CASE REPORT

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Nasal and paranasal sinus manifestation of Rosai-Dorfman disease*

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SUMMARY

Rosai-Dorfman disease is a rare, idiopathic, benign, histiocytic proliferation usually seen in younger patients. Most commonly neck lymph nodes are involved with a predominant infiltration of sinusoidal histiocytes. Nearly half of the patients have extranodal manifestation. Two cases of Rosai-Dorfman disease involving the nose and the paranasal sinuses are presented. The clinical presentation, radiographic findings, treatment and histological characteristics of the disease are discussed.

Key words: Rosai-Dorfman disease, nose, histiocytosis, lymphadenopathy

INTRODUCTION

Rosai-Dorfman disease is also known as sinus histiocytosis with massive lymphadenopathy (SHML). It was first described in 1969, by Rosai and Dorfman [1]. It is a non-neoplastic lymphoproliferative disease that is usually characterised by bilateral painless lymph node enlargement of the neck, fever, leucocytosis, raised erythrocyte sedimentation rate and polyclonal hypergammaglobulinaemia. The disease develops most frequently in the first and second decades of life. Involvement of lymph nodes other than neck lymph nodes is rarely observed. In approximately 30-43 % extranodal manifestations are seen, 75% of which occur in the region of the head and neck [2, 3]. Histological features of the disease include marked proliferation of sinus histiocytes, which often contain phagocytosed lymphocytes (emperipolesis) [1]. To date, no specific cause of the disease has been found. It is speculated that its pathogenesis could be an as yet unidentified infectious agent or possibly also an altered immune response. The disease typically begins insidiously, with a protracted active disease phase and occasionally spontaneous remission, and, in some cases, is followed by several recurrences [1, 4, 5].

We describe two cases of Rosai-Dorfman disease with extranodal involvement in the region of the nasal cavity and the paranasal sinuses and discuss the different treatment possibilities.

Case 1

A 38-year-old male patient complained of nose obstruction, posterior rhinorrhoea and rhinophonia clausa. He had occasionally noted blood-streaked nasal secretion. In addition, there had been frontal headaches of varying severity. He had suffered from bilateral nasal polyps since the childhood which had not been further investigated. For the first few years at the age of 20, the polyps had responded to oral steroids. The installation of topical steroids during the last years has not changed the situation. Additionaly the patient suffered of intermittent bilateral knee pain related to exercise since three years. On examination, endoscopy of the nose showed bilateral nasal polyps with nearly complete obstruction of the nasal lumen (Figure 1). Macroscopically the polyps were yellowish, coarse and fibrous and showed minimal bleeding on biopsy. Further ENT examina-

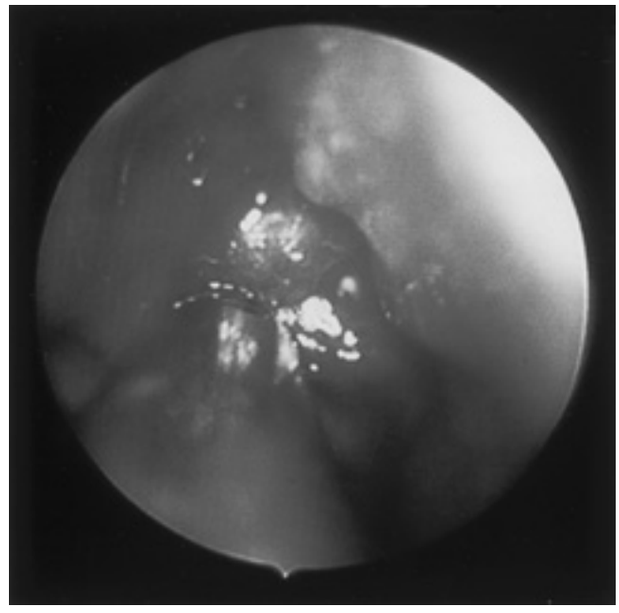

Figure 1. Nasal polypoid masses (arrow) in Rosai-Dorfman-disease visible on the endoscopic view.

