*Q J Med* 2008; **101**:591–598

# Correspondence

QJM

## The hidden anti-phospholipid antibody syndrome

Sir,

Kalita and colleagues report three interesting cases of women with cerebral venous sinus thrombosis leading to intracerebral haemorrhage.[1] However, they cited that the underlying conditions could not be identified, I disagree. The authors performed prothrombotic screenings but failed to include anti-phospholipid antibody syndrome (APS) among other differentials. These are common disorders, which might be the hidden causes in the patients[2] And cerebral venous sinus thrombosis is a well known complication of such disorder.[3,4] I believe that anti-cardiolipin antibodies and lupus anticoagulant must be screened in the authors' patients.

Last but not least, 'APS must be detected for any unknown hypercoagulable states'.

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## References

1. Kalita J, Bansal V, Misra UK, Jain SK. Intracerebral haemorrhage due to cerebral venous sinus thrombosis. *Q J Med* 2008; **101**:247–9.
2. Levine JS, Branch DW, Rauch J. The antiphospholipid syndrome. *N Engl J Med* 2002; **346**:752–63.
3. Stam J. Thrombosis of the cerebral veins and sinuses. *N Engl J Med* 2005; **352**:1791–8.
4. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. *Lancet Neurol* 2007; **6**:162–70.

doi:10.1093/qjmed/hcn063

Advance Access published on 12 May 2008

## A case of prolonged fatigue following an acute rickettsial infection

Sir,

We note the recent publication by Unsworth *et al.*[1] where a survey of individuals with chronic illness showed evidence of exposure to rickettsiae. Here, we report a case of prolonged fatigue following a serologically proven acute rickettsial illness in an otherwise well young man from Sydney, Australia.

A 33-year-old man, who lived in urban Sydney, presented with an acute febrile illness associated with rash. Symptoms began to develop 5 days prior to presentation. These were fevers, fatigue, decreased appetite, stiff joints and intermittent non-colicky right upper abdominal pain. The day of presentation, he developed a widespread rash.

The only medication was paracetamol for the acute symptoms. There was no significant past medical or psychiatric history. He lived in an urban area and worked as an accountant. On weekends, he was a 'surf life saver' on a beach near bushland in the northern suburbs of Sydney. This required a high level of physical fitness and activity. Three weeks prior to his presentation, he had travelled to Tasmania where he camped in bushland.

He appeared unwell was febrile (>38°C) and tachycardic. There was an erythematous macular and papular rash. The lesions were approximately 5 mm in diameter. The rash was distributed over the trunk and limbs, including the palms and soles (see Figures 1 and 2). No tick or eschar was detected. There was no lymphadenopathy. There was some mild abdominal tenderness in the right upper quadrant.

The lymphocyte count was $0.9 \times 10^9$/l (1.5–4.0). The neutrophil count was normal. C-reactive protein was 98 (mg/l) (<3). The erythrocyte sedimentation rate was normal. Urea, creatinine and electrolyte parameters showed no significant abnormalities. The liver function tests were initially normal. The alanine amino-transferase subsequently increased to 160 U/l (5–40). The chest X-ray was clear.

Urine microscopy and culture was negative. Blood cultures were negative.

A presumptive diagnosis of a rickettsial illness was made and this was confirmed on acute and convalescent serological testing (see Table 1). Rickettsial PCR testing on acute and convalescent specimens of blood was negative.

Doxycycline therapy was commenced and continued for 14 days. The majority of symptoms resolved over the next 72 h.

