The Journal of Laryngology & Otology
July 2000, Vol. **114,** pp. 565–567

Rosai-Dorfman disease of the larynx

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Abstract
We present a case of an 81-year-old man with a history of worsening dysphonia of six months duration. A year before a sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) was diagnosed on a submandibular lymph node biopsy. On presentation the patient showed a mass in the left subglottic area with a modest reduction in the airway space. The patient underwent an endoscopic CO_2 laser excision of the mass, without post-operative complications. Histopathological examination and electron microscope images confirmed the previous diagnosis of Rosai-Dorfman disease. The clinical and pathological features of this entity are discussed.

Key words: Larynx; Histiocytosis; Sinus; Laser surgery

Introduction

Rosai-Dorfman disease (or sinus histiocytosis with massive lymphadenopathy, SHML) is a rare, benign proliferative disorder of histiocytes, sometime showing familiar incidence. It is characterized in the majority of cases by painless bilateral lymph node enlargement in the neck, often associated with fever, leucocytosis, and polyclonal hypergammaglobulinaemia. Moreover, other peripheral or central lymph nodes groups can be affected with, or without, cervical disease.[1,2] It presents mainly in the first or second decades of life, but any age group can be affected, especially in its extranodal form.[3] SHML should be kept in mind for differential diagnosis of neck masses, especially in childhood.[4] Although the geographic distribution is widespread, reportedly there has been a high incidence of the disease amongst black African races.

Microscopically the disease is characterized by a marked dilatation of the lymphatic sinuses that are found to contain lymphocytes, plasma-cells, and numerous histiocytes in whose cytoplasm whole lymphocytes may be found. This feature that has been described as emperipolesis or lymphocyto-phagocytosis, is important for diagnosis.[1,5] Immunohistochemically, the sinus histiocytes are strongly positive for S-100 protein and for markers of antigens associated with phagocytosis and lysosomal activity, for alpha-1-antichymotrypsin and for *Leu*-M1. The immunophenotypic profile suggests, moreover, an origin from macrophage-histiocyte cell types.[6,7] A cytogenetic analysis showed a normal prevalent clone and a small hypodiploid clone and no detectable involvement of the *c-fms* proto-oncogene was found.[7] The hypotheses formulated regarding the aetiology of the disease include a possible viral infection (Epstein Barr virus), and/or an undefined immunological alteration.

TABLE I
COMMONEST SITES OF SHML IN THE HEAD AND NECK AREA

Nasal cavity and paranasal sinuses
Orbit
Parotid and submandibular gland
Larynx
Nasopharynx
Temporal bone
Infratemporal fossa
Meninges

In more than 40 per cent of cases, an extranodal involvement may be found, especially in the region of the orbit, the upper respiratory tract, skin and subcutaneous tissue, and central nervous system.[8] It has also been described in the larynx (Table I).[9,10]

The evolution of the disease is somewhat variable, from complete spontaneous remission in some cases, to a protracted clinical course for years in others, with the possibility of involvement of vital organs and death.

Case report

An 81-year-old man presented in July 1994 with a history of worsening dysphonia of six months duration but no other subjective symptoms. About a year beforehand the patient had undergone a surgical biopsy of multiple cutaneous nodules and excision of a left submandibular adenopathy, that had arisen in the previous few months quite asymptomatically. The histological and immunocytochemical findings had indicated Rosai-Dorfman disease.

On presentation fibre-optic-laryngoscopy demonstrated a mass in the left subglottic area, covered by intact mucosa, with hypomobility of the homolateral vocal fold and a modest reduction in the airway space. Objective examination did not indicate any palpable adenopathy nor other lesions in the upper aero-digestive tract. Blood tests revealed a normal complete blood count. All other

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Accepted for publication: 6 March 2000.

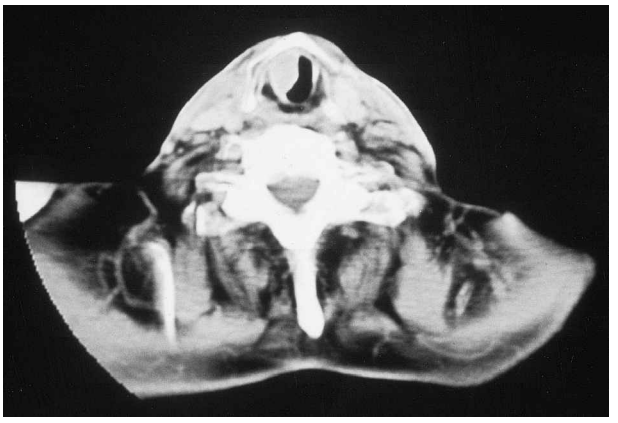

FIG. 1

An axial plane CT scan showing a left homogeneous egg-shaped subglottic mass, with a modest reduction in the airway space.

haematochemical tests proved to be within the norm of values except for an increase in total protein count (8.6 g/dl) and of gammaglobulin level (= 37.3 per cent) with an IgA monoclonal component with type K light chains. A general medical examination excluded any systemic involvement of the disease. A cervical CT scan showed the limits of the mass that did not infiltrate the paraglottic space or laryngeal cartilage (Figure 1).

