


Is syndrome of inappropriate antidiuretic hormone secretion an extra-articular manifestation of rheumatoid arthritis?

Sir, Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a disorder of fluid and electrolyte balance which results from the excessive release of antidiuretic hormone (ADH) that leads to hyponatraemia. Systemic diseases of many types and various groups of drugs have been associated with SIADH. The association of SIADH with rheumatoid arthritis (RA) is not very well established. We report a patient with recent onset RA and SIADH whose hyponatraemia improved upon control of the inflammatory arthritis.

An 84-yr-old woman with a background of osteoarthritis and ischaemic heart disease, who had been previously fit, well and independent, was admitted to the hospital with complaints of nausea, profound lethargy and tiredness. She had noticed increasing pain, stiffness and some swelling in her hands and feet in the 4 weeks prior to the admission. One day prior to coming into hospital she felt weak in her legs and had difficulty with standing and walking. She had no other significant past medical history.

Her medications included isosorbide mononitrate, propranolol, diclofenac and low-dose aspirin. She was a non-smoker. Her examination at this point revealed synovitis of her metacarpophalangeal joints in a bilateral symmetrical distribution. She also had tenderness over her metatarsophalangeal joints. Full neurological assessment revealed generalized muscle weakness, grade 4/5, in the upper and lower limbs but there was no clinical evidence of a specific neuromuscular disorder. The rest of her examination was unremarkable. Her initial investigations revealed sodium (Na) 115 mmol/l, potassium (K) 3.9 mmol/l, urea 3.7 mmol/l and creatinine 68 mmol/l. Her full blood count showed haemoglobin (Hb) 11.5 g/dl, platelets 545 $\times$ 10^9/l and a white cell count (WCC) of 12.9 $\times$ 10^9/l. C-reactive protein (CRP) was 127.4 mg/dl and the erythrocyte sedimentation rate (ESR) was 75 mm/h.

She was fluid restricted to 1 l/day. Her diclofenac was discontinued. However, repeated measurement of Na continued to show low levels. Investigations looking into the possibility of SIADH revealed a low serum osmolality (248 mmol/kg), increased urine osmolality (334 mmol/kg) and sodium excretion (44 mmol/l) confirming the diagnosis of SIADH [1]. Further tests which included cortisol levels, a short synacthen test, thyroid function, blood glucose, myeloma screen, chest X-ray, echocardiogram and a

![Fig. 1. The relationship between Na levels and CRP concentration in a patient with rheumatoid arthritis and syndrome of inappropriate antidiuretic hormone secretion.](https://example.com/fig1.png)
computed tomography (CT) scan of her brain were all normal. Two weeks of fluid restriction produced only a modest improve-
ment in her sodium levels bringing it up, at best, to 120 mmol/l.

The rheumatoid factor was strongly positive with a titre of
1/1024. The X-rays of her hands revealed peri-articular osteopenia.
The rest of her autoantibody screen was negative. She satisfied
American Rheumatism Association criteria [2] for a diagnosis of
RA and inflammatory control was achieved initially with 120 mg
of intramuscular methylprednisolone; she was later started on
sulphasalazine EC. Further improvement of her RA was gradual
over the following months and Fig. 1 compares her CRP and Na
levels at various points in time.

It is clear from Fig. 1 that there was an inverse relation-
ship between the levels of Na and CRP, reflecting the effect of
active inflammation on Na levels. Furthermore, controlling disease
activity with sulphasalazine EC as a monotherapy without any
further long-term steroid supplement was effective in bringing
the Na levels gradually toward normal values. There have been
two case reports [3, 4] from Japan that discuss the occurrence
of SIADH following infections in patients with RA. Their
hyponatraemia resolved on treatment of their infective process.
To our knowledge this is the first case to be reported where SIADH
was associated with active RA, which improved on adequate
control of inflammation. Based on this it is tempting to speculate
that inflammation is probably responsible for increased ADH
secretion through a common pathway, which when stimulated
results in the release of CRP and ADH. The possibility of increased
production of interleukin-6 (IL-6) in the inflammatory lesions
leading to excessive release of ADH and CRP from the pituitary
gland and the liver respectively has been postulated [5].