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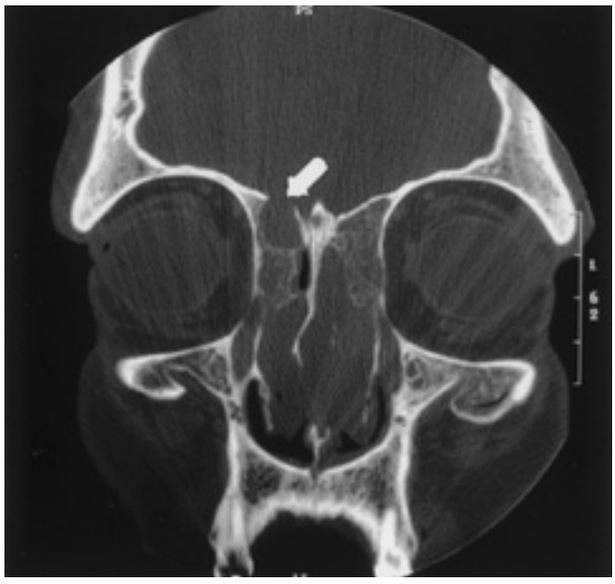

Figure 2. Coronal CT-scan showing subtotal obstruction of the nose due to soft-tissue and a mucocele of the ethmoid with a virtual defect of the frontal skull base (arrow).

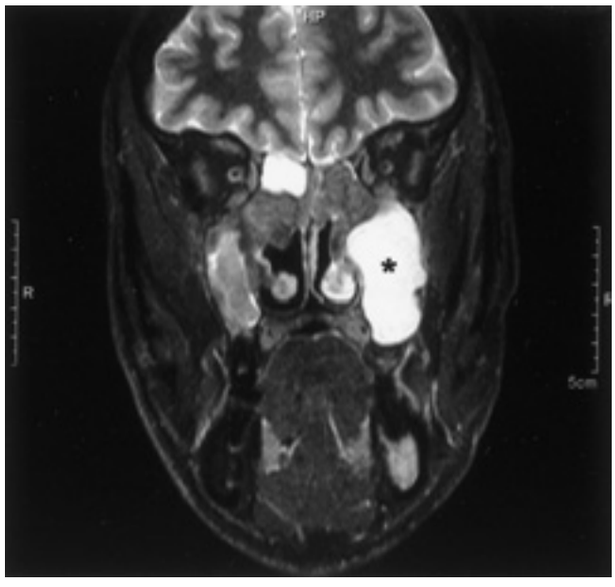

Figure 3. MRI in T2 showing a hyperintense signal (mucocele) in the right ethmoid and the left maxillary sinus (asterix).

tion was unremarkable; in particular there were no enlarged neck lymph nodes. Computed tomography (CT) and magnetic resonance imaging (MRI) of the skull revealed soft tissue dense obstruction of the entire paranasal sinuses and nasal cavity with osteolytic changes in the ethmoidal cells bilaterally, with a virtual defect of the bony skull base because of a mucocele (Figures 2, 3). Both CT and MRI showed neck lymph nodes, reaching a maximum of 7 mm in size, at the level II and III bilaterally. Further radiological examination showed osteolysis in both tibiae. Laboratory blood examinations revealed a slightly raised C-reactive protein (CRP) of 12 mg/l and a leucocytosis of 11.2 x 109/l. Histologically, the biopsy of the nasal polyps showed polypoid soft tissue covered with ciliated epithelium, well-structured lymph follicles and well-developed germinal centres. In addition, there was a perivascular infiltrate composed of densely packed plasma cells. Overall, the picture showed loose connective tissue with numerous macrophages with partially vacuolated cytoplasm and isolated giant cells of the foreign body type. The giant cells showed focal intracytoplasmic accumulation of nuclear debris and lymphocytes (emperipolesis) which is characteristic for Rosai-Dorfman-disease (Figures 4a, 4b). Immunohistochemical examination showed intense immune reactivity of the histiocytes/macrophages to S-100 protein. No malignant neoplastic tissue was detected. Biopsies taken from the proximal tibia lesions

