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Letters to the Editor

Biochemical diagnosis of myocardial infarction? Cardiac enzymes or *caveat emptor*

Sir,

The use of biochemical markers, and in particular serum creatine kinase (CK) activity, in the diagnosis of myocardial infarction has received renewed interest because of the advent of thrombolytic therapy,[1] which has resulted in pressure to make an early diagnosis in order to maximize the efficacy of treatment. Unfortunately, CK is also present in skeletal muscle and is released following muscle trauma, ischaemia or any inflammatory episode.[2] This limits its diagnostic specificity as a test for myocardial infarction. We wish to report a case of initial misdiagnosis in a patient at high risk of myocardial infarction because of familial hypercholesterolaemia, who was subsequently found to have a drug-induced skeletal myopathy caused by a lipid-lowering drug.

A 46 year old man with known coronary artery disease was admitted to the coronary care unit following several episodes of crushing central chest pain. An electrocardiogram (ECG) showed no evidence of ischaemia but his serum CK activity was 1,380 U/l (reference range 24-195). In view of the history and high serum CK activity a diagnosis of myocardial infarction was made. Over the next 48 hours, he experienced no further chest pain and no ECG changes developed, However, the serum CK activity continued to rise, reaching 5,825 U/l at 48 hours. A possible skeletal muscle origin for the CK was therefore considered. There had been no muscle trauma or vigorous exercise. He denied excessive alcohol intake. He was biochemically euthyroid. Serum CK-MB concentration was normal (less than 10 ng/ml), and cardiac troponin-T was undetectable in all samples. On subsequent questioning it emerged that he had been commenced on treatment with simvastatin for familial hypercholesterolaemia 10 days before admission. The most likely cause for the rise in serum CK activity was therefore a simvastatin-induced myopathy. Treatment was stopped, the serum CK activity peaked within 72 hours and then fell to normal levels within 21 days. The original diagnosis of myocardial infarction was revised to unstable angina.

There is a greatly increased incidence of ischaemic heart disease in familial hypercholesterolaemia.[3] Many patients with this condition are now treated with an HMG CoA reductase inhibitor such as simvastatin. Skeletal myopathy is a rare complication of treatment, although subclinical myopathy with a rise in serum CK activity is commoner.[4] It follows that there is a small but significant possibility of misdiagnosis of myocardial infarction if a patient on treatment with an HMG CoA reductase inhibitor presents with non-infarcting ischaemic chest pain. The absence of ECG evidence of myocardial infarction in the presence of a very high serum CK activity is the initial characteristic feature of this presentation, and subsequent measurements will fail to demonstrate the expected fall in CK activity after 24 hours. Measurement of serum CK-MB[2] or cardiac troponin T[5] levels are valuable second line investigations. Above all, we believe that the clinician should be aware of this cause of misdiagnosis of myocardial infarction, especially when considering treatment with potentially hazardous thrombolytic therapy.

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Thrombophlebitis and Reiter's syndrome

Sir,

Seronegative asymmetric arthropathy, urethritis and conjunctivitis make up the characteristic triad that most commonly defines Reiter's syndrome.[1,2] Different complications have been reported, among them thrombophlebitis of leg deep veins.[3] However, the intimal-coagulation abnormality is unknown. We describe herein a patient with Reiter's syndrome who developed this complication in the acute stage of his disease and in whom a thorough coagulation study failed to find any abnormality.

A 29 year old man was admitted because of urethritis and polyarthritis of metatarsophalangeal joints. He was well until 5 days after an unprotected sexual contact with a prostitute when he experienced dysuria and a purulent urethral discharge. Three days later, he developed arthritis in the metatarsophalangeal joints of both feet and in the left knee. On physical examination there were slight conjuctival injection in both eyes, along with signs of arthritis in those joints. No stomatitis was present but a few painless, superficial erosions with surrounding erythema were evident on the glans penis.

Blood cell counts were normal and the ESR was 77 mm/hour. There were slight increases in transaminases and a polyclonal increase in gammaglobulins. Other biochemical parameters were normal including C_3 and C_4 measurement. The VDRL and the FTA-ABS tests were

negative as were the serum *Chlamydia trachomatis* antigen by ELISA, rheumatoid factor and antinuclear antibodies. HLA B27 was positive. A bone scintigraphy revealed an abnormal uptake in the left knee and metatarsophalangeal joints. The synovial fluid of the left knee revealed: normal glucose protein 72 g/l, many red and white cells with 79% neutrophils.

The urine culture was negative. Gram stain of the urethral discharge disclosed Gram-positive cocci, but the culture was negative, perhaps because the patient had been previously treated with doxycycline. The patient, with a clinical diagnosis of Reiter syndrome, was put on indomethacin with some improvement and was discharged home. Two days later, the patient was newly admitted with swelling of his left leg below the knee. A venography revealed several defects on the femoral venous system indicative of a deep venous thrombosis.

Parameters of coagulation and fibrinolysis were normal, including the number of platelets, prothrombin, partial thromboplastin and thrombin times, antithrombin III functional antigen, functional plasminogen levels, functional plasminogen activator inhibitor, and the protein S and C activity. Anticardiolipin antibodies were negative. The patient was anticoagulated with rapid resolution of the picture. Nine months later he remains well.

Hypercoagulable state defines a concept which has been related to several rheumatic diseases as well as different conditions.[4] In our patient we could not find any abnormality in the coagulation system, so that other unknown mechanisms could have taken place.

Although Csonka described the occurrence of thrombophlebitis in Reiter's syndrome many years ago,[5] we have been unable to find reports from other authors in a review of the literature using MEDLINE files back through 1966. Moreover, in no reported case has the patient undergone a complete coagulation study to exclude underlying coagulation abnormalities. Although infrequent, thrombophlebitis should be considered as another complication of Reiter's syndrome. However, the intimal coagulation abnormality remains unknown.

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Poisoning from topical salicylic acid

Sir,

Treatments applied to the skin may have unwanted systemic effects. We report a patient who suffered poisoning from topical salicylic acid.

A 42 year old woman who suffered from psoriasis was prescribed 10% salicylic acid in white soft paraffin by her general practitioner. This was intended for application to localized areas of hyperkeratosis but the patient used it widely on her trunk and limbs. We estimate that she applied 50 g of the ointment daily over a 10 day period. She was not taking any oral medication; her body weight was 45 kg. Her psoriasis deteriorated and she was admitted to hospital. Two days before admission she had developed deafness and nausea.

On admission almost her entire skin was affected by psoriasis. She was agitated and had a pyrexia and a tachycardia. Serum salicylate (measured 14 hours after the last application of the ointment) was 2.6 mmol/l (therapeutic range up to 2.2 mmol/l). Serum bicarbonate was 13 mmol/l (normal range: 22–28 mmol/l); renal and hepatic function were normal. The topical salicylic acid was discontinued and supportive treatment was given. Twenty-four hours later her symptoms had resolved and her vital signs were stable; serum bicarbonate was normal and serum salicylate had fallen to 1.5 mmol/l.

The patient suffered poisoning primarily because a high concentration of salicylic acid was applied to a wide area. Her low body mass made her more susceptible to toxicity. Absorption of the drug was increased because of the inflamed condition of the skin. Chronic administration of salicylic acid may produce intoxication at serum levels lower than those seen in acute poisoning.[1]

Most previous reports of salicylate poisoning have arisen during intensive treatment of ichthyotic conditions in hospital.[2–4] Our report illustrates that salicylate poisoning may also occur in ambulant patients. It is often difficult to ensure that treatment is applied according to instructions in such patients. We advise caution in the use of high concentrations of salicylic acid.

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