Simultaneous presentation of sarcoidosis and Sjögren's syndrome

Sir, A 32-yr-old woman presented with pretibial painful red nodules. She had a 6-month history of migratory pain and swelling of several joints. She complained of daily progressive oral dryness, thirst, impaired swallowing and blurred vision with a feeling of dry eyes for more than 3 h a day. Her medical, family, occupational and environmental histories were non-contributory. She used an oral contraceptive and ibuprofen. Physical examination showed oedema of the ankles and erythema nodosum on both legs. Laboratory investigations revealed an erythrocyte sedimentation rate of 44 mm/h (normal value <10) and a C-reactive protein (CRP) level of 42 mg/l (normal value <3). Routine haematological laboratory and blood chemistry values were all within the normal ranges. Urine analysis showed no erythrocytes. Creatinine clearance was normal, with a slight proteinuria of 300 mg/24 h. Serum lysozyme was elevated at 9.7 mg/l (normal range 0.6–2.6) and angiotensin-converting enzyme (ACE) was 134 U/l (normal value <45). Antinuclear antibody, antibodies to extractable nuclear antigens and anti-double-stranded DNA (Farr assay) were all negative. Antibodies against SS-A (Ro) were positive. IgM rheumatoid factor was elevated at 105 kU/l (normal value <15). The IgG
concentration was 19.2 g/l (normal range 8.5–15.0), IgA was 5.4 g/l (normal range 0.9–4.5) and IgM was 2.2 g/l (normal range 0.6–2.6). No cryoglobulins were found. A tuberculin test with purified protein derivative was negative. A chest radiograph showed extensive mediastinal and bilateral hilar lymphadenopathy. Pulmonary function tests were normal. Ophthalmological examination demonstrated a normal Schirmer’s tear test [10 and 9 mm/5 min for the right and left eye respectively (normal value ≥ 5.5 mm/5 min)] but a decreased tear film break-up time of 2 s for both eyes (normal value ≥ 10 s) and positive Rose Bengal staining (Van Bijsterveld score 5 and 3 for the right and left eye respectively; normal value <3.5), consistent with keratoconjunctivitis sicca. Sialometric analysis revealed reduced unstimulated and stimulated (2% citric acid) flow of whole saliva. The reduced unstimulated flow of whole saliva was caused by a very low rate of secretion of all individual salivary glands (<0.01 ml/min), whereas the reduced stimulated flow of whole saliva was caused mainly by very low secretion from the parotid glands (0.02 ml/min per gland; normal range 0.05–0.5 ml/min). Sialochemistry revealed elevated sodium concentrations and a normal amylase concentration in whole, parotid and submandibular/sublingual saliva. Sialography of the right parotid gland showed globular sialectasis. Histopathological examination of parotid tissue showed epithelial cell granuloma as well as periductal lymphocytic infiltration and epimyoepithelial islands. Immunohistochemical staining showed a polyclonal plasmacytic infiltrate and a shift in the relative number of IgA-bearing plasma cells in favour of IgG-bearing plasma cells. A labial salivary gland biopsy revealed extensive epithelial cell granuloma and lymphocytic infiltration with a positive focus score of 1 (normal value <1). The patient was diagnosed as having sarcoidosis, presenting as Löfgren’s syndrome, with coexisting Sjögren’s syndrome. During a 2 yr follow-up, laboratory investigations revealed normalization of CRP and ACE activity and persistence of anti-SS-A antibodies. Repeated sialometric analysis showed persistent reduction in the unstimulated and stimulated flow of whole saliva, with further reduction in submandibular/sublingual salivary secretion and persistent elevation of sodium concentration. A chest radiograph showed a major reduction in mediastinal and hilar lymphadenopathy. Until now, the patient has been treated symptomatically for her sicca complaints.

Currently, seven sets of international criteria for the diagnosis of Sjögren’s syndrome are being used which incorporate the exclusion criterion of sarcoidosis [1]. Nevertheless, the present case demonstrates that sarcoidosis and Sjögren’s syndrome can coexist. Although the reduced stimulated secretory function of the parotid glands observed in our patient could also be caused by sarcoidosis, the observed elevation of salivary sodium concentration and the globular sialectasia on the sialogram are distinctive features in Sjögren’s syndrome and have not been described previously in association with sarcoidosis. The normalization of ACE activity, the persistence of sialometric and sialochemical abnormalities and anti-SS-A antibodies during 2 yr of follow-up support the persistence of Sjögren’s syndrome. Histopathological examination of salivary gland specimens revealed periductal lymphocytic infiltration and epimyoepithelial islands, as well as clear evidence for sarcoidosis [2]. Occasionally, epimyoepithelial islands were found in association with sarcoidosis. The decreased percentage of IgA-bearing plasma cells further supports coexisting Sjögren’s syndrome [3]. However, it is unknown whether an increased percentage of IgG- and/or IgM-bearing plasma cells may occur in the salivary glands of patients with sarcoidosis. The HLA-DR3 phenotype is associated with primary Sjögren’s syndrome, a subgroup of patients with SLE and SS-A antibodies, and a subgroup of patients with sarcoidosis. In our patient, the HLA-DR3 phenotype was absent. In the majority of cases, sarcoidosis is associated with SLE [4]. Some cases have been reported that are suggestive of sarcoidosis and coexisting Sjögren’s syndrome [5–10]. The incidence of sarcoidosis and Sjögren’s syndrome may be much higher than is suggested by this relatively small number of case reports, because the presence of sarcoidosis is one of the exclusion criteria for Sjögren’s syndrome. We emphasize that both disease entities might be present in a subset of patients, as illustrated in this case, with possibly common immunopathogenic mechanisms. Furthermore, the presence of Sjögren’s syndrome may be easily underdiagnosed, because extensive epithelial cell granuloma may dominate the histopathological specimen, especially in minor salivary gland biopsies. Careful use of exclusion criteria for Sjögren’s syndrome is warranted in order to define subgroups of patients with overlapping clinical syndromes. We propose that the exclusion criteria currently used in diagnostic criteria sets for Sjögren’s syndrome need to be reconsidered with regard to the exclusion of sarcoidosis.

A. A. van de Loosdrecht, W. Kalk, H. Bootsma, J. M. L. Henselmans, J. Kraan, C. G. M. Kalenberg

Divisions of Haematology, Rheumatology, Pulmonology and Clinical Immunology, Department of Internal Medicine, Department of Oral and Maxillofacial Surgery, Academisch Ziekenhuis Groningen, Hanzeplein 1, 9713 GZ, Groningen and Department of Neurology, Hofpoort Ziekenhuis, Polanerbaan 2, 3447 GN, Woerden, The Netherlands

Accepted 4 August 2000

Correspondence to: A. A. van de Loosdrecht, Department of Haematology, Vrije Universiteit Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands.

3. Bodeutsch C. De Wilde PCM, Kater L et al. Quantitative immunohistologic criteria are superior to the lymphocytic focus