The patient underwent a microlaryngoscopical CO_2 laser excision-biopsy of the mass with vaporization of the implantation area at 5 watts; no haemorrhagic or oedematous complications were observed intra- and post-operatively. The patient began to eat 24 hours after operation without inhalation.

Histopathological examination showed infiltration by lympho-plasmocytes and histiocytes with focal signs of 'lymphocytic phagocytosis', in agreement with the previous diagnosis of Rosai-Dorfman disease (Figure 2). Most of the histiocytes strongly expressed S-100 protein and CD68 by immunohistochemistry (Figure 3). This extranodal case of SHML was documented by an electron microscope study (Figures 4 and 5).

The patient is alive and free of disease 54 months post-operatively with normal laryngeal function and without signs of systemic involvement.

Discussion

Rosai-Dorfman disease is a benign condition characterized frequently by spontaneous remission. It manifests mainly

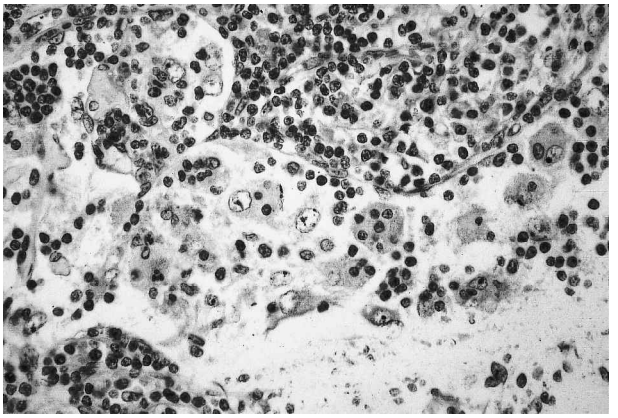

FIG. 2

Photomicrograph showing emperipolesis of lymphocytes by histiocyte-type cells (H&E; ×40).

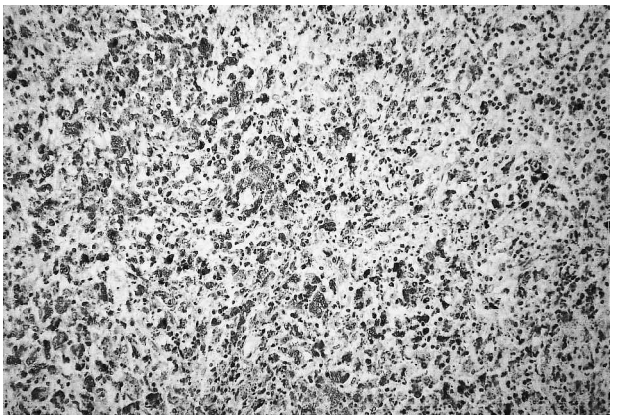

FIG. 3

Photomicrograph showing numerous histiocytes strongly positive for S-100 protein in their cytoplasm (H&E; ×20).

with an asymptomatic latero-cervical lymphadenopathy, occasionally associated with an extranodal location of the disease, which may, at times, represent its only pathological expression. The illness usually takes on an insidious and self-limiting course, unless there happens to be an important involvement of vital organs.

In its extranodal form, which usually affects an older category of patient, it may take the form of numerous inflammatory and granulomatous lesions of the soft tissues, and therefore needs to be differentially diagnosed from other inflammatory conditions of the upper aero-digestive tract.[11] SHML has also been described in human immunodeficiency virus (HIV)-patients.[12]

The histological features of the extranodal form are quite similar to those of the lymph node form of the disease, even if the feature of lymphocyto-phagocytosis is sometimes less evident. In our case this characteristic feature of 'emperipolesis' has been demonstrated at electron microscope examination. The differential diagnosis, sometimes very difficult, should consider some conditions, including benign inflammatory and fibrohistiocytic lesions (Table II).

