Letters to the Editor

Water balance in rheumatoid arthritis

Sir, Kaushik and Binymin raise the interesting suggestion of a link between rheumatoid arthritis and the syndrome of inappropriate antidiuretic hormone (SIADH) [1]. The serum and urine osmolality results and urine sodium excretion do not, however, confirm the diagnosis of SIADH. Previous serum urea and creatinine concentrations and clinical features such as oedema, blood pressure and pulse are not described and liver function tests are not recorded.

The differential diagnosis includes the possibility of sick-cell syndrome [2] as part of a chronic inflammatory condition, hyper-volaemic hyponatraemia secondary to chronic liver disease, or a reset osmostat [3]. The latter may have been induced by long-term diclofenac therapy. Non-steroidal anti-inflammatory drugs may potentiate the effect of antidiuretic hormone (ADH), leading to water retention [4]. This is mediated by a reduction in renal synthesis of prostaglandins, which normally antagonize the action of ADH.

These other mechanisms were not investigated by a water load test, hypertonic saline infusion test or plasma vasopressin estimations. Fluid restriction to one litre per day is only a weak therapy for SIADH and the ADH antagonist demeclocycline was not given a therapeutic trial.

My interpretation of the data presented for this case is that the findings suggest a probable drug effect, with diclofenac resetting the osmostat, and a possible acute-phase sick-cell syndrome with reduced ability of the cell membrane sodium pump to correct hyponatraemia. The gradual improvement in serum sodium with control of disease activity favours the latter mechanism, with a reduction in inflammation leading to the recovery of cell membrane sodium pump function.

In conclusion, I do not believe that this case report provides convincing evidence that inflammatory arthritis is another cause of SIADH.

The authors have declared no conflicts of interest.

C. VAN HEYNINGEN

Department of Pathology, Southport District General Hospital, Southport, UK
Accepted 25 February 2005
Correspondence to: E-mail: charles.vanheyningen@southportandormskirk.nhs.uk

Rheumatology 2005;44:956–957
doi:10.1093/rheumatology/keh624
Advance Access publication 29 March 2005

Water balance in rheumatoid arthritis: reply

We are grateful to Dr van Heyningen for his remarks and interesting comments regarding our letter, in which we highlight a possible causal relationship between rheumatoid arthritis and the syndrome of inappropriate antidiuretic hormone secretion (SIADH) [1]. However, we are surprised by the arguments used to analyse the data given and the subsequent conclusions he has made. He claims ‘The serum and urine osmolality results and urine sodium excretion do not however confirm the diagnosis of SIADH!’ Dr van Heyningen failed to outline why and how these biochemical data do not confirm a diagnosis of SIADH. He also failed to cite any reference or other diagnostic criteria that support his claim. We reported the serum osmolality at 248 mmol/kg, urine osmolality at 334 mmol/kg and urine sodium excretion of 44 mmol/l, confirming the diagnosis of SIADH. The criteria laid down by Bartter and Schwartz (Table 1) [2] (referenced in our letter) for diagnosis of SIADH were fulfilled in our patient. The clinical and biochemical abnormalities reported in our case satisfied the five cardinal features of SIADH. At the time of her symptomatic hyponatraemia she excreted concentrated urine, which was inappropriate to her hypo-osmolar state. We stated that there were no other systemic disorders apart from rheumatoid arthritis. Relevant investigations done in an attempt to identify an alternative cause for hyponatraemia were outlined in detail in our letter. Because of manuscript constraints, we were not able to list all other less relevant tests and normal results. Thus, most of the conditions known to cause SIADH were effectively ruled out.

Dr van Heyningen also stated that ‘the data presented for this case is that the findings suggest a probable drug effect, with diclofenac resetting the osmostat’. We have great reservations about his interpretation and reasoning. Here we would like to discuss two issues related to this statement.

(i) He failed to notice that the urine osmolality in our patient is much higher than the serum osmolality. This feature, when identified, would completely exclude the diagnosis of reset osmostat. Therefore, the acute water loading test, often used to establish a state of reset osmostat, was deemed unnecessary. Patients with reset osmostat syndrome have normal osmoreceptor responses to changes in serum osmolality, although the threshold for antidiuretic hormone (ADH) release is reduced [3]. Therefore, the serum Na levels are below normal but stable, usually between 125 and 130 mmol/l, unlike in our patient, who presented with far lower serum Na concentrations. Furthermore, with reset osmostat syndrome, the urine osmolality is maximally dilute, generally less than 100 mmol/kg [4].

(ii) We stated in our letter that her diclofenac was discontinued, despite which hyponatraemia persisted for more than 6 months. The serum Na levels of most patients with NSAID-associated hyponatraemia usually return to normal within days of withdrawing the responsible drug [5]. We might agree that diclofenac could be responsible for initiating hyponatraemia, but we are not clear how diclofenac therapy could be implicated in propagating hyponatraemia in this patient.

Dr van Heyningen concluded that there is no convincing evidence that inflammatory arthritis is another cause of SIADH.

Table 1. Essential criteria of SIADH

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<th>Description</th>
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<tr>
<td>Hyponatraemia with hypo-osmolality (&lt;275 mmol/kg)</td>
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<td>Inappropriate urinary concentration (urine osmolality &gt;100 mmol/kg)</td>
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<td>Elevated urinary sodium (&gt;20 mmol/l) (except during sodium and water restriction)</td>
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<td>Absence of clinical evidence of volume depletion or overload</td>
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<td>Normal renal function, absence of hypothyroidism and glucocorticoid deficiency and recent diuretic therapy</td>
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and he chooses to ignore the striking correlation between the clinical course, Na level and CRP concentration, as presented in our letter. He admits, however, that the Na level recovery after the prolonged course of hyponatraemia is probably due to better control of underlying inflammation.

It should be pointed out that correction of chronic hyponatraemia is often an elective procedure, because there are no pernicious symptoms or adverse events related to this type of hyponatraemia. If the decision to initiate treatment is made, fluid restriction remains the mainstay of treatment. The fact that this patient did not receive anti-ADH treatment—as she remained asymptomatic after discharge from hospital—provided an excellent opportunity to uncover and study the natural history of chronic SIADH in patients with inflammatory arthritis.

We believe that the inflammatory process secondary to rheumatoid arthritis was in great part responsible for initiating and propagating hyponatraemia in this instance. The proposed explanation for this was a possible chemokine-induced release of ADH. We were unable to identify another possible cause for SIADH, and Dr van Heyningen, in his comments, failed to provide a convincing alternative diagnosis.

V. V. KAUSHIK, K. BINYMIN
Department of Rheumatology, Southport and Ormskirk Hospital NHS Trust, Southport, UK
Accepted 25 February 2005
Correspondence to: K. Binymin, Southport District General Hospital, Town Lane, Southport PR8 6PN UK. E-mail: kbinymin2001@yahoo.co.uk