This letter raises the possibility that SIADH can occur with
inflammatory conditions, and appropriate control of the under-
lying inflammation would lead to improvement in Na levels. At
present, due to the paucity of similar reports, we recommend that
hyponatraemia in patients with active RA be investigated in the
traditional way in order to identify the more common causes
associated with SIADH. However, in the absence of an obvious
underlying cause for SIADH, the possible association with active
inflammation should be considered. Furthermore, the lack of
response of hyponatraemia to the standard treatment with fluid
restriction is another clue to the presence of an on-going active
process (inflammation in this case) responsible for propagating
SIADH. Recognizing this clinical association may save patients
with inflammatory arthritis going through an exhaustive list
of investigations in an attempt to identify another cause for
their SIADH.

The authors have declared no conflicts of interest.

V. V. KAUSHIK, K. BINYMIN

Department of Rheumatology, Southport and Ormskirk Hospital
NHS Trust, UK

Accepted 27 August 2004

Correspondence to: K. Binymin, Department of Rheumatology,
Southport District General Hospital, Town Lane, Southport PR8
6PN, UK. E-mail: kbinymin2001@yahoo.co.uk

1. Bartter FC, Schwartz WB. The syndrome of inappropriate secretion

2. Arnett FCS, Edworthy M, Bloch DA et al. The American
Rheumatism Association Revised Criteria for the classification of

3. Ota K, Kamoto Y, Hoshimoto K. Unexpected impaired conscious-
ness in RA: a rare complication of SIADH induced by increased IL-

Hyponatremia in a patient with chronic inflammatory disease. Intern

Rinsho Byori 1999;47:408–16.

Reversible focal myositis in a patient taking venlafaxine

Sir, A previously healthy 30-yr-old man presented with a 4-day
history of a tender and painful left thigh. He had no history of
trauma, and had not performed any unaccustomed exercise. He
had not felt generally unwell. Since the symptoms were progressive,
he was referred to hospital by his GP. It was noted that these
symptoms had presented 2 months after he had started venlafaxine
(Efexor) for anxiety. Venlafaxine is a serotonin and noradrenaline
re-uptake inhibitor, used in the treatment of anxiety and depres-
sion, which has gained a considerable market share.

The patient had had a possible diagnosis of coeliac disease as a
child, but his symptoms had settled many years earlier and he was
no longer eating a restricted diet. Venlafaxine was his only medi-
cation. On examination he was generally well, apyrexial and able
to walk unaided. His left leg showed no swelling or erythema. The
posterior aspect of his left thigh was tender proximally and medi-
ally. He had a full range of movement of his hip and knee, but
extension of the knee increased the pain. Reflexes and peripheral
pulsations were normal. There were no cutaneous symptoms.

Blood investigations had been performed by his GP, and were
repeated upon admission. The striking abnormality was a serum
creatine kinase of 5286 U/l (normal range 0–180) on the day
before admission; the day after, this had increased further to 7700.
His other blood results on admission were normal, including an
erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)
and a full blood count. His urine tested negative for myoglobin.
Further blood tests for rheumatoid factor, antinuclear antibodies
(ANA), antineutrophil cytoplasmic antibodies (ANCA), parietal
cell antibodies, mitochondrial antibodies and smooth muscle
antibodies gave negative results. A plain X-ray of his femur
showed no abnormality. He was admitted to hospital and treated
with diclofenac and codydramol. The venlafaxine was stopped on
admission.

An MRI scan of the thigh demonstrated increased signal
intensity within the hamstring compartment of the left thigh on
T2-weighted images (Fig. 1A). Fat-suppressed axial images using
the short T1 inversion recovery method to achieve fat suppression
clearly demonstrated hyperintensity within the left hamstring
muscles (Fig. 1B), extending throughout the semimembranosus
and semitendinosus muscles on a coronal image (Fig. 1C).
These signal changes indicate considerable oedema in the ham-
string musculature, and were considered to be consistent with
myositis. A computed tomography (CT) guided biopsy of the
abnormal tissue was performed (Fig. 2). The biopsy showed the
muscle fibres to be largely intact, although there were changes in
staining to suggest some may be undergoing regeneration. In
one fragment, a modest sprinkling of mononuclear cells was seen.
The appearances were considered to be consistent with a patchy
myositis. The immunohistochemistry report showed CD45 posi-
tive, CD3 positive, CD79 negative cells; these T lymphocytes are
non-specific, but consistent with a myositis.

Although there was no immediate change in the patient’s
symptoms, his serum creatine kinase level started to drop very
soon after admission to hospital. The day after admission his