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Clinical Records

Extranodal Rosai-Dorfman disease: an uncommon cause of persistent nodule in the ear

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Abstract
A 40-year-old woman presented with a nodule over the tragus of the right ear. A biopsy was initially reported as showing non-specific inflammation. In view of the persistence of the lesion, the histological material was reviewed, leading to revision of the diagnosis to Rosai-Dorfman disease, a diagnosis further confirmed by immunoreactivity of the histiocytes for S-100 protein. This case represented the extranodal form of Rosai-Dorfman disease in the absence of lymph node involvement.

Introduction

Rosai-Dorfman disease (sinus histiocytosis with massive lymphadenopathy, SHML) is an uncommon reactive histiocytic proliferative disorder of unknown aetiology. It typically presents as massive enlargement of lymph nodes, but about 40 per cent of cases show involvement of extranodal sites such as upper respiratory tract, bone, soft tissues, skin and central nervous system, sometimes to the exclusion of lymph node involvement (Foucar *et al.*, 1990). The disease pursues a self-limiting course, but a small proportion of patients may succumb to extensive disease involving vital structures, associated immunological abnormal-

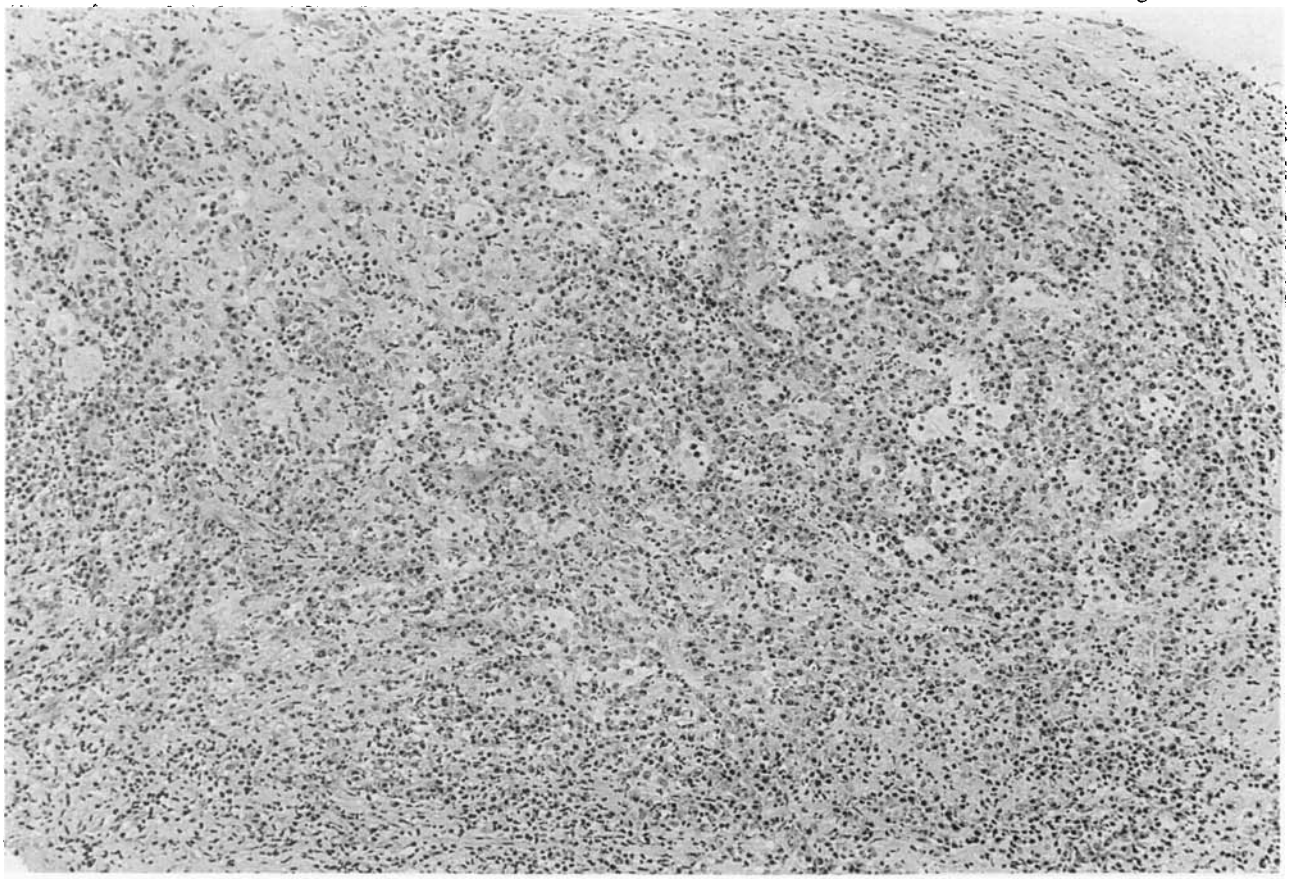

Fig. 1
Low power view of the nodule showing sheets of dark-staining plasma cells punctuated by multiple pale foci. H&E, ×100.

