Rosai-Dorfman Disease: Simultaneous Parotid and Thymus involvement with invasive behaviour: Radiology and Pathology Findings

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Abstract
Rosai-Dorfman Disease (RDD) is a rare benign proliferative disorder of unknown etiology which usually presents with marked painless enlargement of the cervical lymph nodes. However, it can affect any body organ. Here, we describe a case of simultaneous involvement of the left parotid gland and the thymus. The thymic component of the disease was locally aggressive with direct invasion of the pericardium and the sternum. In addition, we describe the radiologic and pathologic manifestations of the disease and discuss the treatment and prognosis.

Keywords: Rosai-Dorfman Disease, Parotid, Thymus.

Introduction

Rosai-Dorfman Disease (RDD) or Sinus Histiocytosis with Massive Lymphadenopathy (SHML) is a proliferative disorder of unknown etiology. It is a rare entity manifested by abnormal histiocytic/phagocytic cell proliferation.[1] Although painless enlargement of the neck lymph nodes is the most common manifestation of the disease, it may present as enlargement of lymph nodes anywhere in the body or can also be extranodal.[2] The extranodal manifestation of RDD is not uncommon and can be seen in up to 43% of the patients.[3] Children and young adults are most commonly affected.[4] The disease can be locally aggressive despite its benign nature and therefore may mimic malignant disease. We report a case of a left parotid and simultaneous mediastinal/thymic RDD with direct invasion of the sternum and pericardium.

Case Report

A 62-year-old non-smoker female presented initially with a chronic progressively growing painless swelling in the left parotid region for 6-8 months. She has a past medical history of epilepsy, type 2 diabetes mellitus, dyslipidemia, depression and glaucoma. On physical examination, a 2 cm firm mass was palpated in the region of the left parotid tail. There was no involvement of the overlying skin. No palpable cervical lymph nodes were identified. The patient had 2 prior biopsies of the mass which were non-diagnostic, but the last biopsy revealed aggregate of epithelioid histiocytes, some with multinucleation, intermixed with inflammation and rare degenerated epithelial cells.

A CT scan of the neck with (intravenous) IV contrast showed a 3.2 x 2.6 x 2.5 cm lobulated, mildly heterogeneous enhancing soft tissue mass within the superficial part of the left parotid gland (Fig. 1). There was no cervical lymphadenopathy. In addition, a partially imaged lobulated anterior mediastinal mass was also observed on the same examination (Fig. 2) and further evaluation with CT scan of the thorax, abdomen and pelvis was recommended. At this time, the clinical/radiological differential diagnosis included histiocytic diseases and granulomatous diseases including tuberculosis and lymphoma. The possibility of a malignant left parotid tumor with mediastinal metastasis was felt less likely. A CT-guided biopsy of the anterior mediastinal mass was performed and showed abundant stroma, fibroblasts, numerous plasma cells and some spindle cells. The mediastinal mass remained stable on follow up after 9 months from the initial examination.

