

# Rosai-Dorfman disease

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## ABSTRACT

**Sinus histiocytosis with massive lymphadenopathy, also known as Rosai-Dorfman disease, is a rare histiocytic proliferative disorder of unknown aetiology. The classic presentation of Rosai-Dorfman disease is massive, bilateral, painless cervical lymphadenopathy. Extranodal disease is also common, often with a particular predilection for the head and neck regions. We report a rare case of Rosai-Dorfman disease with nodal and multiple extranodal manifestations in a 13-year-old girl. The patient had cervical and mediastinal lymphadenopathy, multiple soft tissue swellings of the scalp, bilateral proptosis and goitre due to thyroid gland involvement. She responded to steroids, with remission of the swellings and symptoms. This case is being reported for its rarity, multiple extranodal manifestations and thyroid gland involvement. Thyroid gland involvement in Rosai-Dorfman disease has rarely been reported in the literature.**

**Keywords: emperipolesis, goitre, lymphadenopathy, Rosai-Dorfman disease, sinus histiocytosis**

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## INTRODUCTION

Sinus histiocytosis with massive lymphadenopathy, also known as Rosai-Dorfman disease (RDD), is a rare and benign histiocytic proliferative disorder of unknown aetiology. It usually presents with painless cervical lymphadenopathy with or without extranodal manifestations.

## CASE REPORT

A 13-year-old girl, born of a non-consanguineous marriage, had multiple painless soft tissue swellings over her scalp, enlargement of the neck glands and thyroid swelling for six months (Fig. 1). She also had a low-grade



**Fig. 1** Photograph shows cervical lymphadenopathy and thyroid swelling in a 13-year-old girl.

fever, malaise, anorexia and nausea for the same duration. She had developed a gradual protrusion of her eyeballs and swelling of the eyelids for the last 20 days, as well as dry cough and breathlessness for the last 15 days. No history of haemoptysis, weight loss, arthralgia, rashes, photophobia, bleeding manifestations, high-risk sexual behaviour or contact with animals was noted. The patient also had no history of intake of drugs such as phenytoin or carbamazepine. No significant family history was present.

Physical examination of the patient revealed an average build and nutrition, a regular pulse at 98 beats/minute, blood pressure of 110/70 mmHg and a respiratory rate of 26 breaths/minute. Pitting oedema, jaundice and cyanosis were absent. Multiple cervical and submandibular lymph nodes, which were 2–3 cm in diameter, non-tender, movable, firm, discrete and free from superficial and deep structures, were present. The isthmus and the left lobe of the thyroid gland were moderately enlarged and non-tender. Five soft tissue swellings over the scalp were palpable; these swellings were approximately 4 cm in diameter, globular and non-tender, with no local rise in temperature. The skin over the swellings appeared normal. Bilateral proptosis with periorbital swelling, more toward the left side, was observed. Sternal percussion revealed dullness. The patient had bilateral vesicular breath sounds, with prominent inspiratory and expiratory rhonchi and no crepitations. The other systems revealed no significant abnormality.

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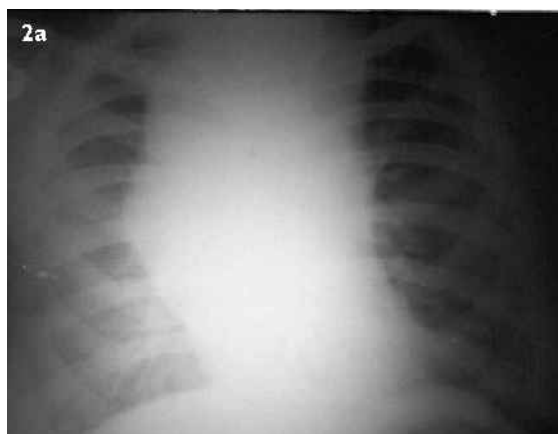
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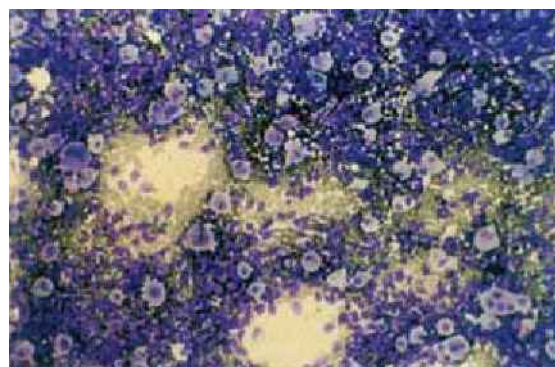
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**Fig. 2** Chest radiographs in (a) posteroanterior view and (b) right lateral view show mediastinal lymphadenopathy.

