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Clinical Record

# Polypoid intranasal mass caused by Rosai–Dorfman disease: a diagnostic pitfall

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**Abstract**

Background: Rosai–Dorfman disease is a rare, idiopathic, histiocytic proliferative disorder with a distinctive microscopic appearance, which was formerly thought to be a disease process limited to lymph nodes. However, extranodal involvement has been documented in less than half of the reported patients, but rarely without associated lymphadenopathy.

Case report: We report the case of a 43-year-old Senegalese woman who presented with a polypoid, intranasal mass caused by Rosai–Dorfman disease. A diagnosis of a granulomatous process, including rhinoscleroma, was initially discussed. The correct diagnosis was made histologically by demonstrating aggregates of histiocytes with large amounts of cytoplasm, emperipolesis and protein S100 antigen expression. Despite using ancillary methods (molecular biology and electron microscopy), we failed to demonstrate any associated pathogen.

Conclusion: Diagnosis of Rosai–Dorfman disease can be very difficult, in particular in adults from Africa with pure, isolated, intranasal localisation, in whom clinical and radiological features may mimic other infectious or neoplastic disorders. The diagnosis is made based on the histological presence of large histiocytes with lymphophagocytosis. Moreover, immunohistochemical analysis of these histiocytes using anti-protein S100 antibody shows strong positivity.

**Key words: Rosai-Dorfman Disease; Nasal Polyp; Paranasal Sinuses**

## Introduction

Inflammatory and infectious diseases may have various rhinosinusal granulomatous findings as part of the disease state (as may neoplasms), particularly in patients from certain geographic regions such as Africa. The otorhinolaryngologist must be aware of the differential diagnosis of such inflammatory states, in order to formulate optimal evaluation and ongoing management for these patients.

One of these conditions, Rosai–Dorfman disease (i.e. sinus histiocytosis with massive lymphadenopathy) is a rare disorder which usually occurs within lymph node sinuses in children, and which is characterised by non-malignant proliferation of distinctive histiocytic cells.[1–3] Extranodal Rosai–Dorfman disease is documented in less than half of reported patients, but rarely without associated lymphadenopathy, which may develop later in the course of the disease.[2,3] Almost every organ system can be affected, isolated from or associated with immunological disorders.[2,3] The diagnosis of Rosai–Dorfman disease can be difficult in an adult with pure, isolated extranodal localisations, in whom clinical and radiological features may mimic chronic granulomatous infectious diseases and malignant neoplasms.

We report an adult patient from Africa who presented with an isolated, intranasal, polypoid mass caused by Rosai–Dorfman disease, and for whom the diagnosis of another granulomatous process, in particular rhinoscleroma, was initially discussed.

## Case report

A 43-year-old Senegalese woman presented with progressive left nasal obstruction, epistaxis and pain. She was a smoker and was human immunodeficiency virus (HIV) seronegative. Her symptoms had worsened progressively over the previous six months.

The patient's past history included lung tuberculosis and, one year prior to the current presentation, endoscopic sinus surgery for a polypoid mass of the left nasal cavity. Histopathological examination of the latter mass had shown granulomatous inflammation with associated giant cells, numerous plasmocytes and a few large, 'foamy' histiocytes. An infectious aetiology had been discussed, but various serodiagnostic and microbiological cultures (in particular to detect for infection by treponema, bartonella, yersinia, pasteurella, klebsiella and mycobacteria species) and tissue staining methods (i.e. Giemsa, Zielh-Neelsen, periodic acid Schiff, Gram, Warthin-Starry and Gomori-Grocott) had been negative. However, despite a negative tissue culture, a diagnosis of a chronic granulomatous disease probably caused by *Klebsiella rhinoscleromatis* had been made, since numerous large, foamy histiocytes similar to Mikulicz cells were noted, associated with plasma cells with Russell bodies. Therapy with tetracycline and steroids had then been commenced.

One year later, the patient was admitted to hospital with recurrent left nasal obstruction. No cervical lymph nodes were palpable.

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A chest X-ray and biological tests were normal. Rhinoscopy showed a large mass in the left nasal cavity, partially involving the maxillary sinus. This polypoid mass was grey-white, firm and partially ulcerated. A computed tomography (CT) scan revealed an infiltrating, extensive soft tissue tumour occupying the left nasal cavity and left maxillary sinus, with septal deviation (Figure 1).

Several diagnoses were considered, particularly non-Hodgkin lymphoma, carcinoma and recurrent rhinoscleroma. Chest and abdominal CT scans showed no other localisations.

A large biopsy of the nasal lesion was performed. The specimen consisted of a $5 \times 4 \times 4$ cm mass. A diagnosis of a lymphoid lesion rich in histiocytes, without malignancy, was made from the frozen section.