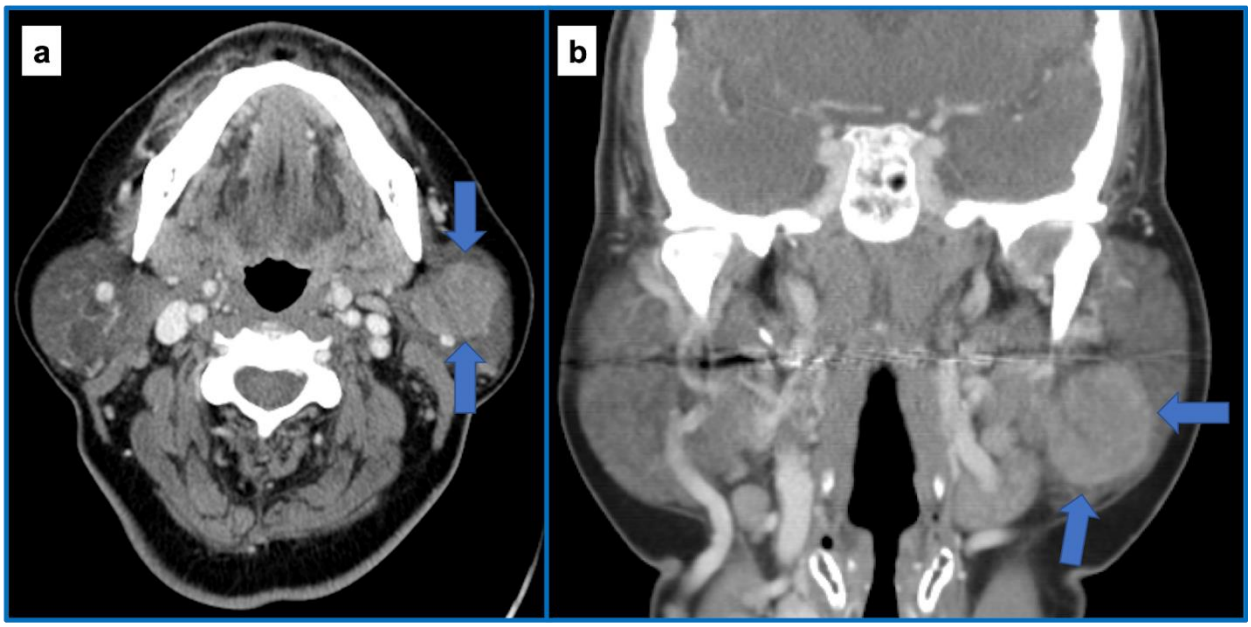

Figure 1

Figure 1: Contrast enhanced CT scan of the neck, axial (a) and coronal reconstruction (b) demonstrating a well-defined slightly heterogeneous soft tissue mass with smooth outline within the superficial part of the left parotid gland (arrows).

