Compartment syndrome during an ischaemic forearm exercise test

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THE CASE
A 32-year-old man presented with a history of progressive exercise intolerance, exertional myalgia and cramps since childhood. He also complained of shortness of breath on exertion, without any orthopnoea. On examination he had mild proximal upper and lower limb weakness. His facial muscles and neck flexors were normal and there was no scapular winging. His tendon reflexes and sensory examination were normal. Serum creatine kinase (CK) levels were mildly raised at 493 IU/L (reference range < 180 IU/L).

He underwent an ischaemic forearm exercise test, exercising for 40 s, and his effort was felt to be very good. However, later that afternoon he was reviewed because he was complaining of continuing pain in his forearm and inability to extend his fingers. He was treated with analgesia. CK levels were re-checked at this point and were markedly elevated at 4930 IU/L (reference range < 180 IU/L).

The patient had clearly developed a compartment syndrome and was referred to the orthopaedic surgeons. He underwent emergency fasciotomy. At operation he required release of both the superficial and deep fascia of the forearm. His recovery was incomplete and he has been left with persistent sensory loss in the distribution of the median nerve.

A muscle biopsy was performed at a later date and confirmed the diagnosis of glycogen storage disease type IV (Fig. 1).

GLYCOGEN STORAGE DISEASE TYPE IV (ANDERSEN’S DISEASE)
Andersen’s disease is an autosomal recessive condition caused by branching enzyme deficiency, typically affecting liver and muscle. The clinical pattern depends on the age of onset. The classical presentation is of failure to thrive, hepatomegaly and progressive hepatic failure. There may also be evidence of myopathy and cardiomyopathy. Onset is usually in infancy but childhood onset is also described and usually presents with cardiomyopathy (Bao et al. 1996). Adult onset is much rarer and presents with myopathy and proximal weakness, as in our patient. This must be distinguished from Adult Polyglucosan Body Disease, which is a clinical variant also due to branching enzyme deficiency; these patients have mixed upper and lower motor neuron involvement, sphincter problems and dementia.

Figure 1. Muscle Biopsy. (A) Transverse section showing glassy, pale but eosinophilic material around the edge of the fibre. Special stains showed this to be glycogen. (B) Electron micrograph showing glycogen storage material in muscle.
The diagnosis is based on liver or muscle biopsy that shows accumulation of abnormal glycogen and PAS positive material, polyglucosan bodies, as well as a deficiency of glycogen branching enzyme activity.

THE ISCHAEMIC FOREARM EXERCISE TEST

The ischaemic forearm exercise test is used as a screening tool to look for metabolic myopathies, in particular glycogenoses. The rationale is that, during vigorous exercise, muscle normally generates lactate through anaerobic metabolism of glycogen, and this can be measured in venous blood draining the forearm. It has been argued that the addition of ischaemia causes more vigorous production of lactate, although this hypothesis has been challenged (see below). Ammonia is also produced.

The most widely practised method of performing this test (there is slight variation between centres) begins with a baseline antecubital venous sample taken for lactate and ammonia levels, ideally without the use of a tourniquet. A sphygmomanometer cuff is then applied to the upper arm and inflated to well above systolic blood pressure, e.g. 200 mmHg. The patient is asked to perform vigorous repetitive forearm exercise, such as squeezing a ball at one grip every 1–2 s, aiming to continue for at least a minute. The normal patient is unlikely to exceed 90 s while patients with metabolic myopathies are unlikely to exceed 40 s. The duration of the exercise are documented. The cuff remains inflated for another minute. Further venous samples for serum lactate and ammonia are taken on release of the cuff, at 2 mins and then at 5, 10 and 20 mins. Urine passed over the next 12 h may be sent for myoglobin analysis if it is discoloured.

A normal response is at least a three-fold rise in lactate on the immediate sample postexercise and then a gradual decline. The ammonia level should also rise, five- to 10-fold. An abnormally attenuated lactate response (i.e. less than a three-fold rise) suggests a glycogenosis because lactate cannot be generated anaerobically in these patients. If ammonia levels fail to rise then a low lactate level may be due to submaximal effort. Alternative diagnoses may be revealed by this test. A flat ammonia response with a normal, or even slightly reduced, lactate response, is suggestive of myoadenylate deaminase deficiency (Livingstone et al. 2001).

THE AVOIDABLE COMPLICATION

Our patient suffered what must be an extremely rare but serious complication of the ischaemic forearm exercise test. This has been previously reported in a patient with McArdle's disease in very similar circumstances (Lindner et al. 2001). Compartment syndrome is caused by muscle swelling within fascial planes leading to muscle ischaemia and oedema, thereby setting up a vicious cycle of further swelling and muscle necrosis. This is an emergency and the degree of permanent damage is determined by the rapidity of surgery. Therefore, after the test, any patient with prolonged pain and contractures should be closely observed. Failure of these symptoms to resolve, tense forearm muscle groups and the development of paraesthesiae should lead to an urgent orthopaedic assessment. Loss of the radial pulse is a late sign and suggests irreparable damage has already occurred.

Pain and brief contractures are a much more common complication of the test, particularly in patients with metabolic myopathies. In McArdle's original case described in 1952, the ischaemic forearm test produced a painful contracture within a minute. McArdle himself felt that this response resembled the reaction of a fish poisoned by iodoacetate, which he knew blocked glycolysis (Bradley et al. 1996). Chui et al. also described painful contractures lasting between 4 and 10 minutes post-exercise in a family with McArdle's syndrome (Chui & Munsat 1976). Rhabdomyolysis is potentially the most serious complication. Meink et al. reported a patient who developed a painful contracture and excessive myoglobinuria after the ischaemic forearm test (Meink et al. 1982).

REDUCING THE RISK IN THE FUTURE

One question raised is whether the risks involved in the ischaemic forearm exercise test could be reduced while still maintaining accuracy. Bruno et al. inflated the cuff to, but not above, mean arterial pressure, their main aim being to see if this variation on the test improved compliance in paediatric patients without reducing accuracy (Bruno et al. 1998). Only two patients suffered mild forearm pain and none experienced contractures. However, the test was felt to be unreliable in patients under the age of 10 because of poor cooperation. In all 20 cases with a negative ischaemic forearm test the muscle biopsy was normal, and the two patients with a positive test both had an abnormal muscle biopsy.
It has also been suggested that occluding the blood supply at all is unnecessary because it adds little benefit while increasing the risk of contractures. Initially during exercise, the aerobic process and fatty acid oxidation provide energy. However, if particularly vigorous, the circulation is unable to deliver sufficient oxygen and fatty acids and the muscle quickly begins to provide energy by anaerobic glycogenolysis and lactate is produced. As a consequence there may be little merit in performing the exercise under ischaemic conditions (Hilton-Jones 2001). A small study involving nine patients with McArdle’s disease and nine controls has suggested that a non-ischaemic forearm test is well tolerated and reliably differentiates between the two groups (Kazemi- et al. 2002). A prospective study would be able to compare different methods, their accuracy and the frequency of adverse effects (such as duration of contractures and severity of pain). Due to the low risk of most complications this would need to be a multicentre study.

We believe that standard practice should be reviewed and reformed, either by performing the test without a cuff or with the cuff inflated to no more than mean arterial pressure.

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REFERENCES