Phenytoin-Induced Pseudo-Sjögren's Syndrome

Sir—Phenytoin-induced 'pseudo-lymphoma syndrome' is a rare but well-recognized entity with fewer than 200 cases reported in the literature [1]. We describe a patient with generalized lymphadenopathy, bilateral parotid hypertrophy and a serological abnormality associated with Sjögren's syndrome. The complete disappearance of the clinical and serological abnormality on withdrawal of the drug suggests that phenytoin can cause not only pseudolymphoma syndrome, but also a syndrome which can be better called pseudo-Sjögren's.

A 75-yr-old woman was referred to the rheumatology clinic with a history of generalized tiredness, weakness and progressive painless swelling of both parotids of 3 months duration, associated with increasing dryness of her mouth and grittiness in her eyes. She also admitted to mild polyarthralgia, involving her large joints. She was also found to have positive anti-Ro antibody in her blood on more than 20 occasions. She had persistently positive anti-Ro antibody and an ESR of 39 mm of Hg. The complement levels were normal. A chest X-ray showed features of a previous operation and an ultrasound of the parotids showed mixed echogenicity with no growth of previous operation and an ultrasound of the parotids showed mixed echogenicity with no growth of underlying bony tissue.

Submandibular salivary gland biopsy showed a mixed seromucinous salivary gland, densely infiltrated with lymphocytes and plasma cells. The diffuse infiltration formed lymphoid follicles and replaced some of the acini, while others looked atrophic. The lymphocytes were a mixture of T and B cells, and suggestive of a benign lymphoepithelial lesion. There was no evidence of lymphoma (Fig. 1).

She was treated with Glandosane spray and Hypromellose eye drops, and was reviewed 2 weeks later, when further enquiry revealed that the diagnosis of epilepsy was based on rather 'soft' signs. The patient had no definite history of 'fits', but she volunteered that many years ago, while an in-patient, she had felt very giddy one night and one of the junior doctors had started her on this drug. No further evaluation of this therapy had taken place since. Apparently, she had never had any tongue bite or incontinence, and there was no family history of epilepsy. A computerized brain scan was normal.

It was, therefore, felt by the rheumatologist (KC) that there was very little clinical evidence of epilepsy and phenytoin could be discontinued. She was also requested to reduce her prednisolone to 15 mg a day. She was reviewed after about a week of stopping the phenytoin and appeared to have had a total transformation of her facial appearance. Her parotids were no longer visible and the other regional lymph nodes were not palpable. The steroid therapy was reduced further and her morphine sulphate was stopped.

She has been reviewed in the clinic and became totally asymptomatic within 3 months. Repeat serological screening showed no evidence of anti-Ro antibody. She has been followed up for more than a year and had no recurrence of epilepsy, Sjögren's syndrome or seroconversion. Her present drug therapy includes prednisolone 7.5 mg daily, enalapril 5 mg daily and ranitidine 300 mg at night.

Phenytoin has been associated with numerous complications, including generalized lymphadenopathy, which is called 'pseudo-lymphoma syndrome' (PLS). Our patient, however, not only had generalized lymphadenopathy, but also had bilateral painless parotid hypertrophy, sicca symptoms with positive Schirmer's test and positive anti-Ro antibody, suggesting that she had an underlying autoimmune disease such as Sjögren's syndrome.

PLS associated with phenytoin therapy usually occurred 1 week to 2 yr after exposure to the drug.
Our patient had been receiving the drug for ~3 yr and her sicca symptoms became rather profound over recent months, associated with severe swelling of the parotids. It is difficult to be certain about how long she had had positive serology for the Ro antibody in her blood as it was tested soon after the development of the sicca symptoms. Although anti-Ro is commonly associated with various connective tissue diseases, none of these were present on clinical examination.

The clinical presentation of our patient had raised several possibilities, including metastatic carcinoma, but the lymph node biopsy finding was reassuring as it had no evidence of secondaries or primary lymphoreticular malignancy. The lymph node biopsy showed no evidence of focal necrosis, or eosinophilic or histiocytic cell infiltrate which is a characteristic feature of PLS [2-5].

It was most interesting to note the transient serological abnormality, which took ~3 months to become normal together with complete resolution of her symptoms. The dramatic effect of withdrawal of the drug on the size of her parotid glands was also remarkable.

Our case highlights problems in many areas of clinical management, including multiple unproven diagnoses, polypharmacy and perhaps indiscreet duration of therapy. An aggressive but cautious approach to the reduction of steroid had met with no untoward effect and she remains well at a considerably lower dose of steroid. Her blood glucose control is very much improved and it is possible that she may not require any anti-hypertensive therapy in future.

To our knowledge, this is the first case of pseudo-Sjögren's syndrome associated with phenytoin therapy and rheumatologists should be aware of this reversible clinical entity.

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Cervical Spondylodiscitis in a Patient with Ankylosing Spondylitis

SIR—First described in 1937, spondylodiscitis is an uncommon but well-recognized complication in patients with ankylosing spondylitis (AS) [1]. The literature suggests that such lesions are invariably confined to the thoracic and lumbar spines [2]. We report here the case of a 58-yr-old man with a 22 yr