Case Report

Extranodal Sinonasal Rosai-Dorfman Disease-A Rare Entity

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Abstract

Rosai-Dorfman disease is a distinct non-malignant clinicopathological entity involving both nodal and extranodal tissue. Its clinical presentation can mimic other benign and malignant lesions. We report a lady presented with sinonasal mass suspicious of malignancy. Various investigation modalities were employed to achieve the diagnosis. She was managed conservatively and remained well. This report serves to highlight such rare clinical entity which follows a significantly different natural course than malignant disease despite sharing similar initial presentation.

Keywords: Rosai-Dorfman disease; extranodal tissue; lymphadenopathy

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Introduction

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a distinct clinicopathological entity involving both nodal and extra nodal tissues. Originally described by Destombes in year 1965, but only formally characterised by Rosai and Dorfman in year 1969, it is a non-malignant disorder mimicking malignant conditions by virtue of confusing clinical presentations to the inexperienced clinicians unfamiliar with the entity, owing partly to its rarity and lack of comprehensive scientific understandings of the disease itself. We present an unusual presentation of this unusual disorder.

Case Report

A 54 years old lady, with underlying hypertension, presented with right nasal blockage with intermittent sneezing for 1 year. It was associated with right-sided throbbing headache for the same duration for 4-5 times per week, with each episode lasted for few hours, requiring regular oral analgesics. She was otherwise well with no other otological or ocular symptoms, epistaxis, and neurological deficit. She was also free from constitutional symptoms. On examination she had no external nasal deformity, and anterior rhinoscopy showed no abnormal intranasal mass. Ear examination and Intraoral was unremarkable. There was no abnormal neck mass or palpable cervical

lymphadenopathy. Other systemic examinations were unremarkable. Rigid nasoendoscopy showed a mass occupying the space between right middle turbinate and nasal septum with adenoid hypertrophy. The nasopharyngeal clefts were symmetrical and the Eustachian tube openings were normal. First biopsy of the right nasal mass showed inflamed granulation tissue, while a repeat biopsy reported chronic inflammatory process. However, a contrast-enhanced computed tomogram (CECT) of paranasal sinuses reported a soft tissue mass within the sphenoid sinus, ethmoidal air cells, nasopharynx and left middle ear cavity and external ear which was associated with bony destruction of central skull base affecting basisphenoid, clivus, basiocciput and petrous apex (FIG 1). Laboratory investigations done and reported normal blood counts with no blast cells seen in peripheral blood film, raised erythrocyte sedimentation rate (ESR) of 54mm/hour and slightly-raised serum immunoglobulin G at 18.03 g/L (reference range 7-16). Other autoimmune screenings including RPR, VDRL, rheumatoid factor and anti-nuclear antibodies were non-reactive. Her liver function tests were all within normal range.

In view of the locally-aggressive features shown in imagings, she underwent an examination under anesthesia with biopsy of right nasal mass.

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Intraoperative findings showed thick left middle ear effusion, and a friable mass with contact bleeding arising from sphenothmoidal region and extending posteriorly to the right nasopharynx. The anterior bony sphenoid surface was exposed. Large generous tissue biopsy was taken from the right nasal cavity mass and right nasopharynx, with both specimen reported as showing chronic histiocytic inflammation in favour of Rosai-Dorfman Disease (FIG 2a & 2b)

She was managed conservatively, with follow-up repeat nasoendoscopy in clinic four months post-diagnosis showed the mass within the nasal cavity had reduced remarkably in size (FIG 3). She was clinically well with almost total resolution of her nasal symptoms.

Discussion

RDD is a disease of non-malignant histiocytes infiltrating lymph nodes (predominantly in the

Figure 1: Axial view computed tomography of paranasal sinus showing heterogeneously-enhanced mass occupying right sphenoid and ethmoid with local bony erosion.

Figure 2: Histopathological examination (H&E stain, high power) showed emperipolesis of lymphocytes and erythrocytes by macrophage.

Figure 3: CD68 staining positive demonstrated for the RDD histiocytes

Figure 4: Nasoendoscopy on right nasal cavity showing small residual mass with minimal mucosal adhesions

head and neck) and a variety of extranodal tissues, commonly including skin and soft tissue, central nervous system (CNS), and less commonly, gastrointestinal tract (GIT)¹. Typical presentation of RDD include fever, leucocytosis, and non-painful cervical lymphadenopathy, mimicking presentation of lymphoma, commonly in second and third decades of life with male gender predominance. Night sweats and weight loss can occur, as well as painless maculopapular skin eruptions are reported in literature. However, our reported patient presented atypically in the sense of painless suspicious mass at extranodal site with demographic difference, showing that this entity should be included in consideration of differential diagnoses.

