Short report

The forearm ischaemic work test — hazardous to McArdle patients?

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SUMMARY A 57-year-old patient suffering from late-onset McArdle's disease developed myoglobinaemia, massive myoglobinuria and marked serum creatine kinase elevation subsequent to a routinely performed forearm ischaemic work test. Twenty hours after the test, enhancement of ^{99m}Tc methylene-diphosphonate activity was demonstrated exclusively in the tested forearm. It is concluded that the forearm ischaemic work test is potentially hazardous to McArdle patients, as it might induce myoglobinuria sufficient to result in acute myoglobinuric renal failure.

The forearm ischaemic work test is established as a useful tool for differentiating between myopathies with and without defects of anaerobic glycogenolysis and glycolysis. So far no dangerous effects of this test have been described. We report a case of late-onset McArdle's disease¹ (glycogenosis V²), in which massive myoglobinaemia and myoglobinuria developed subsequent to this test. By means of conventional whole body bone scanning, local rhabdomyolysis was demonstrated in the tested forearm.

Case report

A 57-year-old male patient complained of weakness and rapid fatigue of his shoulder and arm muscles as well as intermittent claudication-like cramps in his legs in the four years prior to admission (1980). Since 1979, elevated serum creatine kinase (120–560 μl , normal range: 2–70 μl) and creatinine (101–160 $\mu\text{mol/l}$, normal range: 44–97 $\mu\text{mol/l}$) levels were noted. Initially these complaints and symptoms were ascribed to chronic arterial occlusive disease and alcoholic polyneuropathy, since the patient had been an alcoholic and a heavy smoker. There was no history of excretion of dark urine, of myoglobinuria, or of acute renal failure, nor was there any evidence of exercise-induced contractures. In retrospect, however, a typical "second wind" phenomenon was described. There was no relevant family history. In March 1980, the patient underwent abdominal surgery for duodenal ulcer, and did not drink alcohol thereafter. However, his complaints of muscular weakness

increased, and serum creatine kinase and creatinine levels remained high. Serum lactate dehydrogenase (normally below 195 μl) was observed between values of 163 and 263 μl . Repeated ECGs and tests of left ventricular function (measured scintigraphically by means of gated blood pool imaging) were normal.

Neurological examination revealed atrophy and paresis (degrees III to IV on the MRC scale) of the shoulder girdle and proximal arm muscles including bilateral scapula winging, and paresis of the ankle dorsiflexors. Deep tendon reflexes were brisk in the arms, but weak or lacking in the legs. Abdominal and plantar reflexes were normal, but the palmomental, glabellar, and snout reflexes were positive. There was a stocking-like sensory loss for touch, pin-prick, and vibration in his legs, and ataxia was evident when he stood with his eyes closed. Orthodromic measurement of sensory conduction velocities (right sural and left median and ulnar nerves) revealed no nerve compound action potentials. The motor nerve conduction velocity of the right peroneal nerve was 40 m/s and distal motor latency 5.2 ms (both values abnormal), whereas in the left median nerve they were within the normal range. Electromyography of the shoulder and proximal arm muscles revealed disseminated low-intensity fibrillation and positive sharp waves. Motor unit potentials were on the whole normal, but there were a few shortened (2–5 ms) as well as polyphasic and prolonged (15–30 ms) potentials as well. In the ankle dorsiflexors, typical and distinct signs of a neurogenic alteration were observed. These findings were interpreted as indicating an alcohol polyneuropathy plus either a toxic shoulder girdle amyotrophy, or a spinal muscular atrophy. In order to exclude chronic regional alcohol rhabdomyolysis as a possible cause of serum creatine kinase elevation, a whole body ^{99m}Tc methylene-diphosphonate scan was performed which yielded no abnormal findings. Biopsies from the biceps and quadriceps muscles revealed increased fibre diameter, rare phagocytosis within muscle fibres, rimmed vacuoles, and vacuoles located in the periphery of several muscle fibres.

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after deflating the cuff, and excessive myoglobinuria was observed during the subsequent night (fig A). In order to prevent renal failure due to myoglobinuria, the patient was instructed to drink at least 3 l per day in the following days, and serum creatinine levels remained in the pre-test range during the next week. The serum creatine kinase initially remained at the pre-test level, too, but the following morning was found to be about 10 000 μ /l. Both myoglobinuria and increased serum creatine kinase fell to the base line levels in the following days, the creatine kinase showing a delayed decline.

Because of suspected iatrogenic rhabdomyolysis due to the forearm ischaemic work test, a whole body scan was performed about 20 hours after the test. A distinct enhancement of ^{99}Tc methylene-diphosphonate was found to be restricted to the musculature of the right forearm (fig B). Six weeks later, a scan showed normal distribution of the tracer.

Discussion

From these results it seems that local rhabdomyolysis in the right forearm and subsequent myoglobinuria were induced by the ischaemic work test. As our patient exhibited the typical features of late-onset McArdle's disease,^{1,4,5} muscle phosphorylase deficiency is most likely the basis for iatrogenic rhabdomyolysis. However, one might speculate as to whether his previous alcoholism played an additional role in the pathogenesis of myophosphorylase deficiency and local rhabdomyolysis in our patient. Although alcoholism may impair muscle phosphorylase activity (see ref 6), virtual absence—enzyme-histochemically as well as biochemically—of phosphorylase activity from striated muscle, as well as the fact that the patient had not consumed alcohol since his abdominal surgery one year prior to the biopsies, militate against his phosphorylase deficiency as being due to chronic alcoholism. However, an additional sensitisation of the primarily diseased muscle metabolism is possible.

Generally, the forearm ischaemic work test is well tolerated, and the outcome of this diagnostic procedure in our patient contrasts with its apparently good tolerance even by McArdle patients. However, it must be remembered that more than 50% of McArdle patients show myoglobinuria, and renal failure due to myoglobinuria was reported in 8%.⁷ Moreover, Kula *et al*⁸ and Swift and Brown⁹ reported signs of focal rhabdomyolysis and creatine kinase elevations after the ischaemic work test, but did not follow myoglobin levels in serum and urine. Our case report shows that myoglobinuria and serum creatine kinase might increase after the test to levels at which—particularly under unfavourable circumstances such as dehydration or low urinary pH—acute myoglobinuric renal failure might occur.^{6,10,11} Moreover, if our patient did not drink large quantities of water, myoglobin

concentrations in urine would have most probably increased to substantially higher levels.

The forearm ischaemic work test must therefore be considered potentially hazardous to McArdle patients. Therefore renal function as well as creatine kinase and myoglobin levels should be carefully checked after this test. A sufficient diuresis should be induced, simply by prescribing large quantities of water. In addition, a ketogenic diet possibly prevents rhabdomyolysis and creatine kinase elevation after the test in McArdle patients⁸.

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