Blood examination of the patient revealed haemoglobin 10.29 gm%, packed cell volume 33%, mean corpuscular haemoglobin concentration 33 g/dl, reticulocyte count 1%, total leucocyte count 8,100/mm<sup>3</sup> with neutrophil 77%, lymphocyte 21%, eosinophil 1% and monocyte 1%, platelet count 240,000/mm<sup>3</sup> and erythrocyte sedimentation rate 55 mm/hour. Red blood cell morphology revealed mild hypochromia and anisocytosis, along with few target cells. Routine urine examination and culture were normal. Thyroid function test was within the normal limit. Ultrasonography (US) of the whole abdomen showed no organomegaly or lymph node enlargement. US of the thyroid gland revealed a large space-occupying lesion of homogeneous echotexture in the left lobe and isthmus. The right lobe appeared normal. Chest radiograph and computed tomography of the thorax revealed mediastinal lymphadenopathy (Fig. 2). Skull radiograph showed multiple soft tissue swellings of the



**Fig. 3** Photomicrograph shows cytomorphologic features of fine needle aspiration cytology from the cervical lymphnode, comprising mixed population of lymphoid cells with a preponderance of activated lymphocytes, a large number of histiocytes with evidence of lymphophagocytosis (emperipolesis), multinucleated giant cells and few plasma cells (Haematoxylin & eosin,  $\times 100$ ).

scalp without any bony involvement. Bone marrow study was normal. Fine needle aspiration cytology (FNAC) from the cervical lymphnode was suggestive of RDD (Fig. 3). FNAC from the thyroid gland and scalp mass showed similar cytomorphologic features. The patient was finally diagnosed to have RDD with lymphadenopathy and multiple extranodal involvements.

## DISCUSSION

RDD is an uncommon disease that was reported by Juan Rosai and Ronald F Dorfman in 1969. It is a benign self-limiting histiocytic proliferative disorder of unknown aetiology, which usually occurs in the first two decades of life. It is believed to be a reactive process, and infection by a virus (HHV-6) or an undefined immunological defect initiated by some other organism is believed to be responsible for the disease. RDD usually presents with painless massive cervical lymphadenopathy. Extranodal involvement is common and is found mainly in the head and neck regions.<sup>(1-4)</sup> However, it may also involve the skin, orbits, eyelids, salivary glands, upper respiratory tract, peritoneum, bone, kidneys, testis and central nervous system. Fever, weight loss, tonsillitis, nasal discharge and obstruction may also be presenting features of this disease.

FNAC is a useful and reliable tool for the diagnosis of RDD, and as such, biopsy is avoidable.<sup>(5-7)</sup> Cytology usually reveals numerous large histiocytes with abundant pale cytoplasm and phagocytosed lymphocytes (emperipolesis). In emperipolesis, the lymphocytes are not attacked by enzymes and appear intact within the histiocytes (in contrast to phagocytosis). The phenomenon of emperipolesis

is highly useful for the diagnosis of RDD using FNAC. Differential diagnoses, such as Langerhans cell histiocytosis (LCH), lymphoma and nonspecific sinus hyperplasia, lack lymphohagocytosis. Immunohistochemical stains help in diagnosing RDD. In RDD, histiocytes are strongly positive for S-100 protein, negative for CD1a and variably positive for CD68. LCH is positive for both S-100 protein and CD1a, and the cells of LCH ultrastructurally reveal characteristic rod-shaped Birbeck granules. RDD is benign and usually involves spontaneous or steroid-induced regression of symptoms with complete recovery. Treatment (medical or surgical) is necessary, particularly when the disorder becomes life- or organ-threatening.

Our patient presented with a low-grade irregular fever with anorexia and nausea, along with painless bilateral, cervical and mediastinal lymphadenopathy, and multiple extranodal manifestations. Multiple soft tissue masses on the scalp and bilateral proptosis with periorbital oedema were observed. The isthmus and the left lobe of the thyroid gland were also involved. FNAC from the scalp, thyroid and cervical lymph nodes revealed similar cytomorphologic features (lymphohagocytosis). The patient responded to a short course of steroid therapy, with regression of the lymphadenopathy, proptosis, and the scalp and thyroid swellings. Thyroid swelling is uncommon in RDD, and only seven cases of thyroid enlargement with or without hypothyroidism have been reported in the literature.<sup>(8-14)</sup>

RDD with lymphadenopathy is commonly misdiagnosed as lymphoma, and cases with extranodal involvement are suspected to have other neoplasms, depending on the site of involvement. Thyroid swelling with lymphadenopathy in RDD may be misdiagnosed as thyroid malignancy with lymph node metastasis, leading to unnecessary thyroidectomy. A

high degree of suspicion is required to diagnose this rare, benign and self-limiting disease in order to avoid unnecessary intervention to the patients.

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