

An elevated creatine kinase in a healthy young man

Commentary by **COREY CUNNINGHAM** MB BS, FRACGP, MSpMed

What are the possible causes of this young man's raised creatine kinase level, and how relevant is this finding?

Case scenario

A 28-year-old Australian (Caucasian) engineer who had been living and working in China for the past three years returned for a holiday and requested a full physical check up. For the two months before his return he had been very busy and had not been exercising much, but prior to that he had been going to the gym regularly and playing rugby. A history revealed no obvious past health problems, safe (heterosexual) sex practices, erratic nutrition (eating take away meals regularly) and regular heavy alcohol intake (at least six standard drinks daily). He was not taking any medications and had a very occasional cigarette (tobacco). His only health complaint was that he often had pains in his knees and ankles and frequently suffered from 'shin splints'.

A physical examination was basically normal (although his BMI was 29 kg/m²). A general blood screen showed elevated lipids but, of more interest, an elevated C-reactive protein (CRP) level of 7.6 mg/L (reference range 0-5.0 mg/L) and creatine kinase (CK) of 408 IU/L (normal value <180 IU/L). His liver function tests were normal.

What could be the significance of this elevated CK?

Commentary

CK is a large molecular weight protein found predominately in muscle and released into the circulation following damage to muscle tissue. A level of 408 IU/L is elevated, but given the relatively normal history and examination, it is unlikely to be of

clinical significance in this case. A 'check up' often reveals isolated clinical and biochemical abnormalities, and it is important that these are interpreted in clinical context.

It is generally thought that CK levels in excess of 1000 IU/L suggest the possibility of rhabdomyolysis, with potential renal toxicity. However, CK levels as high as 10,000 IU/L have been observed in ultra-distance marathon runners with no evidence of significant renal toxicity or metabolic abnormality.

Possible causes of a moderately raised CK in this patient include:

- unaccustomed exercise
- alcohol myotoxicity
- inflammatory muscle disease (myositis)
- hypothyroidism
- infection.

Unaccustomed exercise

Unaccustomed exercise is the most likely causative factor of raised CK. CK levels will be highest after unaccustomed, high-intensity and eccentric exercise – events that cause the greatest amount of structural muscle damage. A peak level is usually reached between days two and seven after the exercise. However, CK is not considered to be a reliable objective indicator of the extent of muscle damage because there is significant variation in response to exercise among individuals. Training allows improved muscle fibre recruitment and muscle fibre adaptation, resulting in lower CK levels.

Compared with males, females will have a lower CK response to the same type and intensity of exercise. Age, race and body composition appear to have no significant impact on the CK response to exercise. The statin group of lipid-lowering agents (which may be indicated in this patient), are known to exacerbate exercise-induced skeletal muscle damage and cause

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Clinical case review

continued

myalgia or muscle cramps in up to 5% of patients. For all of these reasons, CK is not routinely measured in the assessment of muscle pain in recreational and elite athletes (Figure).

Alcohol intake

Alcohol is directly myotoxic, and this man's regular heavy alcohol intake may be a contributing factor to the elevated CK.

Myositis

Myositis should be considered in light of the patient's elevated CRP; however, it is unlikely in this man in the absence of myalgia and proximal muscle weakness on examination.

Hypothyroidism

Hypothyroidism is associated with raised CK and should be excluded in this patient.

Infection

Infection can result in elevated CK levels. Malaria, influenza, salmonella and HIV infection should be considered, given that this man has spent a prolonged period of time in China.

Other possible causes

The clinical history of pain in his knees and ankles, along with 'shin splints' is most likely the result of biomechanical overload, exacerbated by being overweight. Shin splints generally refer to tibial pain and can include the spectrum of periostitis, stress fracture and chronic exertional compartment syndrome (CECS). It is possible that CECS results in muscle damage and elevated CK, but this patient's lack of exercise in the past two months, before his return, makes this an unlikely cause of his raised CK.

Other causes of lower limb pain should also be considered, including popliteal artery entrapment syndrome, referred pain from the lumbar spine and the presence of an extra muscle such as accessory soleus.

Direct muscle trauma, especially in the form of a crush injury, is one of the most common causes of a raised CK. The history does not suggest recent injury.

Summary

It would be worth addressing this patient's heavy alcohol intake, repeating the CK measurement seven days after any exercise and, if it is still elevated, arranging further investigation to exclude hypothyroidism and infection. The moderately increased CK in this man is unlikely to be as significant as the need to manage his heavy alcohol intake, elevated lipids and increased weight. MT

DECLARATION OF INTEREST: None.