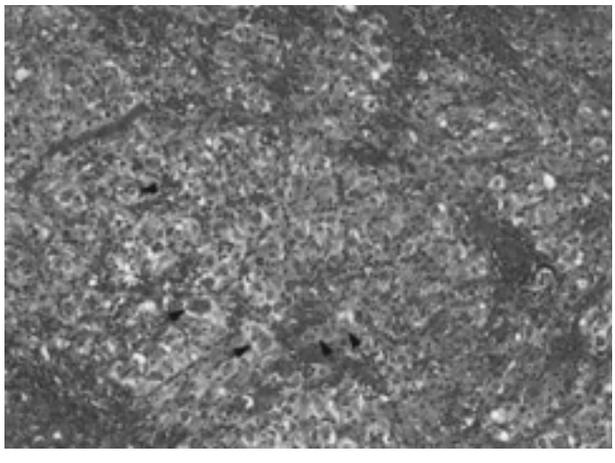

Figure 4a. Histology of nasal polyp showing loose connective tissue with perivascular infiltrate composed of densely packed plasma cells, lymphocytes and macrophages with partially vacuolated cytoplasm and isolated giant cells with intracytoplasmic accumulation of lymphocytes (emperipolesis) (arrows); HE 10x.

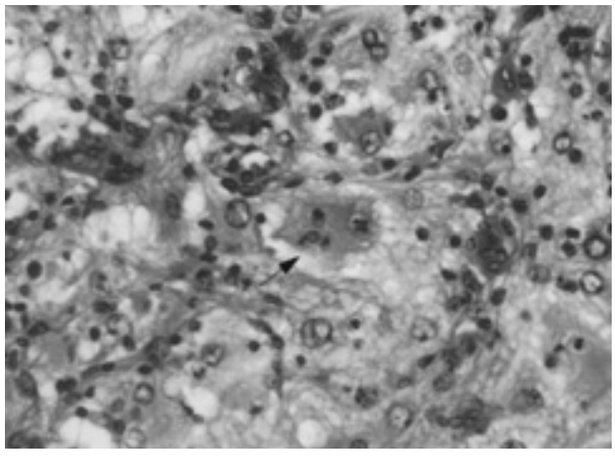

Figure 4b. Giant cell with intracytoplasmic accumulation of nuclear debris and lymphocytes (arrow); HE 40x.

also showed the characteristic histology of Rosai-Dorfman-disease. With systemic steroid therapy starting with 50 mg prednisone/day and tapering of the dose over three months, there was a clear decrease of the pain in the region of the knee without further progression of the osteolysis in this area. The nasal tumour and the nasal symptoms showed no effect to the application of steroids. Therefore in order to prevent a defect of the frontobasis, endonasal tumour debulking was undertaken (Figure 1). During operation the tumour occurred to be only little harder than normal nasal polyps. The boarder to the surrounding tissue was clearly marked within the nasal cavity and no unusual strong bleeding occurred. The multidisciplinary tumour board subsequently decided that fractionated low-dose radiotherapy was indicated because steroids had not achieved any improvement of the nasal symptoms, and this was given in the region of the paranasal sinuses with a total dose of 20 Gy. During the last 18 months there was no further progression of the disease and the patient remained almost free of symptoms.

