Bilateral submandibular gland lymphoma in Sjögren's syndrome

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Summary: Salivary gland lymphoma is associated with Sjögren's syndrome. A case of bilateral submandibular gland and sublingual gland lymphoma, arising in Sjögren's syndrome, is presented. A lymphoma involving more than one salivary gland may occur in Sjögren's syndrome, and there is an increased risk of developing an extrasalivary lymphoma.

Introduction

Since Mikulicz¹ first described the condition of bilateral enlargement of the lacrimal, parotid and submandibular glands, it has become incorporated in a number of syndromes, including Sjögren's syndrome. The association between Sjögren's syndrome and lymphoma has been recognized since 1964.² Sjögren's syndrome histologically demonstrates myoepithelial sialadenitis within the salivary gland, but these pathological features may be present without the full clinical syndrome. A lymphoma may also occur in cases of myoepithelial sialadenitis in the absence of Sjögren's syndrome.^{3,4} These associated lymphomas may arise either within or outside the salivary gland, and are chiefly non-Hodgkin's lymphomas of the B cell type. There are no reports of an association between T cell lymphomas in salivary glands, and myoepithelial sialadenitis.

A case of follicle centre cell lymphoma arising in myoepithelial sialadenitis is described, and features indicating the development of lymphoma in this disorder are discussed.

Case report

A 58 year old woman presented with a 2-month history of painless bilateral submandibular gland enlargement. A similar episode, which had occurred 7 years previously, settled spontaneously. She also suffered from variable tear production, but no xerostomia or joint symptoms.

Examination revealed rather coarse features, and

obvious bilateral submandibular gland, and sublingual gland enlargement. The parotid glands were normal, but the lacrimal glands were both palpable. There was no lymphadenopathy, although the spleen was palpable 4 cm below the left costal margin.

Investigations were as follows: haemoglobin 11.3 g/dl, white cell count $5.2 \times 10^9/l$ with a normal differential, and an erythrocyte sedimentation rate of 44 mm/h. Electrolytes and liver function tests were normal. The serum thyroxine was $< 25 \text{ nmol/l}$, and the TSH was 19 $\mu\text{u/l}$. An autoantibody screen was positive for thyroid and gastric parietal cell antibodies, the rheumatoid factor was negative. Protein studies demonstrated an elevated serum IgM and an IgM kappa paraprotein in the gamma component on electrophoresis.

She underwent bilateral submandibular gland, and right sublingual gland excision. At operation, the excised salivary glands were enlarged, but not locally adherent.

Histological examination of all the glands revealed a grade 1 diffuse lymphoma of follicle centre cell origin, composed of small follicle centre cells, arising in Sjögren's syndrome. Immunoperoxidase studies demonstrated two zones; one a periacinar proliferation of lymphoid cells, staining positively for IgM, corresponding to the malignant proliferation, and the second, a diffuse area in which IgG kappa staining was prominent, due to the high background activity of the reactive plasma cell infiltration. The cytological appearances of the lymphoid infiltrate, in conjunction with the monoclonal IgM pattern, confirmed the diagnosis of a follicle centre cell lymphoma.

Staging of the lymphoma included a bone marrow aspiration which was normal, an abdominal computed tomographic (CT) scan which confirmed the splenomegaly but revealed no para-aortic lymphaden-

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opathy, and a lymphangiogram which demonstrated no abnormal lymph node architecture.

Treatment with chlorambucil 20 mg/day was recently started.

Discussion

The association between malignant lymphoma and myoepithelial sialadenitis takes two forms; lymphoma within the salivary gland and extrasalivary lymphoma.

Salivary gland lymphoma had been considered an unusual condition, with only 43 cases reported up to 1976.⁵ Since then further series have been reported.^{4,6} The majority of salivary gland lymphomas arise in the parotid gland (76%) but the submandibular (20%), sublingual (3%), and palatal glands (1%) may be implicated. In 10% of patients more than one gland is involved; of these half are synchronous tumours, and half are metachronous.⁷ Multiglandular enlargement should not therefore give a false impression of benign disease.

A significant proportion of salivary gland lymphomas are found in conjunction with myoepithelial sialadenitis. In 24% of patients with an intrasalivary gland lymphoma, epimyoeplithelial islands, as seen in myoepithelial sialadenitis, were also observed.⁷ Therefore, a rapidly enlarging mass in the salivary gland of a patient with Sjögren's syndrome should raise the possibility of a lymphoma, as the clinical diagnosis of a benign condition is not acceptable.

Extrasalivary non-Hodgkin's lymphoma of the B cell type is associated with myoepithelial sialadenitis, with or without autoimmune disease.⁴ Patients with

the sicca syndrome have a 43.8 times greater risk of developing a malignant lymphoma in an extrasalivary site, compared with the normal population.⁸

In one series of patients with myoepithelial sialadenitis,⁴ the immunohistological findings of the salivary glands in 27 of 34 cases showed focal staining for a monoclonal immunoglobulin; most commonly this was an IgM kappa paraprotein. This monoclonal staining occurred in confluent proliferation areas composed of immunoblasts and lymphoplasmacytoid cells. Of the patients producing a monoclonal immunoglobulin, 8 had extrasalivary lymphoma at the time of diagnosis while 10 subsequently developed the lymphoma 2 months to 12 years later. Extrasalivary lymphoma only developed in patients with myoepithelial sialadenitis showing a monoclonal immunoglobulin pattern. The immunohistology of the extrasalivary lymphoma in the patients with myoepithelial sialadenitis displayed the same monoclonal immunoglobulin pattern and the same lymphoplasmacytoid cell infiltration as seen in the salivary gland biopsies. This suggests that intrasalivary lymphoma should be diagnosed when a monoclonal lymphoplasmacytoid proliferation is seen within the confluent proliferation areas of myoepithelial sialadenitis, even in the absence of a documented extrasalivary lymphoma.⁴

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