

Primary Sjögren's syndrome associated with inappropriate antidiuretic hormone secretion

A case report

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Summary

A patient in whom primary Sjögren's syndrome and inappropriate antidiuretic hormone secretion were associated is reported. This is the first report of such an association. The possible pathophysiological mechanisms are discussed and vasculitis proposed as the underlying pathogenetic mechanism.

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Sjögren's syndrome is an auto-immune disorder with a predilection for multisystem involvement.¹ Xerophthalmia and xerostomia from a destructive mononuclear infiltration of the lacrimal and salivary glands are characteristic. Central nervous system (CNS) involvement includes recurrent aseptic meningo-encephalitis, necrotising spinal arteritis and unifocal and multifocal cerebral disease.^{2,3} Inappropriate secretion of arginine vasopressin (SIADH) is a form of hyponatraemia in which there is an elevated level of antidiuretic hormone (ADH) inappropriate to any physiological stimuli present that normally affect ADH secretion.⁴ Among the causes are malignant tumours, chest infections and CNS disturbances.⁴

A patient in whom primary Sjögren's syndrome and inappropriate ADH secretion were associated is reported. This is the first report of such an association. The possible pathophysiological mechanisms are discussed.

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Case report

A 56-year-old woman presented to hospital with a generalised convulsion. She was not hypovolaemic and, apart from a decreased level of consciousness, the neurological system was normal.

The serum sodium level was 111 mmol/l (normal 133 - 146 mmol/l), chloride 74 mmol/l (normal 96 - 106 mmol/l), urea 2,1 mmol/l (normal 3,3 - 6,5 mmol/l), uric acid 0,18 mmol/l (normal 0,20 - 0,45 mmol/l) and osmolality 237 mmol/kg H₂O (normal 275 - 290 mmol/kg H₂O). Serum potassium, glucose and creatinine values were normal. Urinalysis revealed a normal sediment, no proteinuria or glycosuria and a sodium content of 63 mmol/l, potassium 123 mmol/l, chloride 94 mmol/l and osmolality 488 mmol/kg H₂O (normal 50 - 1 400 mmol/kg H₂O). The full blood count was normal, the erythrocyte sedimentation rate was 100 mm/1st h (Westergren) and the C-reactive protein 49 mg/l (normal < 10 mg/l).

Blood culture and toxicology screening for phenothiazines, ethanol, paracetamol, barbiturates and benzodiazepines were negative. An ECG, chest radiography, blood gas analysis, thyroid function tests and the cortisol level were normal and screening for porphyrin in urine and stool was negative. Computed tomography of the brain and cerebrospinal fluid examination were non-contributory, while electro-encephalography showed nonspecific diffuse changes compatible with a metabolic encephalopathy.

SIADH was diagnosed and fluid intake restricted to 500 ml/24 h. In addition, 200 ml of 5% saline was administered twice 8-hourly. The serum sodium level rose to 126 mmol/l within 24 hours and the patient became fully conscious. Serum and urine electrolyte values and osmolality returned to normal and remained so.

Further enquiry revealed a 3-year history of dry eyes and mouth and swelling of the left parotid gland. There was no history of skin rashes, Raynaud's phenomenon, oral or genital ulcers, photosensitivity, serositis or musculoskeletal symptoms. The patient denied any drug intake. No salivary gland enlarge-

ment or lymphadenopathy were present but an absence of pooling of saliva in the floor of the mouth was noted. Slit-lamp examination of the eyes showed a diminished tear film and punctate areas of epithelial loss were demonstrated with 1% rose bengal drops. Liver function tests, serum creatine kinase, aldolase, calcium, magnesium, phosphate and complement levels was normal. Cryoglobulins were negative and a hyperglobulinaemia of 42 g/l with increased IgA and IgG levels were demonstrated.

The rheumatoid factor was positive on three and the Rose-Waaler test on two occasions (titres of 1:80 and 1:20). Antinuclear antibodies ranged from 1:10 to 1:1280 (speckled pattern) and anti-Sm and anti-RNP antibodies were positive on three occasions. Anti-double-stranded DNA, anti-Ro (SAA) and anti-La (SSB) antibodies were persistently negative. A labial salivary gland biopsy revealed focal mononuclear cell infiltration. The patient was treated with artificial tears and has remained well for 26 months.

Discussion

SIADH was first described by Schwartz *et al.*⁵ Diagnostic criteria for this syndrome have subsequently evolved and include: (i) hyponatremic hyponatraemia; (ii) urine osmolality higher than would be anticipated for the degree of hyponatraemia; (iii) normal renal, adrenal and pituitary function; (iv) excretion of appreciable quantities of sodium in the euvolaemic patient; (v) absence of hypovolaemia or dehydration; (vi) absence of a condition associated with generalised oedema or ascites; and (vii) correction of both the hyponatremic hyponatraemia and natriuresis by severe fluid restriction.⁴ Our patient fulfilled all these criteria and was on no medication, such as diuretics and non-steroidal anti-inflammatory agents, which can cause a SIADH-like picture.⁶ The hypo-uraemia and hypo-uricaemia present in our patient have been well described in SIADH.^{7,8}

In a small number of patients with SIADH no cause can be identified, but Martinez-Maldonado⁹ advises caution in diagnosing 'idiopathic' SIADH, since the syndrome might precede overt disease, specifically cancer, by months or years.

The diagnosis of primary Sjögren's syndrome (sicca syndrome) was made by the triad of keratoconjunctivitis sicca, xerostomia and mononuclear cell infiltration in a labial salivary gland biopsy, and the clinical and serological exclusion of other connective tissue disease.^{10,11} When diminished tear secretion and punctate keratitis coexist, keratoconjunctivitis sicca is considered present. No entirely satisfactory clinical or laboratory tests are as yet available for the diagnosis of the oral component of Sjögren's syndrome. The most reliable signs are probably the absence of pooling of saliva in the floor of the

mouth and unilateral, episodic parotid gland enlargement, both of which were present in our patient.¹⁰ Focal lymphocytic infiltrates in minor salivary glands are seen in over 70% of patients with Sjögren's syndrome.¹⁰

A computer-assisted search of medical publications revealed no previous report of an association between primary Sjögren's syndrome and SIADH. This association could be entirely fortuitous. The rarity of idiopathic SIADH and the patient's well-being 26 months after diagnosis suggest that there is a true association between the two conditions.

Possible pathogenetic mechanisms to explain CNS manifestations of Sjögren's syndrome include vasculitis, direct mononuclear cell infiltration of CNS tissue, antineuronal auto-antibodies and cerebral vasospasm.² An association between peripheral vasculitis, CNS involvement and anti-Ro (SSA) antibodies has been described in primary Sjögren's syndrome.^{2,3} Vasculitis probably accounts for a significant proportion of CNS complications in Sjögren's syndrome.¹⁰ The diversity of CNS manifestations in Sjögren's syndrome is comparable to that of systemic lupus erythematosus and it is conceivable that the underlying pathogenetic mechanisms, including vasculitis, may be similar.^{5,12} Systemic lupus erythematosus vasculitis has previously been reported as a cause of SIADH, with immune-mediated inflammation postulated to have caused release of ADH from the neighbouring neurohypophysis.⁹

In similar fashion, we propose a direct association between primary Sjögren's syndrome and the subsequent development of SIADH in our patient, with vasculitis as the possible underlying pathogenetic mechanism.

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