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Bilateral and multicystic major salivary gland disease: a rare presentation of primary Sjögren's syndrome

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Abstract
We present a case of a 15-year-old girl with bilateral parotid and sub-mandibular salivary gland enlargement as the sole presentation of primary Sjögren's syndrome. The clinical, radiological, immunological and pathological features have been discussed. The relevant literature has been reviewed. To our knowledge this is the only reported case of Sjögren's syndrome presenting as multicystic disease with bilateral major salivary gland involvement.

Key words: Sjögren's syndrome; Salivary gland diseases; Cysts; Immunology

Introduction

Sjögren's syndrome is an autoimmune disease characterized by inflammation and destruction of exocrine glands, mainly the lacrimal and salivary glands. The syndrome is classified as primary when it exists on its own and secondary when associated with other autoimmune diseases such as, rheumatoid arthritis, systemic lupus erythrematosus, systemic sclerosis, polymyositis and primary biliary cirrhosis. An autopsy study in 1957 estimated the incidence of disease to be one case per 255 persons, therefore second in frequency to rheumatoid arthritis (Hudson, 1986). Sjögren's syndrome is more common in females and the onset is at any age from 15 to 65. It is, however, uncommon in young adults and children (Saito *et al.*, 1994).

The exact aetiology is unknown but is considered to be an interaction between genetic and environmental factors resulting in autoimmunity. Epstein-Barr virus and cytomegalovirus have been implicated in triggering the autoimmunity (Flescher and Talal, 1991). We present a case of a young girl with primary Sjögren's syndrome.

Case report

A 15-year-old girl presented to the ENT department with a painless and progressive swelling of left parotid gland for the last six to seven months. There were no associated oral, ocular or generalized symptoms. She was otherwise well with no significant family history.

On examination, she had diffuse enlargement of both parotid glands with a discrete mass in the left parotid. Submandibular salivary glands on both sides were also clinically palpable but not grossly enlarged and therefore escaped the patient's attention. No other abnormality was found in the upper respiratory tract and systemic examination was unremarkable.

The peripheral blood picture was normal with an ESR of 15 mm/hour. Fine needle aspiration of the left parotid gland showed lymphocytes without any malignant cell. Chest X-ray was normal. An immunological screen was carried out which showed raised immunoglobulins. The

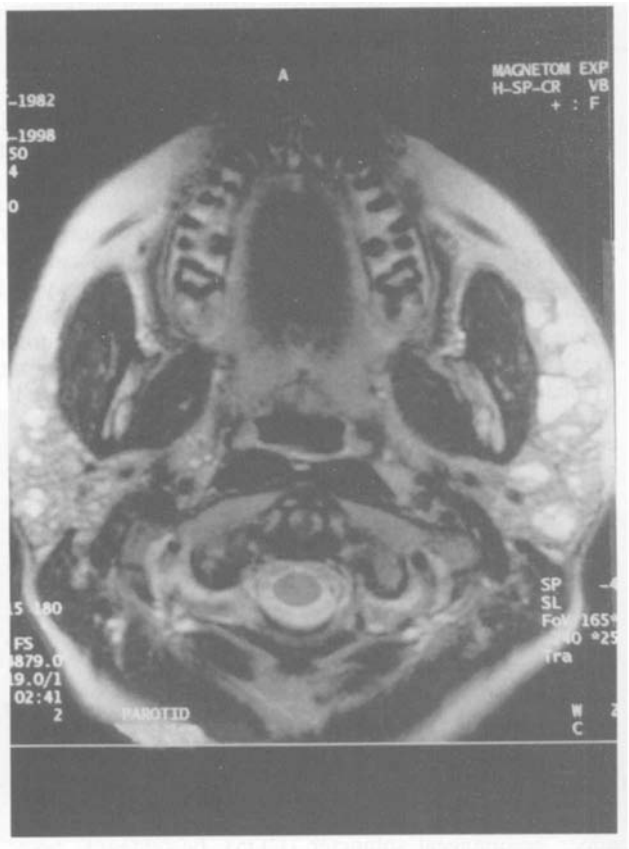

FIG. 1
Axial T2-weighted MRI showing multiple cystic changes in both parotid glands. The changes are more florid on the left side.

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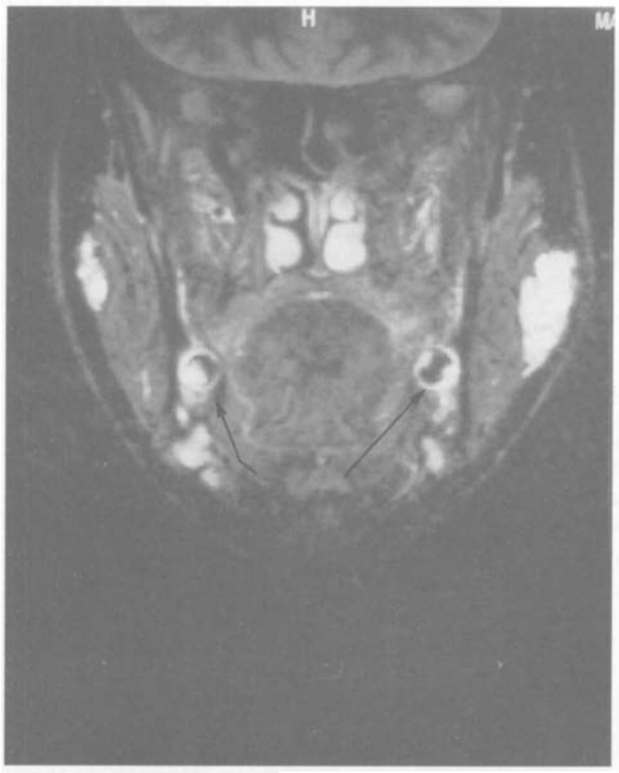

FIG. 2
Coronal T2-weighted MRI showing cysts (arrows) in both submandibular glands.