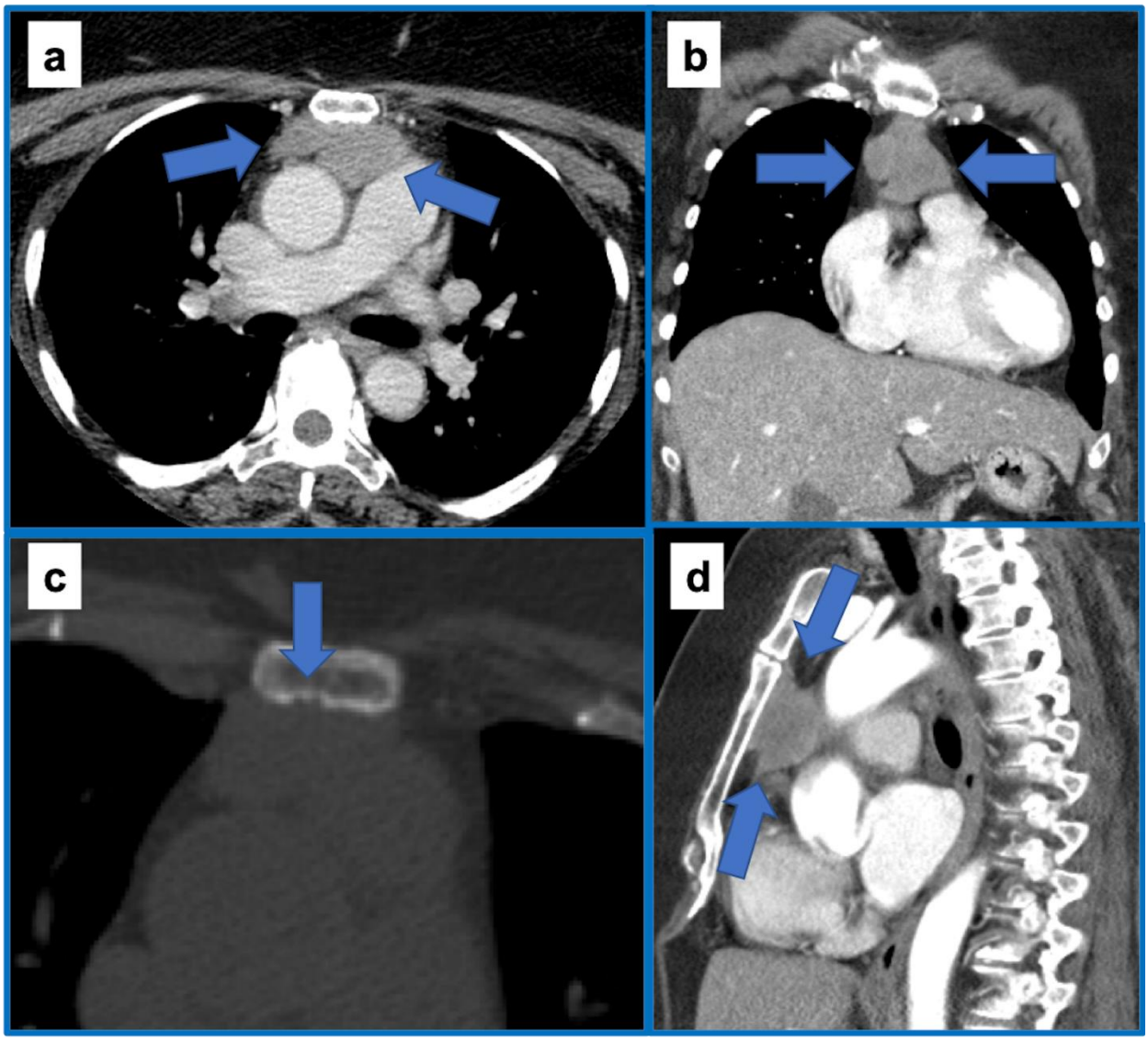

Figure 2

Figure 2: (a) axial image of the initial CT scan of the neck at the level of the mediastinum. (b, c and d) follow up CT scan of the chest with IV contrast with coronal reconstruction (b), zoomed in image with bone window (c) and sagittal reconstruction (d). Incidental findings of a thymic mass on the initial CT neck examination (arrows in a). The mass is inseparable from the pericardium. It is also inseparable from the sternum. The follow up contrast enhanced CT scan of the chest 9 months later (b, c and d) demonstrates stable size of the thymic mass. Note the erosion of the posterior cortex of the sternum (arrow in c).

The patient then underwent left parotidectomy at 9 months from the initial presentation. Gross pathological examination showed an ill-defined tumour measuring 1.8 x 1.4 x 2.6 cm. Hematoxylin and eosin (H&E) stained sections showed a well circumscribed tumor composed of large pale histiocytic cells intermixed with fibroblasts and collagen against an inflammatory background of plasma cells and neutrophils. Emperipolesis (inflammatory cells within the histiocytes) was seen

(Fig. 3). No mitotic activity was appreciated. Immunohistochemical stains showed that the histiocytic cells were positive for S100, CD68 and CD45 and negative for cytokeratins, CD1a, ALK1, CD30, and Melan A. The findings were similar to those seen on the mediastinal mass biopsy (Fig. 4) and a diagnosis of Rosai-Dorfman disease was made.