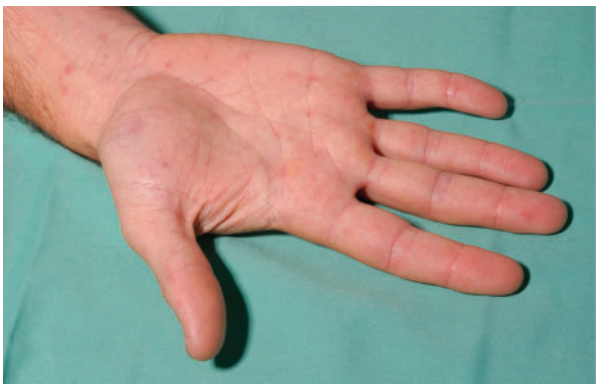

**Figure 1.** Rash on the palm of the hand.

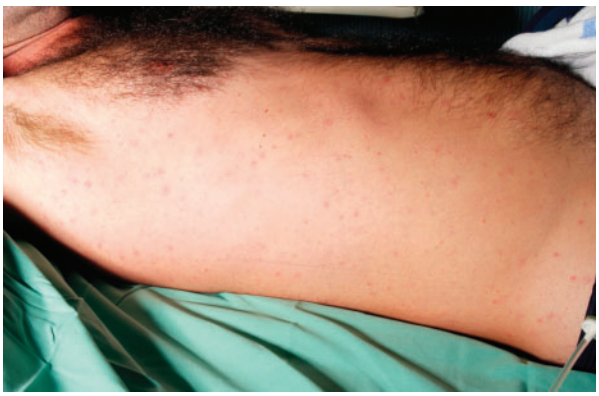

**Figure 2.** Rash on the trunk.

Fatigue was the most significant ongoing symptom. He described this as a lack of stamina or energy. This was associated with poor concentration, discomfort in the knees, muscular aches, frontal headache, reduced appetite, unrefreshing sleep and increased sleep duration. He denied substance abuse, depression or anxiety. He described feeling significant frustration at his decreased level of activity.

Investigations for other underlying medical causes of fatigue were negative and additional courses of doxycycline (up to 4 weeks) had no discernable effect.

He did not return to work for 7 weeks after the acute illness. The fatigue and other symptoms gradually resolved over ~2 years.

The main differential diagnoses of the acute rickettsial illness were the two tick-borne spotted fevers known to exist in Australia. Queensland tick typhus is caused by *Rickettsia australis* and Flinders Island Spotted Fever is caused by *Rickettsia honei*. *Rickettsia australis* infection has been contracted in the northern suburbs of Sydney where this man was a 'surf life-saver' and *R. honei* infection has occurred where he was camping in Tasmania.[2,3] However, due to the cross reactivity of human antibodies to rickettsial antigens it was not possible to confirm the identity of the causative organism.

The lack of response of the chronic symptoms to repeated courses of anti-microbial therapy is consistent with a post-infectious phenomenon rather than a chronic infection.

Unsworth *et al.*[1] document exposure to rickettsia in a cohort suffering from chronic symptoms. This is a novel case of prolonged fatigue occurring after an acute rickettsial infection.

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**Table 1** Rickettsial microimmuno-fluorescence serology results

| Rickettsial antigens | Dates of serum collection and titres<br>Positive titre ⩾128, negative titre <128 | | | |
|---|---|---|---|---|
| | Day of presentation | 22 days post-presentation | 35 days post-presentation | 562 days post-presentation |
| Spotted fever group[a] | <128 | 8192 | 4096 | 512 |
| Typhus group[b] | <128 | 4096 | 2048 | 128 |
| Scrub typhus group[c] | <128 | <128 | <128 | <128 |

[a] *Rickettsia australis* (Queensland tick typhus), *R. honei* (Flinders Island spotted fever).
[b] *Rickettsia prowazekii* (Epidemic typhus), *R. typhi* (Murine typhus).
[c] *Orientia tsutsugamushi* (Scrub typhus).

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## References

1. Unsworth N, Graves S, Nguyen C, Kemp G, Graham J, Stenos J. Markers of exposure to spotted fever rickettsiae in patients with chronic illness, including fatigue, in two Australian populations. *Q J Med* 2008; **101**:269–74.
2. Baird RW, Stenos J, Stewart R, Hudson B, Lloyd M, Aiuto S, *et al.* Genetic variation in Australian spotted fever group rickettsiae. *J Clin Microbiol* 1996; **34**:1526–30.
3. Unsworth NB, Stenos J, McGregor AR, Dyer JR, Graves SR. Not only 'Flinders Island' spotted fever. *Pathology* 2005; **37**:242–5.

