Serum angiotensin converting enzyme in Sjogren’s syndrome—a case report and study of 21 further cases

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Summary

We report the case of an elderly woman with primary Sjogren’s syndrome and abnormal liver function tests indicative of primary biliary cirrhosis. She was found to have a raised serum angiotensin converting enzyme activity. We proceeded to study 21 further cases of Sjogren’s syndrome to discover whether raised levels of this enzyme were a feature of Sjogren’s syndrome. None of them had any features to suggest associated primary biliary cirrhosis. The cases included 12 with associated rheumatoid arthritis, two with systemic sclerosis, three with systemic lupus erythematosus and four with primary Sjogren’s syndrome. In only two of these 21 patients was a raised serum angiotensin converting enzyme obtained, the elevation being modest. We conclude that a raised activity of the enzyme is not usually associated with primary or secondary Sjogren’s syndrome, and that discovery of such an abnormality should prompt a search for an associated condition.

KEY WORDS: primary biliary cirrhosis, rheumatoid arthritis, systemic sclerosis, systemic lupus erythematosus.

Introduction

Serum angiotensin converting enzyme (SACE) has been shown to be elevated in certain conditions, most notably sarcoidosis, but also in other granulomatous disorders such as tuberculosis, leprosy, and primary biliary cirrhosis (PBC) (Studdy et al., 1978, 1979). Primary Sjogren’s syndrome (SS) may resemble sarcoidosis in many features, including parotid swelling, keratoconjunctivitis sicca, and lymphadenopathy. We report a case of primary SS in whom the diagnosis of sarcoidosis was originally considered, and in whom SACE levels were estimated and found to be raised. This led us to question whether SACE levels were regularly raised in SS or whether some associated condition, such as PBC in our case, was necessary before altered SACE levels were seen.

Case report

An 82-year-old white female was referred for investigation of progressive ataxia and paraesthesiae below the knees. Examination revealed anaemia and bilateral parotid swelling. Finger clubbing was present and bilateral basal crackles were audible in the chest. The liver was smoothly enlarged, but no stigmata of chronic liver disease were noted. Signs of a mild sensorimotor peripheral neuropathy were present in her legs.

Investigations revealed the following results: haemoglobin 8.8 g/dl; white blood cell count 2.4 x 10⁹/l; platelet count 352 x 10⁹/l; erythrocyte sedimentation rate 140 mm/hr (Westergren); raised serum alpha₂-globulin and gamma globulin; rheumatoid factor titre of greater than 1/5120; antimitochondrial antibody (AMA) titre greater than 1/40; antinuclear antibody titre greater than 1/640; SSB antibody not present; corrected calcium, phosphate, urea and electrolytes were within normal limits; Kveim test negative; serum angiotensin converting enzyme (SACE) 78 and 87 nmol/min/ml (normal less than 53 nmol/min/ml); bilirubin 13 μmol/l; albumin 31 g/l; alkaline phosphatase 520 iu/l (normal); aspartate transaminase (AST) 76 iu/l (normal); gamma glutamyl transferase (γGT) 174 iu/l (normal); Schirmer’s test—tear production less than 5 mm/5 min; Rose Bengal staining confirmed keratoconjunctivitis sicca; labial salivary gland biopsy revealed grade 4 changes of SS on histology (Chisholm and Mason, 1968). Respiratory function tests showed a moderately severe restrictive defect.

Primary SS was diagnosed on the evidence of keratoconjunctivitis sicca, parotid swelling and the positive lip gland histology, without evidence of...
connective tissue disorder. In addition she was felt to have PBC because of the antimitochondrial antibody and the pattern of elevated hepatic enzymes. Liver biopsy was considered not ethically justified in view of her age. Following this case other patients with SS were investigated looking for raised levels of SACE and any evidence of associated PBC.

**Patients and methods**

Twenty-one further patients with SS were studied. SS was diagnosed on the basis of having four or more of the symptoms of SS described by Anderson et al. (1972); a positive Schirmer's test (filter paper strips being damped to less than 5 mm in 5 min, ± positive Rose Bengal staining; and a positive labial salivary gland biopsy appearance (grade 4 according to the criteria of Chisholm and Mason, 1968). These included all the patients known to have SS in our department at the Whittington Hospital, and four further cases from University College Hospital. All the patients were female, aged 42–82 years. Twelve had associated rheumatoid arthritis, two had systemic sclerosis, three had systemic lupus erythematosus, and four had primary SS with no associated connective tissue disorder. SACE was measured using the method described by Friedland and Silverstein (1976).

AMA was measured by indirect immunofluorescence in a modification of the method of Walker et al. (1965) using quick fixed tissue. Bilirubin, alkaline phosphatase, AST and γGT were measured by autoanalyser.

All patients gave their informed consent to the study and approval was given by the hospital's ethical committee.

**Results**

No patient had detectable AMA, nor did any patient have elevation of bilirubin or hepatic enzymes to suggest PBC.

SACE levels were within the normal range in all but two patients. These two (one with primary SS and one with SS and rheumatoid arthritis) had only a modestly elevated level of 62 nmol/min/ml in each case.

**Discussion**

SS has been described as the result of lymphocyte mediated destruction of exocrine glands leading to a reduction or absence of glandular secretions. Extraglandular associations have been reported, and altered cellular and humoral immunity are manifested by hypergammaglobulinaemia and auto-antibody formation (Moutsopoulos et al., 1980). Sica features have been reported in 70–100% of patients with PBC (Golding et al., 1970; Alarcon-Segovia, Diaz-Jouanen and Fishbein, 1973). In most of these cases SS has been considered secondary to PBC, and histocompatibility studies have supported this concept (Hamlyn, Adana and Sherlock, 1980). Studies of SACE in sarcoidosis have suggested the increased levels are the result of stimulation of the monocyte/macrophage system. Raised activity has also been found in a variety of granulomatous disorders such as tuberculosis, leprosy and PBC (Studdy et al., 1978). Recently raised activity of SACE has been found in other liver disorders such as chronic active hepatitis, chronic persistent hepatitis and cirrhosis (Matsuki and Sakata, 1982), and in diabetes mellitus with retinopathy (Lieberman and Sastre, 1980). Our study shows that elevation of SACE does not appear to be a feature of primary or secondary SS. If an elevated activity of the enzyme is discovered in a patient with SS it should prompt investigation for an associated condition such as PBC.

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**References**


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