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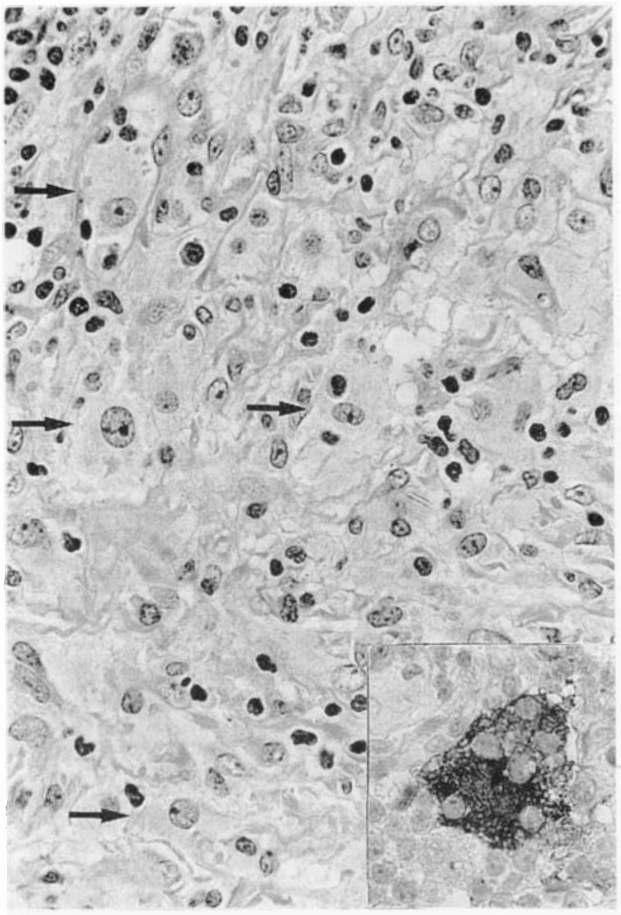

Fig. 2

The pale foci contain small aggregates of large histiocytes with abundant clear cytoplasm, rounded nuclei (arrows) and occasional phagocytosed lymphocytes. Immunostaining for S-100 protein is positive, which also highlights the phagocytosis (inset). H&E, ×375; inset, immunostain for S-100 protein ×375.

ities or unusual infection. We report an unusual case presenting as a skin nodule in the tragus of the ear in the absence of lymphadenopathy, and discuss problems related to the histological diagnosis of this uncommon condition.

Case report

A 42-year-old housewife presented in September 1989 with a slowly enlarging painless nodule over the right ear for one month. Her past health was good and she was otherwise asymptomatic. Examination revealed a 3 cm indurated nodule located at the right tragal and preauricular region. There was no lymphadenopathy. X-ray and computerized tomography showed that the mass was separate from the underlying zygomatic bone and temporomandibular joint, both of which were normal. A short course of antibiotics was given with no improvement. A biopsy was performed in October 1989, but it was not diagnostic. A repeat incisional biopsy in January 1990 was interpreted as 'chronic inflammatory lesion'. Since the mass persisted with no change in size as of March 1991, the histological material was reviewed, and yielded the diagnosis of extranodal Rosai-Dorfman disease.