IgG type was 18.5 g/l (normal 5.40–16.10) and IgM 1.91 (normal 0.50–1.90). Antinuclear antibodies were positive in a 1/1600 dilution and rheumatoid factor was also positive. Tests for other auto-antibodies showed anti-R0 (SSA) and anti-La (SSB) antibodies.

A sialogram of the left parotid gland showed sialectasis. The MRI scan confirmed bilateral enlargement of the parotid glands with multiple cystic changes in both parotids (Figure 1) and few in the submandibular glands (Figure 2). Based on these findings, a working diagnosis of Sjögren's syndrome was made. A sub-labial biopsy of minor salivary glands was performed which showed lymphocyte infiltration of the ductules.

Discussion

The diagnosis of primary Sjögren's syndrome was based on the salivary gland involvement, immunological abnormalities, radiological findings and sub-labial biopsy of the minor salivary glands. The clinical picture of primary Sjögren's syndrome has been described as a triad of xerostomia, keratoconjunctivitis and rheumatoid arthritis. In our case, however, no such features were found. Absence of any typical skin rashes, subcutaneous nodules, arthritis, or joint deformities and pulmonary abnormalities helped to exclude secondary Sjögren's syndrome. The possibility of localized lymphoma was excluded on the basis of cytology and there was no significant lymphadenopathy or hepatosplenomegaly suggesting widespread lymphoma. The risk of human immunodeficiency virus (HIV) infection was excluded by careful questioning.

The disease can affect virtually any organ of the body (Fox *et al.*, 1984). Our discussion is mainly based on salivary gland involvement. The cardinal pathological features are inflammation and destruction of the glandular tissue. The changes are predominantly of duct dilatation, acinal atrophy and interstitial fibrosis (Lindvall and Jonsson, 1986).

Clinically there may be bilateral or unilateral swelling of the salivary glands: the parotid gland is most commonly involved. In the differential diagnosis of bilateral parotomegaly, sarcoidosis, cirrhosis of the liver, chronic alcoholism and HIV infection are the important systemic diseases to be looked for. Rarely, a gland may present with localized swelling, which is called pseudotumour because it clinically mimics a primary neoplasm (Bradus *et al.*, 1988). Multiple cysts of varying size in the parotid gland have been described (Som *et al.*, 1981). Rarely presentation may be as one or two large cysts in the parotid gland (Hong *et al.*, 1990), in which case other cystic conditions such as cystic Warthin's tumour, lymphoepithelial cyst, HIV-related parotid cyst and branchial cyst have to be excluded on clinical and histological grounds (Som *et al.*, 1995). Cystic changes in the submandibular glands have not been described before.

The majority of patients have a raised erythrocyte sedimentation rate (ESR) and a mild normocytic anaemia with leucopenia. The production of a variety of auto-antibodies reactive with cellular antigens is seen. The most remarkable feature is the high level of gammaglobulins (IgG), which can be up to 50 g/l. Other types of immunoglubilins, IgM and IgA may be raised. Rheumatoid factor may be positive in both primary and secondary (Martinez *et al.*, 1979). Antinuclear antibodies are usually positive. Anti-Ro (SSA) has been reported most sensitive and anti-La (SSB) most specific for this disorder (Yamagata *et al.*, 1986). All these abnormalities can be seen in other connective tissue disorders but the presence of anti-La and anti-Ro combined with clinical features are suggestive of primary Sjögren's syndrome.

The sialographic findings may vary and can be correlated with the severity of the disease. Features include normal or dilated ducts, punctate or globular collections and cavitary lesions. Computed tomography (CT) scan of the salivary gland can define the extent of the disease and localize the area for biopsy. The scan usually shows an enlarged gland and heterogeneous attenuation with multilocular appearance, representing chronic sialectasis (March *et al.*, 1989). This is not a reliable marker for the differentiation between lymphoma and pseudotumour, however, other local complications such as abscesses and cysts can be readily detected.

Magnetic resonance imaging (MRI) is now a significant diagnostic tool in inflammatory and tumorous lesions of the parotid gland. The typical changes in Sjögren's syndrome are multiple areas of high signals mixed with low signal foci throughout the gland, visible on both T1 and T2 weighted images, known as salt and pepper appearance. The dilated duct system has been reported to appear as a low signal area on the T1 weighted image (Takashima *et al.*, 1991).

Malignancy has been reported from either the lymphoid tissue or the epithelial component of salivary glands in Sjögren's syndrome. The incidence of lymphoma is from five to 10 per cent and is almost always of B-cell type (Kassau, 1978). The young patients are at greater risk (Hurt and Burroughs, 1985). The presence of lymphadenopathy and splenomegaly can be used to identify the patients to follow up closely for the development of lymphoma (Schmid *et al.*, 1982).

Fine needle aspiration cytology of the gland or palpable lump may not be helpful. The biopsy and histology of the sub-labial glands is therefore the most definitive diagnostic test. The typical histological picture is massive lymphocytic

infiltration of glandular tissue with atrophy or destruction and narrowing of the ducts (Jones and Mason, 1980). This was demonstrated in our case.

Conclusion

Multicystic, multiple salivary gland disease is a diagnostic conundrum, which conjures up several interesting possibilities. A high index of clinical suspicion is required if such an atypical presentation of this well known condition is to be picked up.

The diagnostic tools suggested are radiology, immunology and histology. The immunological tests are simple and easy to perform, and therefore should be employed in cases of salivary gland swellings. Potentially serious conditions such as HIV infections and lymphomas need to be excluded. In young patients a long-term follow-up is essential to look for the development of lymphoma, as a complication.

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