After formaldehyde fixation, tissue sections stained with haematoxylin and eosin showed diffuse, granulomatous infiltration without any signs of a proliferation disorder. Sinusal mucosa showed a dense inflammatory cell infiltrate and slight epithelial hyperplasia with partial squamous metaplasia. The infiltrate was partially associated with fibrous septae, and comprised numerous types of lymphoplasmacytic cells in an oedematous stroma mixed with aggregates of histiocytes. These histiocytes had a large amount of clear, foamy cytoplasm. Some of these foamy histiocytes resembled the 'clear' cells seen in rhinoscleroma. However, histiocytes with lymphophagocytosis were frequently seen (Figure 2). Moreover, lymphoid follicles and neutrophil infiltrates with small necrotic areas were observed. Most of the blood vessels were normal, without inflammatory lesions.

Various stains were used (Giemsa, Gram, Gomori-Grocott, periodic acid Schiff, Ziehl-Neelsen and Warthin-Starry) but no microorganisms could be identified.

On immunohistochemical analysis, the different histiocytes stained for cluster of differentiation 68 glycoprotein and protein S100 (Figure 3), confirming the diagnosis of Rosai–Dorfman disease.

A bacterial, mycotic or parasitic infection was ruled out since all tissue specimen cultures were negative.

Analyses for human herpes virus 6, human herpes virus 8, Epstein-Barr virus (EBV) and cytomegalovirus (CMV) were performed with frozen specimens using the polymerase chain reaction and amplimer detection techniques. Ten tissue sections of 10 μm thickness were cut from specimens of frozen nasal lesions. We used the plasmid pZH14 (containing an 8.7 kb portion of the human herpes virus 6 genome), the latency-associated nuclear antigen (ORF73) of human herpes virus 8, the BamHI W fragment of EBV, and a cloned CMV fragment (Digene, College Park, Maryland, USA) to test for human herpes viruses 6 and 8, EBV and CMV, respectively. We detected no DNA for human herpes viruses 6 or 8, or for EBV or CMV. Immunohistochemical analysis with the monoclonal mouse anti-B19 VP1/VP2 antibody R92F6 (Novocastra, Newcastle upon Tyne, UK) was negative.

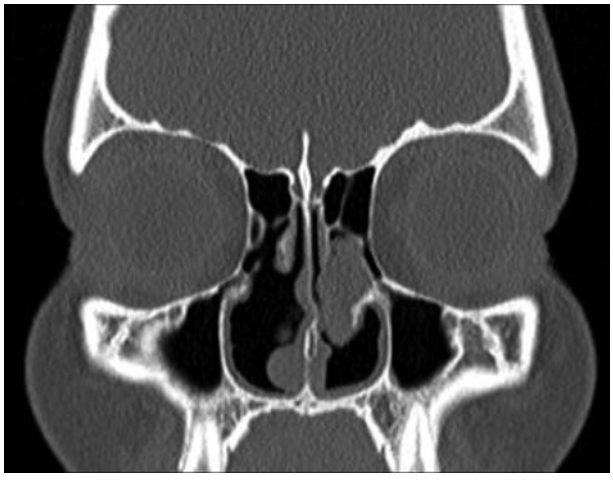

FIG. 1

Coronal computed tomography scan showing a mass of soft tissue occupying the left nasal cavity.

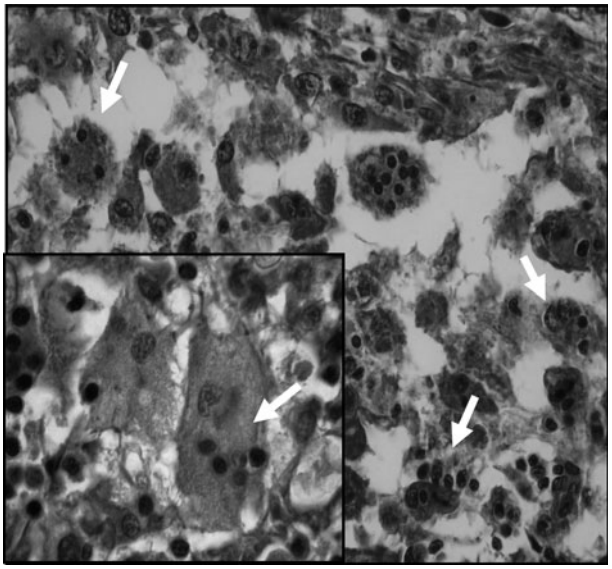

FIG. 2

Photomicrograph showing an aggregate of histiocytes with a large amount of cytoplasm and emperipolesis (arrows) (H&E; ×320). Inset shows histiocytes demonstrating lymphophagocytosis (arrow) (H&E; ×1000).

