Case report

Sarcoidosis in a patient presenting with clinical and histological features of primary Sjögren's syndrome

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SUMMARY A patient presenting with bilateral enlargement of parotid and lacrimal glands, xerostomia, and keratoconjunctiva sicca, whose labial biopsy specimen showed changes consistent with Sjögren's syndrome, is described. The patient was initially misdiagnosed as having primary Sjögren's syndrome (SS). Subsequent investigations, however, performed to exclude an associated lymphoma or sarcoidosis, showed histological changes of the latter. The possibility that early infiltrates of the salivary glands in sarcoid may mimic those of SS is discussed.

Key phrase: labial salivary gland biopsy.

Bilateral salivary and lacrimal gland enlargement and symptoms of dry eyes and dry mouth may occur in sarcoid mimicking the presentation of primary Sjögren's syndrome (SS)^{1,2} and necessitating diagnosis on histological grounds. Parotid biopsy is usually avoided because of attendant surgical complications,³ but labial gland biopsy is simple,⁴ less invasive, and may demonstrate changes similar to those seen in the major salivary glands.⁵ Although in one study typical granulomata were seen in the minor glands of only 58% of known cases of sarcoid,⁶ focal lymphocytic sialadenitis is considered to be an accurate indicator of the oral component of SS.^{3,7} Recently, lip biopsy has been described as useful in discriminating between sarcoid and SS.² We report a patient with clinical and histological features consistent with SS who was subsequently diagnosed as having sarcoidosis. We could find no previous comparable report.

Case report

A 57 year old West Indian woman, resident in England for some years, was referred by her dental

practitioner. She had a nine month history of bilateral parotid swelling and persistent dry mouth with difficulty in chewing, swallowing, and speaking and with alterations in oral sensation and taste. One year earlier her complaint of dry eyes had been treated with hypromellose eye drops by an ophthalmologist. She also complained of general malaise and tiredness which had developed over the previous three to six months associated with a loss of 20 kg in weight. During this period she had had an episode of mild pain and swelling in the right knee which settled over a few months. Thereafter the left knee became similarly involved. There was no other relevant personal, past, or family history. The striking finding on examination was woody enlargement of both parotid and lacrimal glands. The oral mucosa was dry and sticky and the furrowed tongue was found to be heavily infected with *Candida albicans*. There was a small amount of fluid in the left knee, which had a full range of pain free movement and no evidence of synovitis. The liver was just palpable with a smooth edge. Otherwise general examination was unremarkable.

There was a good flow of saliva from the submandibular gland, but no parotid salivary flow could be elicited after application of citric acid to the tongue. A labial gland biopsy specimen showed changes of SS with acinar atrophy, mild fibrosis, and

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heavy periductal focal infiltrates of mixed chronic inflammatory cells, predominantly lymphocytes, equivalent to grade 4 on the Chisholm and Mason scale.³ Schirmer's test was positive with less than 4 mm wetting in five minutes of a standard sterile strip (Coopervision Ltd, Southampton) in either eye. There was staining of the conjunctiva with rose bengal dye but no uveitis on slit lamp examination.

Investigations showed that her haemoglobin was 98 g/l (normocytic and normochromic), erythrocyte sedimentation rate 75 mm/1st h (Westergren), and the C reactive protein raised at 49 µg/l (normal range 0.8–8.0 µg/l). Other haematological indices and routine biochemistry were normal. Antinuclear antibody and antibodies to SS-A, SS-B, Sm, and nRNP were not detected, and latex agglutination was negative. Lung function was normal as were chest radiographs. Knee radiographs showed loss of medial joint space with tibial spurring and osteophyte formation, but radiographs of hands and knees were normal.

Clinically the differential diagnosis lay between sarcoidosis and SS, and lip biopsy changes suggested the latter. Because of the systemic features the patient was investigated to exclude a lymphoma associated with SS.⁸ Bilateral parotid gland sialography showed diffuse enlargement of both glands with no evidence of tumour. Parotid ultrasound examination showed both parotid glands were in excess of 11 cm in length, but again with no evidence of tumour. When the possibility of a more generalised lymphoproliferative disease was pursued it was noted that total IgG and IgA were raised at 31.2 g/l (normal range 6.6–13.2 g/l) and 3.78 g/l (normal range 0.5–2.5 g/l) respectively, and IgM was within normal limits. Serum immunoelectrophoresis showed a polyclonal increase in the γ region but no M band. Monoclonal immunoglobulin light chains in the urine have been reported as an early finding when the benign lymphoproliferation of SS becomes malignant,⁹ but no free α or λ chains were detected on immunoelectrophoresis of a 25-fold concentrate of the patient's urine.