Pathological findings

The first biopsy was small, and consisted of fibrous tissue, lymphocytes and plasma cells only. The second biopsy revealed portions of a partly circumscribed nodule with a fibrotic background, heavily infiltrated by lymphocytes, plasma cells and polymorphs (Fig. 1). In some areas, the inflammation and fibrosis had spilled over into the adjacent skeletal muscle. A pattern of alternating cellularity was observed within the nodule, in which cellular areas of plasma cell infiltration were punctuated by pale foci, which on high-power magnification were found to be occupied by isolated or clusters of large mononuclear cells (Fig. 2). These mononuclear cells possessed abundant pale reticular cytoplasm, rounded open nuclei, and a prominent central eosinophilic nucleolus. Phagocytosis (emperipolesis) of lymphocytes, plasma cells and polymorphs was occasionally observed. Immunohistochemical studies showed that the mononuclear cells were positive for histiocyte marker KP-1 and S-100 protein (Fig. 2). Immunostaining for S-100 protein also highlighted the phagocytosed cells within the histiocytic cell bodies by virtue of their negative image.

Discussion

Rosai-Dorfman disease, a disorder of unknown aetiology, typically presents as painless cervical lymphadenopathy in young individuals (Rosai and Dorfman, 1969; Chan *et al.*, 1985; Foucar *et al.*, 1990). The mean age of the patients is 20.6 years and there is a slight female predominance. Extranodal disease can occur in almost every organ, and occasionally in the absence of lymph node involvement. There may be associated immunological dysfunctions such as autoimmune haemolytic anaemia and polyclonal gammopathy. The clinical course is characterized by waxing and waning of the lymphadenopathy, and in a majority of cases, the disease stabilizes and regresses spontaneously. However, in a small proportion of patients, it behaves aggressively with progressive lymphadenopathy and involvement of vital organs. Most patients require no specific treatment, but surgery and systemic chemotherapy have been applied to the severe debilitating cases.

Rosai-Dorfman disease is characterized histologically by proliferation of large histiocytes with round vesicular nuclei, distinct nucleoli and voluminous pale to clear cytoplasm. Though lymphophagocytosis (emperipolesis) is always present, this is not a pathognomonic feature, and the diagnosis should be based mainly on the distinctive cytological features of the histiocytes. There is invariably a rich infiltrate of plasma cells in the background. The histological diagnosis of Rosai-Dorfman disease in lymph node is usually straightforward. However, the diagnosis in extranodal sites is often more difficult, because this possibility may not be considered at all, lymphophagocytosis is often less prominent, and secondary changes such as fibrosis may obscure the diagnostic features.

In the present case, only small foci in the biopsy are diagnostic of Rosai-Dorfman disease as a result of the extensive sclerosis and lymphoplasmacytic infiltration. However, the presence of dark staining foci alternating with pale foci in areas should have led to a suspicion of the diagnosis. This characteristic low-magnification appearance is found in most cases of Rosai-Dorfman disease irrespective of anatomical location. A firm diagnosis can be rendered on identifying the distinctive histiocytes, which are typically immunoreactive for S-100 protein (Chan *et al.*, 1985; Eisen *et al.*, 1990). This immunostain also facilitates the search for lymphophagocytosis, because the outline of the individual histiocytes can be much better appreciated. The S-100 protein staining must be interpreted on the large histiocytes with round nuclei, and not on the Langerhans' cells (with groove nuclei) which are often abundant in the skin. Rosai-Dorfman disease can also be potentially mistaken for malignancy (such as large cell lymphoma) since the proliferated histiocytes can show some degree of nuclear pleomorphism (Foucar *et al.*, 1990).

Cutaneous involvement in Rosai-Dorfman disease is uncommon, and can occur in the absence of nodal involvement (Foucar *et al.*, 1990). It presents as solitary or multiple papules, patches, plaques, or nodules. The overlying skin may be xanthomatous, erythematous or ulcerated. The lesions can regress, persist or progress but this disease is rarely fatal (Foucar *et al.*, 1990). In the present case, since the presence of extensive sclerosis and

paucity of diagnostic histiocytes suggest that the lesion is regressing, the patient is observed without further treatment.

Conclusion

Cutaneous Rosai-Dorfman disease, though rare, merits recognition because it is often self-limiting and does not require specific treatment such as antibiotics or radical excision.

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