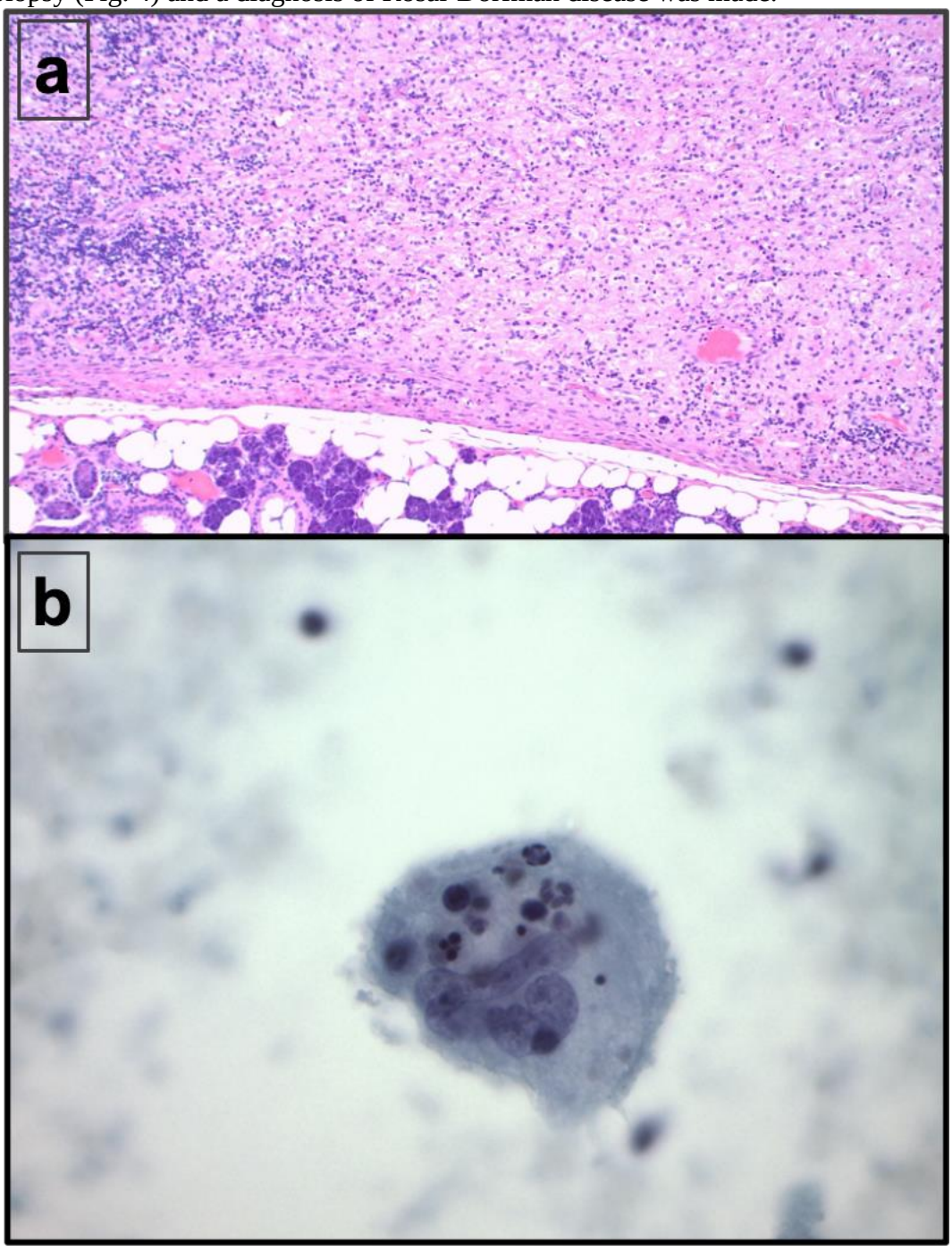

Figure 3: H&E of the parotid mass: A: low power (x200) and B: high power (x1000) showing emperipolesis.