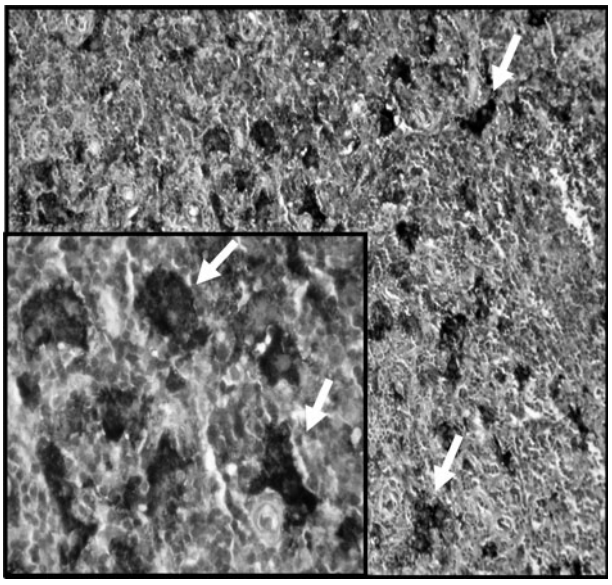

FIG. 3

Photomicrograph of immunohistochemical analysis with anti-protein-S100 antibody, showing numerous positive cells (arrows) (Immunoperoxidase; ×200). (Inset: immunoperoxidase; ×800)

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Finally, electron microscopy performed on a specimen fixed in glutaraldehyde showed no evidence of bacterial or viral particles in the cytoplasm or nuclei of histiocytes.

Two years after complete surgical resection, the patient was doing well. She had undergone no other associated therapy.

## Discussion

Extranodal Rosai–Dorfman disease with no associated lymph node involvement is a very rare disorder.[3] Any organ can be involved, but the most affected extranodal sites include the skin and soft issues.[3] The upper respiratory tract and head and neck can also be affected, mostly in children but also, very rarely, in adults.[4–13]

In patients originating from tropical areas, particularly Africa, the differential diagnosis includes numerous bacterial, fungal and protozoal infections, vasculitis, and neoplastic processes affecting the upper airways.

In the present case, the differential diagnosis included rhinoscleroma, a chronic, progressive, granulomatous infectious disease which can be diagnosed in the upper airway of patients from Africa. Distinguishing between this condition and Rosai–Dorfman disease presented a challenge.[14] Moreover, rhinoscleroma has been found to be associated with Rosai–Dorfman disease in exceptional cases, suggesting a possible relationship between the two diseases in certain patients.[15] Rhinoscleroma is a chronic granulomatous disease of the upper respiratory tract caused by *Klebsiella rhinoscleromatis*.[16] This diagnosis is especially crucial to exclude in small, superficial biopsies in which the presence of extensive squamous hyperplasia could potentially lead to a false negative diagnosis. Long-term use of antimicrobials is important as the disease has a high relapse rate.[16] Moreover, biopsies of the fibrotic stage may be quite non-specific, and cultures are positive in only 50–60 per cent of cases. In our case, the presence of large histiocytes with lymphophagocytosis, and the negative results for Gram staining, cultures and electron microscopic study, allowed us to eliminate a diagnosis of rhinoscleroma.

- **Rosai–Dorfman disease is a rare disorder which usually occurs within lymph node sinuses in children; it is characterised by non-malignant proliferation of distinctive histiocytic cells**
- **This paper describes an adult patient from Africa who presented with an isolated, intranasal, polypoid mass caused by Rosai–Dorfman disease; a diagnosis of other granulomatous processes, in particular rhinoscleroma, was initially considered**
- **Treatment in this case was by surgical excision**

The histogenesis of the proliferative cells seen in Rosai–Dorfman disease is uncertain, but they have features of both Langerhans cells and phagocytes.[1,2] Rosai–Dorfman disease cells express the S100 protein, as do Langerhans cells, but also have regular nuclei and show prominent phagocytosis, in contrast to Langerhans cells. It has therefore been suggested that Rosai–Dorfman disease cells are functionally activated macrophages, and that prominent phagocytosis may result from the presence of an infective agent, viruses in particular.[1,2] Although there is some evidence of an association with human herpes virus 6 and HIV, the pathogenic mechanism of Rosai–Dorfman disease is still unclear.[2,17,18]

Finally, in the present case we failed to detect any associated infectious agent, despite the use of ancillary investigation methods.

## Conclusion

The diagnosis of isolated, intranasal Rosai–Dorfman disease, in particular in an adult patient from geographical regions such as Africa, ultimately requires a high index of suspicion together with clinicopathological correlation. Before making a final diagnosis, it is important to take an accurate history and to perform a thorough physical examination, imaging studies and large biopsies, in order to eliminate other causes of granulomatous processes, in particular infectious disorders which frequently occur in such patients.

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