doi:10.1093/qjmed/hcn064

Advance Access published on 12 May 2008

## The use of the sliding scale also needs to be reviewed

Sir,

Apart from the issue of administration of intravenous insulin to patients who are able to eat normally, and in whom subcutaneous insulin is not contraindicated[1] the other consideration worth addressing is the continuing prevalence of the sliding scale insulin (SSI) regime in clinical practice, exemplified by its use, albeit via intravenous infusion, in 10 of the patients in the study.[1] This should be a cause of concern, given the fact that the American Diabetic Association (ADA) guidelines discourage the use of the SSI, citing concerns about its potential to exacerbate both hyperglycaemia and hypoglycaemia.[2] Indeed, in one study, the sole use of the SSI (without either basal insulin or a separate nutritional insulin order) was associated with a 'daily average glucose reading that was . . . higher than that for those . . . not prescribed a sliding scale at all.'[3] The alternative is to base treatment on an initial evaluation of the admission glycosylated haemoglobin (HbA1c) level, and to calculate the dose of basal insulin on the basis of body weight.[4] The basal requirement should then be supplemented by short acting 'prandial' insulin (dose also based on body weight) administered with each meal so as to dampen down the postprandial surge in blood glucose. Even the subsequent fine tuning of prandial insulin (so-called correction dose insulin) can be made without recourse to SSI, the recommended strategy being a calculation based on a percentage of the initial total insulin dose.[4] Indeed, the ADA guidelines are at pains to point out that correction dose insulin should not be confused with the sliding scale because, as opposed to SSI, correction dose insulin does not refer to a set amount of insulin administered for hyperglycaemia without regard to the timing of the food.[2] Accordingly, it is appropriate to criticise, not only the use the intravenous insulin regime in patients who are able to eat,[1] but also the use of a sliding scale which is based neither on a correction of prandial insulin requirements, nor on the intention to supplement basal insulin requirements. The SSI, however, permeates all aspects of clinical practice, including the management of diabetic ketoacidosis (DKA).[5] In the 'recovery' phase of DKA, the recovery phase being defined as the one characterized by a fall in blood glucose to levels, below 14 mmol/l,[6,7] the main rival to the SSI is a regime based either on a 'match' between the dose of insulin and the dextrose content of the rehydrating fluid,[6] the 'insulin/rehydrating fluid' match or a 'match' between the doses of insulin, the dextrose content of the rehydrating fluid and the patient's body weight,[7] the 'insulin/rehydrating fluid/body weight' match. In the 'insulin/rehydrating fluid' match a 2.5 units/h continuous infusion of insulin is matched with 1 l/4 h infusion of 5% dextrose, and a 10 units/h infusion of insulin is matched with a 1 l/4 h infusion of 10% dextrose).[6] In this regime, the comparison between 2.5 units/h insulin (with matching 5% dextrose) and 10 units/h insulin (with matching 10% dextrose) showed no difference in the rate of resolution of acidosis. However, at the expense of higher final levels of blood glucose (higher by ~2.0 mmol/l), the 10 units/h regime achieved a significantly more rapid resolution of ketonaemia.[6] In the 'insulin/rehydrating fluid/body weight' match insulin 0.05–0.1 units/kg body weight per hour is matched with either 5% dextrose or 10% dextrose.[7] Comparative rates of resolution of acidosis and ketonaemia are not available for the 'insulin/rehydrating fluid/body weight' regime but, in view of the fact that it generates a dose of insulin in the range 2.5–6.0 units/h it is reasonable to extrapolate that it compares favourably with the 'insulin/rehydrating fluid' regime in its rate of resolution of acidosis. In contrast with the evidence base for the rate of resolution of acidosis and ketonaemia obtained from the 'insulin/rehydrating fluid' match,[6] there is no documentation of the rate of resolution of these parameters following the use of the SSI during the recovery phase of DKA. Accordingly, this is one more reason for phasing out the SSI, a reason justified, in my view, by the misgiving that 'the