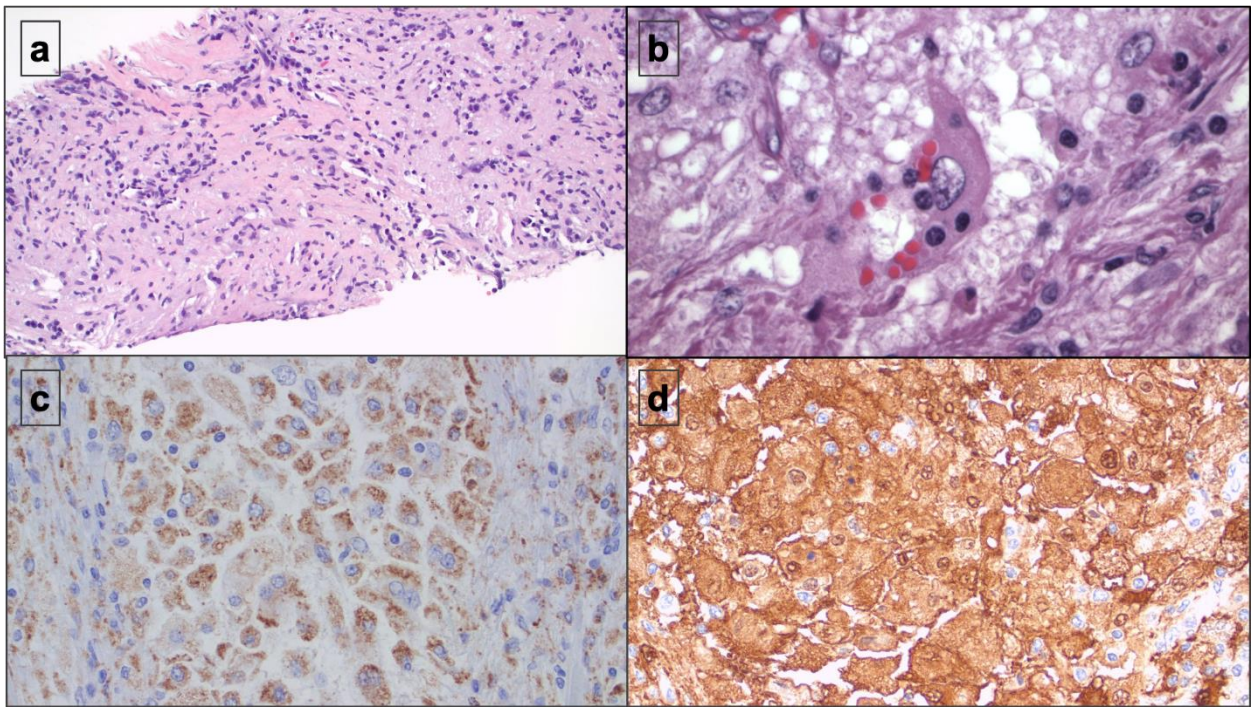

Figure 4: A: H&E (x200) of the mediastinal mass showing fibrosis and mixed lymphohistiocytic inflammation, B: H&E (x400) of the mediastinal mass showing mixed inflammation and emperipolesis, C: Immunohistochemical stain CD68 staining the macrophages (x400) and D: Immunohistochemical stain S100 staining the macrophages (x400).

The patient developed a neck collection in the immediate postoperative period at the surgical site which has been successfully treated with IV and oral antibiotics. No other complications were encountered. Follow up CT scan of the chest with IV contrast was performed at 9 months from the initial CT scan of the neck and demonstrated no significant interval changes in the size and appearance of the anterior mediastinal mass. There was no fat plane between this mass and the anterior pericardium which was suspicious for direct invasion. The mass was abutting the posterior cortex of the sternum with associated cortical irregularity in keeping with direct invasion (Fig. 2). There was no invasion of the heart or the great thoracic vessels.

Discussion

Rosai-Dorfman Disease was first described in 1969 by Juan Rosai and Ronald Dorfman.[5] It is also known as Sinus Histiocytosis with Massive Lymphadenopathy (SHML). RDD is a rare self-limiting non-malignant disorder manifested by abnormal histiocytic/phagocytic cell proliferation.[6] The etiology of RDD is not yet known, however, various factors are thought to play a role in its development. Those factors include autoimmune diseases and viruses such as human herpes virus 6 and Epstein-Barr virus.[3]

Painless enlargement of the cervical lymph nodes in children and young adults is the commonest presentation of the disease. It can also present in other clinical forms and may affect patients of any age groups. Lymph nodes in different body regions other than the neck can be affected. It is

reported that up to 43% of the patients with RDD may have extranodal involvement. In up to 23% of the patients, the disease is exclusively extranodal and the commonest sites include skin, central nervous system, bones, soft tissues, upper respiratory tracts and salivary glands.[6,7] Our patient presented with a slowly growing painless left parotid swelling. Despite its benign nature, RDD could be locally aggressive mimicking malignant diseases.

