

Letters to the Editor

Hyponatraemic rhabdomyolysis in Addison's disease

Sir,
The protean manifestations of rhabdomyolysis include, not only the biochemical derangements listed in the case report by Egan *et al*,¹ but also a spectrum of haematological manifestations, ranging from disseminated intravascular coagulation² to non-specific pancytopenia,³ which can obscure recognition of this syndrome, with consequent diagnostic delay. This was exemplified by an 81-year-old woman admitted to this hospital in February 1993 with a recent fall preceded by generalised aches and pains of a few days' duration. She had clinical stigmata of congestive cardiac failure and a temperature of 38°C. She was taking bumetanide 10 mg, enalapril 5 mg, isosorbide mononitrate 60 mg, and a variable dose of cocodamol daily. Her haemoglobin (Hb) was 9.3 g/dl, mean corpuscular volume = 86.7 fl, mean corpuscular haemoglobin = 27.4 pg, white blood count (WBC) = 1600/mm³, with 84% neutrophils and 4% metamyelocytes. Platelet count = 97000/mm³. The blood film showed a moderate degree of anisocytosis, and many non-segmented neutrophils. Although the electrocardiogram only showed non-specific ischaemia, the total creatine phosphokinase (CPK) level was 3338 with absence of the MB isoenzyme. Other biochemical investigations are shown in the table. Blood and urine cultures were sterile, and the urinary dipstick test showed no abnormality. On admission, and on follow up, significant hepatotoxicity was ruled out by the fact that serum bilirubin and γ -glutamyl transferase levels were normal. In view of pancytopenia, she was also investigated for vitamin B₁₂ and folate deficiency (see table). Her subsequent biochemical tests showed transient hypocalcaemia, and her WBC and platelet counts eventually reverted to the normal range (table). Her management included cessation of enalapril, due to renal dysfunction, and the use of sustained-release morphine for relief of disabling muscle pains. Sixteen days later, she was afebrile, pain free, and independently mobile.

Comment

The association of disabling muscle pains, marked elevation of non-cardiac creatine phosphokinase, transient hypocalcaemia, and reversible renal failure formed the basis for the diagnosis of rhabdomyolysis,⁴ notwith-

standing the normal urinary dipstick tests,⁵ although confirmation by serum myoglobin assay had not been sought because the index of diagnostic suspicion was low, due to the fact that the clinical picture was dominated by the haematological derangements. The latter were initially perceived to be the result of septicaemia, or deficiency of vitamin B₁₂ and/or folate. In the event, as in the case reported by Feldman,² pancytopenia appeared to be entirely consistent with rhabdomyolysis *per se*, the haematological profile possibly being a component of multiple organ dysfunction.⁶ The spurious elevation of serum vitamin B₁₂ might have been the result of the fact that this vitamin, which is stored not only in the liver but also in skeletal muscle,⁷ had been released into the blood stream as a result of rhabdomyolysis.

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- 1 Egan JJ, Davies AJ, Jones MC. Hyponatraemic rhabdomyolysis in Addison's disease. *Postgrad Med J* 1994; 70: 830-2.
- 2 Prendergast D, George CF. Drug-induced rhabdomyolysis: mechanisms and management. *Postgrad Med J* 1993; 69: 333-6.
- 3 Feldman R. Rhabdomyolysis (clinical conference). *N Y State J Med* 1988; 88: 582-8.
- 4 Gabow PA, Kaehny WD, Kelleher SP. The spectrum of rhabdomyolysis. *Medicine (Baltimore)* 1982; 61: 141-52.
- 5 Marcus EL, Rudensky B, Sonnenblick M. Occult elevation of CK as a manifestation of rhabdomyolysis in the elderly. *J Am Geriatrics Soc* 1992; 40: 454-6.
- 6 St John R, Dorinsky PM. An overview of multiple organ dysfunction syndrome. *J Lab Clin Med* 1994; 124: 478-84.
- 7 Chanarin I. Vitamin B₁₂ - nutritional aspects. In: *The megaloblastic anaemias*. Oxford, Edinburgh: Blackwell Scientific Publications, 1969; p 48.

This letter was shown to the authors, who responded as follows:

Sir,
Drs Jolobe and Sen emphasise the importance of recognising occult rhabdomyolysis in clinically complex patients. In a similar fashion to our report, their case demonstrates that unless there is a high index of suspicion, particularly in elderly patients with multi-organ dysfunction, rhabdomyolysis may go unrecognised and contribute to renal impairment in the absence of urinary myoglobinuria.

In our publication we have suggested a causal relationship between severe Addi-

sonian hyponatraemia and the subsequent onset of rhabdomyolysis. In contrast their case appears to describe an association, not a causal relationship, between pancytopenia and rhabdomyolysis in an elderly patient with multiorgan dysfunction.

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Clinical guidelines

Sir,
The recent discussion of clinical guidelines¹ is most welcome. As guidelines are developed and introduced with increasing frequency it is important that clinicians become familiar with the issues surrounding them. I would like to make some additional points.

The article did not define guidelines. The definition of 'practice guidelines' proposed by the Institute of Medicine² may reduce anxieties about them: 'systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances (my italics)'. This definition emphasises the positive role guidelines may play when appropriately developed and implemented. Thus defined they are not the coercive managerial instruments some clinicians fear.

The second point concerns guideline development. Systematic reviews should be pivotal in guideline development. Guidelines based on other types of review or on consensus are prone to bias and may reflect this bias rather than the 'best' evidence. Everyone involved in guideline development or use should ensure that guidelines are not having a detrimental effect on patients, a potential danger of inappropriately developed guidelines. Guidelines based on consensus may have a further drawback. In order to reach agreement the wording of such guidelines may be so vague as to render the guideline useless: 'Consensus means that lots of people say collectively what nobody believes individually.' (Abba Eban)

My final point concerns the effectiveness of practice guidelines. Ideally the impact of a new guideline on patient outcome should be prospectively evaluated. If adverse events are infrequent, and if there is very strong evidence to support a guideline's recommendations, the process of care (the level of

Table Serial biochemical and haematological tests

Date	Sodium (mmol/l)	Potassium (mmol/l)	Urea (mmol/l)	Creatinine (μ mol/l)	Calcium (mmol/l)	Albumin (g/l)	CPK (IU/l)	Hb (g/l)	WBC (mm^{-3})	Platelets (mm^{-3})	Vitamin B ₁₂ (ng/l)
20/2/93	138	4.7	26.0	225			3338	9.3	1600	97 000	
22/2/93	127	4.2	36.1	308	1.94	34.5	2888				2255
2/3/93	133	5.0	34.5	320	2.21	37.9	129	10.1	11 400	417 000	
28/4/93	140	4.4	11.6	161				10.3	5700	285 000	
16/11/94	144	4.7	9.6	116							
23/11/94								11.6	9000	240 000	392
Reference range	135-146	3.5-4.8	2.5-6.5	40-110	2.12-2.63	37-50	38-148				170-900