Microscopy of urinary sediment showed the presence of red blood cells persistently and hyaline casts once. The patient had a creatinine clearance of 83 ml/min and 0.32 g/24 h of proteinuria. Culture and cytology of the urine were negative. An intravenous urogram showed a right duplex kidney and ureter but was otherwise normal. Abdominal ultrasound was normal with the exception of a slightly enlarged liver with no focal lesions. Cystoscopy was normal.

Thus, again, largely because of the histological changes of the lip biopsy specimen, a diagnosis of SS was still favoured. Because the systemic features

Fig. 1 Lymph node almost completely replaced by non-caseating epithelioid granulomas; inset: granuloma. (Haematoxylin and eosin.)

were still unexplained a 1 cm firm supraclavicular lymph node which had appeared some weeks after the initial presentation was biopsied. Histologically, the normal architecture had been replaced by sharply defined compact non-caseating granulomata with occasional multinucleate giant cells (MNGCs) with no evidence of necrosis (Fig. 1). Stains for acid fast bacilli were negative, and mycobacteria were not cultured. The patient had not been immunised against tuberculosis and a 1:100 Mantoux test (100 units of purified protein derivative; Evans Medical Ltd, Greenford, Middx) was negative. Angiotensin-converting enzyme was raised at 94 units/ml (normal range 18–53 units/ml). A Kveim test was performed, and a palpable subcutaneous nodule biopsied at six weeks showed multiple non-caseating granulomas of epithelioid cells and MNGCs, confirming the diagnosis of sarcoidosis.

Within one week of receiving 15 mg of prednisolone the patient felt generally better with dramatic improvement of the oral and ocular symptoms and resolution of her dysphagia. The parotid swelling had almost halved in size, the ESR fallen to 17 mm/1st h, and the C reactive protein to 22.6 µg/l.

Discussion

Sarcoid is known to present with clinical features of SS, and lip biopsy has been advocated for distinguishing between the two conditions.² This case report is instructive because reliance on the histological features of the lip biopsy would have resulted in a misdiagnosis. Primary Sjögren's syndrome was suggested by the positive labial gland biopsy, which showed a focus score of three foci per 4 mm² of tissue, equivalent to grade 4 on the Chisholm and Mason scale and highly indicative of SS.³ This

Fig. 2 Labial salivary gland showing a periductal infiltrate of lymphocytes containing a single Langhans' multinucleate giant cell (arrow). (Haematoxylin and eosin; bar=100 μ m.)

diagnosis was found to be incorrect when a lymph node biopsied primarily to exclude a lymphoma associated with SS⁸ showed changes of sarcoid. With this new information, further serial sections of the labial glands were examined. Typical features of SS were found throughout the tissue, though in one focus an isolated Langhans' type MNGC was seen (Fig. 2). There were no epithelioid granulomata or other features suggestive of sarcoidosis.

It is interesting to speculate on the significance of the single MNGC found in the labial biopsy specimen. Such cells in association with epithelioid granulomata make sarcoid the most likely diagnosis, but isolated MNGCs in a lymphocytic infiltrate are not considered suggestive of sarcoid.² In particular, de Wilde *et al* demonstrated MNGCs in four out of 55 patients with SS, with typical focal lymphocytic sialadenitis.¹⁰ In two of these cases epimyoeplithelial islands were present in association with the MNGC, leading to an appearance resembling epithelioid granulomata. In these cases muramidase staining was useful as it preferentially stained epithelioid cells. In our case no such confusion arose and the appearances were in keeping with those described for SS despite an isolated MNGC.

There are two possible explanations for the

histological changes of SS found in our patient with sarcoid. Firstly, both sarcoid and SS may have been present simultaneously. Both conditions may share aetiological factors¹¹ and result from defective T suppressor cell regulation.¹² We believe a more likely explanation is that early involvement of labial salivary glands by sarcoid, before the development of classical epithelioid granulomata, may result in lymphocytic infiltrates very similar to those seen in SS. This has been postulated before¹¹ but never demonstrated. Thus in patients presenting with the sicca syndrome the finding of focal lymphocytic sialadenitis on lip biopsy should be interpreted with caution, especially in the absence of autoantibodies.

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