The disease has no specific radiological features and most frequently the diagnosis is made on pathology. On imaging, the disease may present with findings similar to other conditions like infectious/inflammatory diseases and neoplasms. Therefore, the initial differential diagnosis is wide and includes tuberculosis, histiocytosis, Castleman disease, granulomatosis with polyangiitis, sarcoidosis, lymphoma, Kaposi sarcoma, carcinoma, metastases and malignant histiocytoses.[3] The clinical history is important in determining the likely diagnosis from those differential diagnoses. For example, infectious lymphadenitis is usually painful and presents acutely. Patients with granulomatosis with polyangiitis, sarcoidosis, lymphoma and metastasis are most frequently demonstrating other features of the disease with involvement of other organs. Patients with Kaposi sarcoma are usually known to have retroviral infection at time of presentation and may demonstrate clinical or radiological involvement of the skin, gastrointestinal or respiratory systems. The radiological investigations of choice include ultrasound (US), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) which are mainly used for detection and characterization of the lesions. The US and CT are also useful for biopsy guidance and for follow up to ensure stability and response to therapy.[3]

Depending on the site of involvement, the radiological findings are variable. For clinically palpable lesions, US is usually enough for the initial workup. However, CT scan is frequently utilized for assessment of disease extent in different body parts. On CT, the lesions are usually lobulated with smooth contours and demonstrate mild homogeneous enhancement. The mass may be locally aggressive and demonstrates invasion of adjacent structures similar to our case where the thymic mass demonstrated pericardial invasion and cortical destruction of the sternum. To our knowledge, there are less than 3 reported cases of thymic RDD without lymphadenopathy elsewhere and among those, our case is unique in the presence of local aggressive features manifested by direct invasion of the pericardium and cortical destruction of the sternum.

Whole body MRI is usually utilized in assessment of disease extent in children and younger patients to avoid excess radiation exposure. The findings on MRI are non-specific and do not usually help in the differentiation from other lesions. The most common findings are isointense T1 signal and hyperintense T2 signal with mild diffusion restriction and low ADC map.[4] The degree of diffusion restriction usually decreases with treatment or spontaneous disease regression. The lesions usually demonstrate avid fluorodeoxyglucose (FDG) uptake on Positron Emission Tomography (PET-CT) which is also useful in monitoring treatment response and disease remission. However, there is increased radiation dose to the patients if the PET-CT is performed for follow up.

On pathology, expansion of sinuses with histiocytes and plasma cells along with lymphophagocytosis or emperipolesis is a characteristic feature of RDD. Normal red blood cells (RBCs), lymphocytes or plasma cells are observed within the cytoplasm of histiocytes. However, emperipolesis is not entirely pathognomonic of RDD and it can be seen in other conditions. If

present, it is more commonly seen in nodal RDD.[6] The positivity of S100 immunomarker is a helpful indicator for RDD in addition to positivity to other markers including CD68, CD14, CD15, CD163 and α-1-antichymotrypsin. CD1a and factor XIIIa immunomarkers are usually negative.[6,8]

The treatment of RDD is controversial due to the rarity of the disease and variable clinical courses and outcomes. The treatment is usually individualized according to the clinical setting. In up to half of the patients with RDD, there has been spontaneous disease resolution.[9] The disease usually has a favourable prognosis with median survival of more than 5 years after diagnosis even in cases where there is extranodal involvement. Corticosteroids are usually used for patients in whom spontaneous response is not observed or where the disease is progressive. However, it has not been documented that corticosteroids are useful for treatment. [9] For localized disease, surgery is usually curative. Radiation with or without chemotherapy have been used in patients who demonstrate disease progression despite steroid therapy. [9]

Conclusion

RDD or SHML is a benign proliferative disorder of unknown etiology and has a wide clinical and radiological manifestations but typically presents as painless enlarged cervical lymph nodes. Here, we described a case of simultaneous involvement of the parotid gland and the thymus associated with sternal invasion. Despite its benign nature, RDD can be locally aggressive and may be confused with malignant conditions. It usually has a good prognosis.

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