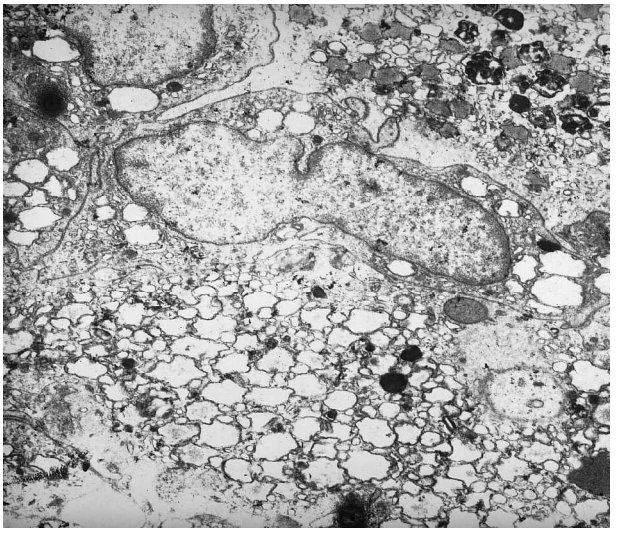

FIG. 4

Electron microscope image showing histiocyte-type cells, some of which contain residues of lymphocytes (lymphocyte phagocytosis) (H&E; ×4400).

https://doi.org/10.1258/0022215001906192 Published online by Cambridge University Press

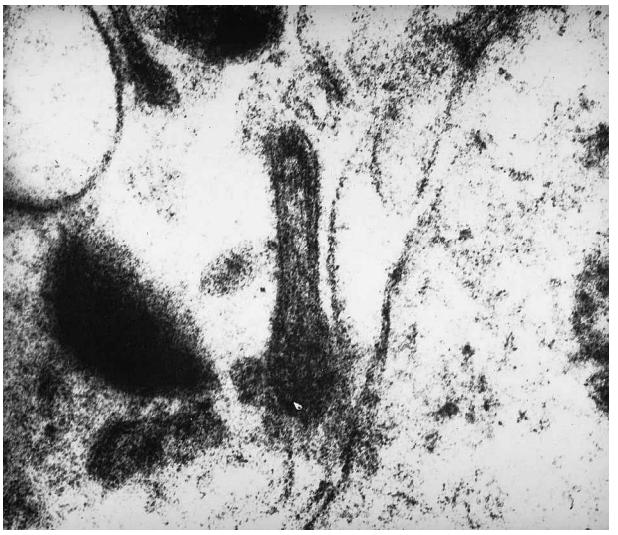

FIG. 5

Electron microscope image showing an histiocyte with cytoplasm that expands into pseudopodia (H&E; ×85 000).

In light of the uncertain aetiological origin of the disease and of its frequent spontaneous remissions, treatment still does not have any set guidelines. A therapeutic approach, when necessary, can take the form of surgical treatment and/or radiotherapy, that when associated with chemotherapy in disseminated diseases with progressive symptoms has allowed for a complete or partial resolution in 50 per cent of cases. The most effective regimens combined a vinca alkaloid with an alkylating agent.[13] Corticosteroid treatment is also a common form of therapy. Some patients however require a surgical, rather radical approach because of the spread of the disease and its tendency to recur.

In the case that we observed, a conservative endoscopic surgical approach, consisting of a microlaryngoscopic CO_2 laser excision of the endolaryngeal mass, showed a good functional result without any local spread of disease. After 54 months of periodic follow-up, the patient had not shown any sign of local recurrence of disease or systemic involvement.

We would like to emphasize, in the case of such a disease, how important a complete medical and clinical screening is, so as to exclude widespread extranodal involvement, and above all, the importance of careful follow-up in order to intervene, when possible, with a conservative surgical approach.

Conclusion

Rosai-Dorfman disease is a rare, idiopathic, benign histiocytic proliferation, most commonly involving cervical lymph nodes. Extranodal SHML occurs in more than 40 per cent of cases, 75 per cent involving a variety of head and neck sites. Because in many cases the disease shows a self-limited clinical course and undergoes complete spontaneous resolution, in selected cases surgery may be limited to excision-biopsy with a strict clinical follow-up.

TABLE II

DIFFERENTIAL DIAGNOSIS OF ROSAI-DORFMAN DISEASE

Hodgkin lymphoma
Eosinophilic granuloma
Fibrous histiocytoma
Dermatofibrosarcoma
Langerhans cell histiocytosis

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Dr P. Aluffi takes responsibility for the integrity of the content of the paper.
Competing interest: None declared