Case 2

A 54-year-old male patient complained of a several months' history of rhinitis and increasing obstruction of nose breathing on the left. He also had an intermittent feeling of pressure over the left maxillary sinus with yellowish-green rhinorrhoea. Inspection showed an extensive coarse, yellowish polyp-like space-occupying lesion in the left nasal cavity. The remainder of the ENT examination was unremarkable. No enlarged lymph nodes could be found. Polypoid cushions of tissue in the nose were excised on several visits, mainly on the left side, in order to improve nose breathing. On each occasion, the histology showed loose connective tissue with strikingly large histiocytes with aggregates of lymphocytes and nuclear debris in the cytoplasm (emperipolesis) which is characteristic for Rosai-Dorfman disease. The only remarkable finding on laboratory blood examinations was a raised CRP, at 87mg/l, and a discrete polyclonal hypergamma-globulinaemia. No further conservative treatment was installed. Two years after the diagnosis had been made, the patient had intermittent pain in the area of the maxillary sinuses and purulent rhinorrhoea, as well as bilateral cervical lymphadenopathy. Radiological investigations with CT and MRI revealed a subtotal obstruction of the osteomeatal complex bilaterally (Figure 5). Functional endoscopic sinus surgery was performed. As in the case described above we found a tumor of a consistence little harder than normal nasal polyps, showing a clearly marked boarder towards the surrounding mucosa. No unusual bleeding occurred from the lesion during surgery. Histology again confirmed Rosai-Dorfman disease. In view of the patient's good general condition after surgery, no further systemic therapy was decided.

After a three-year symptom-free period, the patient again developed increasing nasal obstruction, accompanied by intermittent symptoms involving the anterior ethmoid bilaterally. Because of the progression, systemic steroid therapy (prednisone 100 mg/day tapering the dose over 2 months) was then started. A few weeks later, the patient was symptom-free for nasal breathing, and the neck lymph nodes also showed a clear reduction in size. After the prednisone had been stopped, there was once more progression of nose symptoms. Therefore a steroid therapy with 100 mg/day prednisone was again started for several weeks, which led to rapid regression of all symptoms. During the subsequent clinical follow-up over a period of 3 years, there was spontaneous regression of the ongoing lymph node enlargement without further treatment and the patient continued to be symptom-free.

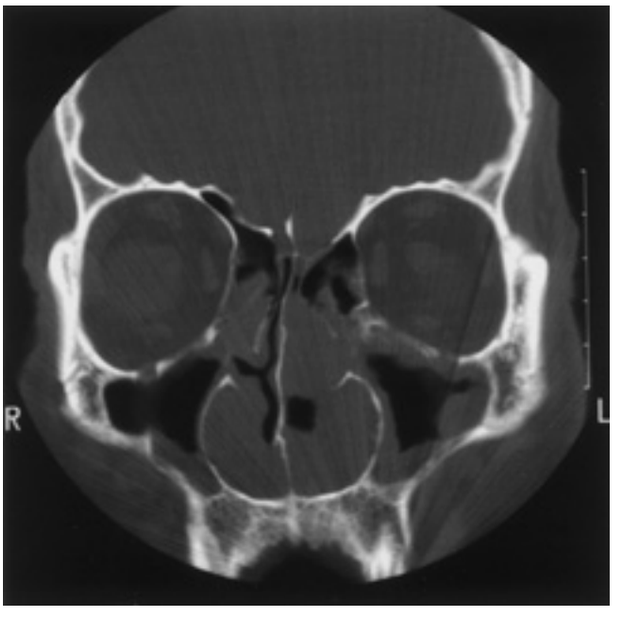

Figure 5. Coronal CT-scan from the second case showing an obstruction of the anterior ethmoid with thickness of the mucosa especially of the left maxillary sinus.

