyelid are also common sites of involvement in Rosai-Dorfman disease, occurring in 7–10% of patients.

CNS involvement with Rosai-Dorfman disease often has no associated lymphadenopathy (up to 70% of patients), and it commonly occurs in adult men, usually in the fourth decade; however, it has also been reported in children [22]. Common locations are the parasellar, cavernous sinus, petroclival, and parafalcine regions; the cerebello-pontine angle; and posterior fossa. Primary osseous involvement with Rosai-Dorfman disease is rare but has been reported to involve the maxilla [23], as in one of our patients, as well as the sphenoid bone and the frontal bone [22].

The nonspecific appearance of cutaneous lesions can lead to a broad differential diagnosis, including other histiocytoses, sarcoidosis, tuberculosis, leishmaniasis, syphilis, and other infectious and infiltrative etiologies. The diagnosis of RDD was only made after performing immunohisto-chemistry on the tissue biopsy. Ear involvement is of particular significance because when present, it can help narrow the clinical and histologic differential diagnosis to include infiltrative and inflammatory processes involving the ear such as leprosy, relapsing polychondritis, perichondritis, pseudocyst of the auricle, and lymphoproliferative disorders. Numerous treatment options have been used for patients with CRDD including radiotherapy, corticosteroids (topical and systemic), chemotherapy, acyclovir, surgical excision, antibiotics, cryotherapy, interferon, dapsone, and retinoids [24].

## Conclusion

The diagnosis of RDD should be considered in any atypical chronic inflammatory lesion with a histiocytic component involving multiple organ systems. The disease often follows a benign clinical course, with poorer prognosis associated with a heavy nodal burden and systemic involvement. The ideal treatment of CRDD has yet to be determined. We propose the development of a national registry of patients for future meta-analyses to help gain a better understanding of the

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disease etiology, clinical features, and future treatment options.

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**Permission from IRB:** Yes

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