While it is vital to differentiate RDD from malignant counterparts such as lymphoma and Langerhans cell histiocytosis, all patients with clinical suspicion of RDD should be worked up

with detailed history and comprehensive physical examination as would be performed for any patient presenting with unexplained adenopathy or mass suspicious of neoplasm. The list of differential diagnoses for RDD is expectedly long; benign etiologies include tuberculosis, Wegener's granulomatosis, sarcoidosis, IgG4-related disease, juvenile xanthogranuloma, glycogen storage disease and other histiocytic disorders such as Langerhans cell histiocytosis, and malignant etiologies include lymphoma, melanoma, leukaemia and Langerhans cell sarcoma. The patient we reported above was clinically suspected for malignant sinonasal lesions such as nasopharyngeal carcinoma and sinonasal squamous cell carcinoma.

Laboratory workup should include baseline haematological and biochemistry tests, in addition to serological viral screening for Epstein-Barr virus (EBV), cytomegalovirus (CMV), HHV-6, HHV-8 and HIV. Suggestive features include elevated erythrocyte sedimentation rate (ESR), polyclonal hypergammaglobulinaemia with reversal of albumin:globulin ratio, leucocytosis with neutrophilia, normochromic normocytic anaemia, positive rheumatoid factor or antinuclear antibody value. RDD is rarely associated with haemolytic anaemia and eosinophilia, which may be useful to guide provisional diagnosis from other similar entities. Bone marrow biopsy may be more useful to exclude other haematological dyscrasias but has unclear role in diagnosis of RDD itself. Imaging modalities such as contrasted computed tomography (CECT) of the neck, chest, abdomen and pelvis can be employed to stage the disease. RDD can cause sclerotic bone lesions but rarely associated with osteolytic bone lesions as seen in Langerhans cell histiocytosis or other malignant entities. The role of MRI is unclear but is generally reserved for assessment of intracranial lesions.

Excisional biopsy ideally should be performed to obtain adequate tissue for histopathological examination (HPE). RDD cells typically exhibit hallmark feature of emperipolesis, which is non-destructive phagocytosis of lymphocytes or erythrocytes. Other findings include (i) distortion of normal lymph node architecture due to massive sinusoidal dilation by histiocytes, lymphocytes, and plasma cells, (ii) reactive lymphoid follicles in the cortex of lymph nodes, (iii) increased plasma cells

in the medullary region, (iv) occasional lipid-laden macrophages. For extranodal EDD, lymph node structure features are absent, for obvious reasons, but fibrosis is more while histiocytes showing emperipolesis are fewer in numbers, making this diagnostic feature less easily picked up for definite diagnosis. Nonetheless, RDD histiocytes are morphologically distinct from Langerhans cell histiocytosis and interdigitating dendritic cells. When in doubt, immunohistochemical stains may be helpful, as RDD histiocytes stains positive for CD68 (KP-1), CD163, and S100; and typically negative for CD1a. In the most ambiguous of cases, BRAF V600E mutations in the setting of RDD are negative, unlike for Langerhans cell histiocytosis, and can help differentiate these two entities in equivocal cases.

Once pathological confirmation of RDD is obtained, further management strategy is usually conservative in view of RDD is non-malignant in nature. RDD is reported to be usually self-limiting and eventually recedes, with spontaneous regression in 20% of cases¹, making aggressive systemic therapy rarely warranted. However, definite treatment is needed in symptomatic patients due to tumour compression such as upper airway obstruction, or vital organ involvement such as CNS disease. These patients usually benefit from surgical excision of the mass, with expected morbidity depending on surgical approach employed. Prolonged disease-free duration after complete excision is the rule, although persistent symptoms after incomplete resection may be further treated with external beam radiotherapy, stereotactic radiotherapy, or any of a variety of systemic therapeutic medications. Corticosteroids are a reasonable first-line treatment option in both classical nodal RDD and extranodal disease, reserving other options with limited usefulness data such as rituximab, interferons, chemotherapy agents for second-line treatment. As with any other rare clinical entities, data on the efficacy of systemic therapy in RDD are limited and therefore cases of RDD should be referred to tertiary care centers for treatment of refractory or widespread disease. Surveillance of patients should be of those employed for lymphoma cases, namely close follow-up for the first two years of 'watch-and-wait' policy after diagnosis,

or complete remission after definitive treatment. Follow-up with 6-monthly examination and laboratory investigation, plus imaging modalities as clinically indicated, would be a sensible strategy to assess for possible relapses and/or treatment-related morbidities. Our patient was thus managed conservatively on this basis.

Conclusion

RDD is a benign histiocytic disorder with locally-enlarging painless mass mimicking malignant lesions. A high degree of suspicion aided by various investigational tools can help

to differentiate it from the exhaustive list of differential diagnoses. Tissue biopsy for HPE can demonstrate emperipolesis in the histiocytes, with or without immunohistochemistry staining positive for S100 and CD68 while negative for CD1a. Most patients with RDD will not require further treatment as spontaneous regression is expected. Healthcare professionals are urged to maintain clinical suspicion for such clinical entity as the therapeutic management differs significantly from malignant lesion otherwise suspected.

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