DISCUSSION

Rosai-Dorfman disease, is a rare, benign, self-limiting disease, which most commonly occurs in the first and second decades of life [2, 5]. The aetiology of the disease is still largely unknown. An association with Epstein Barr virus or herpes virus type II infections has been described in isolated cases, as well as in two cases with malignant lymphomas [2]. Although SHML was originally thought to be a disease limited to the lymph nodes with a predilection for the neck lymph nodes and having a biphasic course (slow progressive lymphadenopathy, followed months later by gradual regression), the disease was subsequently shown to be more complex. About 87% of patients show coarse, painless neck lymphadenopathy, which is usually bilateral [2]. An extranodal manifestation has been described in 43% of patients [1]; in 75% of these patients, the region of the head and neck was involved [3]. In the case of extranodal involvement of the head and neck, about 50% have a manifestation in more than one region. In 73% of cases, the upper airways are affected, in 50% the orbits and in 25% the salivary glands. The SHML occurs most commonly in child-

hood [3] which was seen in our first case with remission and progression phases of the disease until the age of 38.

Patients with involvement of the nose usually present with nasal obstruction and symptoms of rhinitis and sinusitis, as in the presented cases. Epistaxis is another related but unspecific symptom that has been described [6]. The most common examination finding in the case of nasal involvement is "polyposis", where the polyps are coarse and reddish yellow-brown; the typical oedematous, glass-like appearance is not found in this disease [6]. The disease presents itself frequently with subfebrile temperatures and there is often leucocytosis, neutrophilia, a raised erythrocyte sedimentation rate, anaemia and polyclonal hypergammaglobulinaemia [2].

Because of the nature of the disease and its self-limiting course, treatment is not necessary in a large number of patients: often the condition may be allowed to run its natural course [3, 4, 7] and surgical treatment is usually limited to removal of a "biopsy" for the purpose of histological confirmation of the diagnosis. Further surgical treatment is only needed in cases of impairment of function of affected organs in so far as function can be restored by a surgical procedure [4]. While recurrences have occurred following endoscopic nasal surgery, Ku et al. described two patients with a nasal presentation of Rosai-Dorfman disease that remained free of recurrence following endoscopic resection alone [8].

In patients with progressive symptoms, different drug treatments have been tried. Antibiotics and antitubercular drugs have not shown any significant effect [2, 9]. As also occurred in one of our cases, the use of corticosteroids has frequently resulted in a clear improvement and occasionally complete remission. In the series of Komp et al. [10] partial or complete remission of the disease was observed in 4 out of 36 patients, and an improvement in symptoms in 13 of 36 patients. The dose of corticosteroids applied, in the literature varies between 30 mg prednisolone and 150 mg. In our experience the dose of 50 mg prednisolone showed no effect to the endonasale tumor in the first case, whereas in the second case with a dose of 100 mg prednisolone the lesion responded very well to the medication and even after a slow reduction of the daily doses and stopping of the application of steroids the patient remained free of symptoms. The use of different chemotherapeutic agents has also been described. The most effective regimen combined a vinca alkaloid with an alkylating agent and a corticosteroid and achieved partial or complete remission in 7 out of 13 cases [1, 10]. Similar good results were obtained with methotrexate and 6-mercaptopurine [11]. Other substances showed much poorer results.

Radiotherapy has also been applied in some cases. In most, however, the dose of radiation used is not mentioned so that the data on this can be interpreted to only a limited extent. Partial or complete remission following radiotherapy was described in 10 out of 34 patients [4][10].

In our opinion, based on the few experience with the two cases presented, a conservative treatment should be applied first, using a high dose of prednisolone (100 mg prednisolone). In cases where steroid treatment fails within a suitable time and symptoms require further treatment, endoscopic endonasal tumor dubulking is to be considered as next step. To avoid recurrence adjuvant therapy should be considered. In patients having shown no effect to the application of steroids or when high doses of steroids cannot be applied, a low dose radio therapy might be considered, even though according to the literature the effect is not foreseeable. Otherwise an adjuvant postoperative steroid therapy as in case 2 described above might be helpful.

Reddish yellow-brown "polyps" in the nose of high dense consistence could give a clinical hint of SHML and must be considered as a rare differential diagnosis of the usual polyposis nasi. Its slightly different macroscopic aspect and the typical histological characteristics lead to the diagnosis. The need of a therapy depends on the course of the disease, but no consistent therapeutic regimen according to the literature has so far been established.

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