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Clinical Reports

Focal myositis and elevated creatine kinase levels in a patient with phaeochromocytoma

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Summary: A case of phaeochromocytoma with marked transient elevation of creatine kinase levels is presented. No obvious cause for the elevation was found in life, but on autopsy a non-specific focal myositis was discovered. Possible reasons for the raised creatine kinase levels and focal myositis are discussed.

Introduction

Raised catecholamine levels are known to cause focal myocarditis in patients with phaeochromocytoma and similar lesions are seen in rats experimentally infused with large amounts of noradrenaline and adrenaline (Van Vliet *et al.*, 1966). However, focal myositis in skeletal muscle has not been previously associated with phaeochromocytoma.

We report a patient with phaeochromocytoma who presented with muscular symptoms, markedly elevated creatine kinase and was found to have non-specific focal myositis at autopsy.

Case report

A 54 year old unemployed cleaner was admitted with confusion, headache, severe generalized muscle pain and weakness for 3 days. He had a past history of palpitations, anxiety and depression, but had normal electrocardiograms and was normotensive on all the four outpatient visits over the previous one and a half years.

On admission, he was hypertensive and had retinal haemorrhages in both eyes. Muscle tenderness was elicited in most muscle groups in the arms and legs.

Within an hour he developed pulmonary oedema and was given oxygen, diuretics and a salbutamol infusion. The electrocardiogram showed no changes suggestive of myocardial infarction. Emergency investigations at this stage showed early renal failure and a metabolic acidosis with a raised anion gap.

The muscle tenderness persisted and over the next few days he had episodes of sweating, tachycardia and hypertension which continued despite treatment with labetalol initially, and later with phenoxybenzamine. His renal failure progressed, needing repeated dialysis and he suffered cardiac arrests on the sixth day, the sixteenth day and finally on the twentieth day after admission, when he died despite attempted resuscitation. The initial creatine kinase was 775 U/l (normal 10–70) which peaked at 13280 U/l 3 days after admission. The aspartate aminotransferase and lactic dehydrogenase levels were also raised.

A 24 hour urinary collection for 4-hydroxy-3-methoxy mandelic acid (HMMA) was 124 μmol/24 h (normal up to 40 mmol/24 h) thereby supporting a clinical suspicion of phaeochromocytoma. Further evidence was obtained by an ultrasound scan which located a mass behind the liver and elevated plasma catecholamines (noradrenaline 25 pmol/l (normal 1–3 pmol/l), adrenaline 4.4 pmol/l (0.1–0.4 pmol/l) and dopamine 3.0 pmol/l (0.2–0.4 pmol/l)). Tests for myoglobin in urine and serum were negative on two occasions. The initial and repeated blood cultures were negative. Viral antibody titres on paired sera taken 15 days apart were negative for influenza A and B, psittacosis, mumps, adenovirus, mycoplasma, herpes, cytomegalovirus and Coxsackie B viruses.

All electrocardiograms taken showed ischaemic changes, but were not diagnostic of myocardial infarction at any time.

On autopsy a cystic tumour weighing 290 g was present in the right adrenal. Histological examination with electron microscopy showed findings typical of phaeochromocytoma. There was no evidence of tumour metastases. The heart showed left ventricular hypertrophy with minimal coronary atheroma and there was no evidence of myocardial infarction or myocarditis.

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In skeletal muscle non-specific focal myositis was seen. This is illustrated in Figure 1 which shows degeneration of muscle fibres, increase in sarcolemmal nuclei, giant cells and muscle phagocytosis in tissue taken from the diaphragm.

Discussion

The main presenting features in this patient were the muscular symptoms. From the findings of focal myositis at autopsy it is most likely that the source of the raised creatine kinase was skeletal muscle. The absence of myocardial infarction, myocarditis, muscle trauma, intramuscular injections and high viral titres suggests that these are an unlikely cause of the creatine kinase elevation. Shock can cause a rise in many tissue enzymes but the rise in creatine kinase was out of proportion to that of the other enzymes.

Drug-induced focal myopathy (Mastalgia, 1980) is unlikely as our patient on admission was on atenolol and was later given salbutamol, diuretics and antibiotics, none of which cause focal myositis.

Oristrell-Salva' & Miradacanals (1984) in a brief unreviewed report describe a patient with phaeochromocytoma presenting with renal failure, pulmonary oedema and dark red urine accompanied by a creatine kinase level of 30,000 IU/l. The enzyme levels became normal in 7 days and the tumour was later removed successfully. They describe the episode as rhabdomyolysis but do not mention any myoglobin measurements or muscle studies. In our patient the urine was never red and we could not demonstrate any myoglobin in either serum or urine.

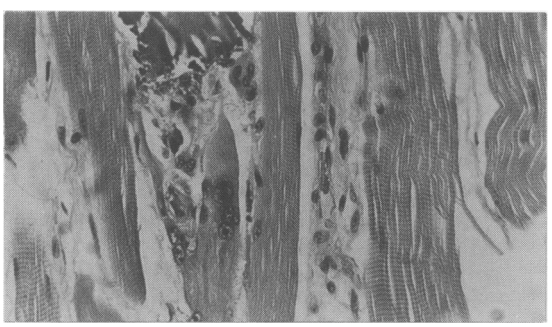

Figure 1 Focal myositis and elevated creatine kinase levels in a patient with phaeochromocytoma.

We postulate that the massive rise in creatine kinase in our patient was due to focal myositis resulting from a large discharge of catecholamines from the chromaffin tumour. No previous association between myositis and phaeochromocytoma has been reported and the mechanisms involved have not been explored.

Under physiological conditions, catecholamines result in increased force of contraction through beta-receptor stimulation (Bowman & Raper, 1967) and enhanced release of acetylcholine at the neuromuscular junction (Goldberg & Singer, 1969). Additionally, glycogenolysis is increased locally in muscle and also in the liver, providing fuel for the extra activity (Himms-Hagen, 1972).

In phaeochromocytoma the release of large amounts of catecholamines could, through vasoconstriction and increase in force of contraction, precipitate ischaemia and necrosis in skeletal muscle. This would also explain the weakness, fatigue and prostration experienced by some patients following a paroxysm.

Myocarditis, which is known to occur in catecholamine excess (Van Vliet *et al.*, 1966) was not seen in our patient. Our patient may have been protected by beta-blockers which have a protective effect (through unknown mechanisms) against catecholamine induced damage to myocardium (Weiner, 1980).

It therefore seems that skeletal muscle damage can result from excessive catecholamine release in phaeochromocytoma and elevated creatine kinase levels may be an indication of focal myositis.

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