CME

Case Report: HyperCKemia: a diagnostic dilemma

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Case description

A previously healthy 45-year-old woman presented with sudden onset of pain in her right leg, which began when she was washing her kitchen floor. She described the pain as starting from the knee and radiating to her hip. The pain progressed to the point that walking was difficult. No abnormalities were found during neurologic examination.

Results of radiographic investigations, including x-ray examination of her lumbar spine, hip, and pelvis and venous Doppler ultrasonography, were normal. Thyroid and parathyroid hormone levels were normal, as were electrolyte levels. The only abnormal finding was elevated creatine kinase at 841 U/L without elevation of the CK-MB fraction. Over the next few weeks, the patient's leg pain gradually improved. Two years later, her symptom had not returned, but her serum CK remained elevated. Results of muscle biopsy were normal, and referral for genetic testing was suggested.

An elevated creatine kinase (CK) level presents a diagnostic dilemma for family physicians. This case and the following discussion of the medical literature will outline an investigational approach to patients with elevated CK levels and describe the first published Canadian case of a rare condition called "idiopathic hyperCKemia," which has very important clinical associations.

Discussion

Family physicians order CK level assessment in several clinical situations. Primary reasons include retrosternal chest pain, muscle pain among patients taking cholesterol medication, and history of trauma. Elevated CK levels are an important marker of myocardial infarction, neuromuscular disease, and rhabdomyolysis.[1,2] Other conditions that can cause elevated CK levels include pregnancy, malignancies, hyperthermia, thyroid and parathyroid diseases, or even physical exercise.[1]

Occasionally, elevated CK levels are observed among people without any symptoms. An investigational approach to asymptomatic patients with elevated CK levels is not well described in the medical literature. A MEDLINE search (1966 to present) using the text word "hyperCKemia" identified 33 publications; most were case reports. Five studies and four review articles were located. One large retrospective study by Prelle et al[1] recently described a diagnostic approach to asymptomatic patients with hyperCKemia. Their approach included an accurate clinical history, physical examination, and laboratory investigations to rule out common causes (including thyroid and parathyroid diseases). Prelle et al[1] mentioned that a muscle biopsy can be useful after these preliminary investigations to establish a diagnosis. They also recommended genetic testing to determine carrier status for Duchenne dystrophy (DD).[1] As well, electromyography was reported as helpful but rarely conclusive.

In 1980, the term "idiopathic hyperCKemia" (IH) was coined by Rowland et al[3] for cases where there was no clinical or histopathologic evidence of neuromuscular disease. The literature reflects differing opinions on what constitutes IH. Brewster and de Visser[4] suggested further exclusion criteria, including hypothyroidism, family history of neuromuscular disease, and medication side effects. Adding to these exclusion criteria, Prelle et al[1] recommended that a case of true IH results only from failure to determine a diagnosis after muscle biopsy.

Very few articles describe cases of IH. No Canadian articles were found in the MEDLINE search. It is unclear whether cases of IH are unknown in Canada or whether previous cases have gone unreported in the literature. Among the articles published, none

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This article has been peer reviewed.
Cet article a fait l'objet d'une évaluation externe.
Can Fam Physician 2005;51:240-241.

documents the prevalence of IH cases. The largest study published reported 114 cases from 1987 to 1999.[1] Another study documented only four cases over a 10-year period, but all affected children.[5] Men appear to be affected by IH more than women are; several studies report approximately 80% of subjects are men.[1,4,5]

Idiopathic hyperCKemia has important clinical associations. Malignant hyperthermia, an autosomal dominant disorder of skeletal muscle, can cause a brief increase in serum CK during a crisis.[6] In one study, malignant hyperthermia susceptibility was discovered in 49% of IH patients.[6] Weglinski and colleagues[6] advised that all patients with IH who have muscle biopsy should also receive malignant hyperthermia contracture testing.

Duchenne dystrophy is another cause of elevated serum CK levels. Elevated serum CK is widely used as a diagnostic marker for carriers of DD.[7] Many of these patients have either symptoms of or a family history of DD. Other authors have described finding DD carriers among their IH populations.[5]

Due to the limited research published on IH, the long-term prognosis of patients with IH is unclear. One recent publication by Reijneld and associates[8] describes a long-term study of 31 patients with IH who demonstrated no clinical deterioration over a mean of 7.2 years. The authors[8] suggested that routine follow up for patients with IH is unnecessary.

Conclusion

Elevated levels of CK occur frequently in family medicine. This article describes an approach to random elevated CK levels. Patients with elevated serum CK levels should undergo thorough initial investigation to determine common and potentially treatable causes of hyperCKemia. If no cause for an elevated CK level is found, the diagnosis of exclusion is IH. This relatively rare condition has been associated with malignant hyperthermia susceptibility and carrier status for DD. After the diagnosis of IH has been confirmed, patients can be reassured that clinical deterioration is rare.

EDITOR'S KEY POINTS

- Family doctors occasionally find elevated creatine kinase (CK) levels. Common causes include myocardial damage, other muscle injury, or heavy exercise; neuromuscular disorders like Duchenne dystrophy; or use of cholesterol-lowering medication. Other less common causes include pregnancy, hyperthermia, and thyroid and parathyroid abnormalities.
- Workup of elevated CK levels should include a careful history, neuromuscular examination, bloodwork, consideration of muscle biopsy, and possible genetic testing for malignant hyperthermia susceptibility.
- If all results are negative, a diagnosis of idiopathic hyperCKemia can be made by exclusion. The condition appears to have no long-term consequences, and patients can be reassured.

POINTS DE REPÈRE DU RÉDACTEUR

- Des niveaux élevés de créatine kinase (CK) sont parfois observés par le médecin de famille. Parmi les causes fréquentes, mentionnons les lésions myocardiques ou autres blessures musculaires et les exercices intenses; les affections neuromusculaires comme la dystrophie de Duchenne; et la prise d'un hypocholestérolémiant. Parmi les causes moins fréquentes, mentionnons la grossesse, l'hyperthermie et les affections thyroïdiennes et parathyroïdiennes.
- Le bilan d'un niveau élevé de CK devrait comprendre une histoire minutieuse, un examen neuromusculaire, un bilan sanguin et éventuellement, une biopsie musculaire et un dépistage génétique pour une susceptibilité à l'hyperthermie maligne.
- Si tous les résultats sont négatifs, on peut poser un diagnostic d'hyperCKémie par élimination. Comme cette condition semble n'avoir aucune conséquence à long terme, on peut rassurer le patient.

Competing interests
None declared

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