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Exercise-induced Elevation of Liver Enzymes in a Healthy Female Research Volunteer

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TO THE EDITOR

In addition to common causes of liver injury, liver enzyme levels can be elevated owing to extrahepatic causes.[1–4] We present a case of an asymptomatic healthy female research volunteer with elevated transaminase levels and a very high creatine kinase (CK) level induced by strenuous exercise. She discontinued her vigorous exercise, and her liver enzyme and CK levels were within the normal range on reevaluation 3 weeks later.

Case Report

A 30-year-old female graduate student presented to determine her eligibility for a pharmacology study involving a new investigational psychiatric drug.

She reported being in excellent physical and mental health and had no complaints. Her review of systems was negative and she denied taking any medications, supplements, or recreational drugs. Alcohol intake was 1 to 2 drinks per week.

The findings on physical examination, including mental status and neurological examination, were unremarkable.

Laboratory assessments consisted of a complete blood count and differential, thyroid-stimulating hormone analysis, comprehensive chemistry panel (that included CK and lactate dehydrogenase assessments), chronic hepatitis B and C serology, HIV serology, urinalysis and urine drug screen, and pregnancy test.

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Laboratory assessment revealed an elevated alanine aminotransferase (ALT) level of 87 U/L (*n* = 0–33) and aspartate aminotransferase (AST) level of 120 U/L (*n* = 0–32), which would disqualify her from participation in the study, as transaminase levels >50% of the upper limits of the reference range were exclusionary. The results of the rest of the laboratory testing were negative except for an elevated lactate dehydrogenase level of 579 U/L (*n* = 113–226) and a very high CK level of 19,654 U/L (*n* = 26–192), suggesting that the probable cause of abnormal levels on laboratory assessments was muscle injury.

When informed about the results, the volunteer stated that she had recently started training for "tough mudder," a 10- to 12-mile military-style obstacle course. She subsequently discontinued her strenuous exercise and remained asymptomatic. On re-evaluation 3 weeks later, her ALT, AST, lactate dehydrogenase, and CK levels were within the reference range (11, 14, 170, and 108 U/L, respectively), and she completed the study without complications.

Discussion

Mild elevations of transaminase levels are often transient.[5] More than 30% of adults with initially elevated AST and ALT levels have normal results on a repeat testing.[5] It is well known that elevations of liver function tests (LFTs) are commonly caused by liver injury due to alcohol, nonalcoholic fatty liver disease, hemochromatosis, hepatitis B, hepatitis C, illegal drugs, dietary supplements, and over-the-counter and prescription medications, including many psychiatric drugs.[1,2]

As transaminase levels are commonly but incorrectly referred to as "liver function tests" and "liver enzymes,"[3] it is sometimes forgotten that they may be elevated owing to extrahepatic causes.[3,4] Although highly concentrated in the liver, AST is also present in the muscle, heart, kidney, red blood cells, brain, and small bowel, whereas ALT is present in the liver, muscle, and kidney.[3] In fact, muscle has more AST and ALT when compared with that in the liver because of a larger tissue mass.[3] Consequently, transaminase levels may be elevated owing to various types of muscular disorders or injury (e.g., heart attack, surgery, and vigorous exercise), hemolysis, and small bowel ischemia.[3,4]

In a study involving healthy men who are used to moderate physical activity, not including previous weightlifting, ALT, AST, lactate dehydrogenase, CK, and myoglobin levels increased significantly after 1 hour of heavy weight-lifting and remained elevated for at least 1 week.[4] Bilirubin, gamma-glutamyl transferase, and alkaline phosphatase levels remained within the reference range.[4]

As CK assessment is not always included in screening blood chemistries for clinical research studies, it may be difficult to interpret the meaning of elevated transaminase levels. For example, if the CK level had not been obtained in our case, the physician could have wrongly assumed that elevated transaminase levels were manifestations of a liver injury, and the volunteer would have been excluded from the participation in the study. Conversely, if the volunteer started her vigorous exercise after screening, during her participation in the study, elevations in LFTs might have been erroneously attributed to study medication.

Therefore, it is prudent to include CK assessment in the screening panel for investigational drug studies and to inquire about exercise habits. Moreover, restriction of vigorous exercise for at least 1 week before the start and during study participation should be considered in studies requiring monitoring of LFTs.[4]

Physicians in clinical practice do not routinely order a CK assessment in the setting of elevated transaminase levels.[3] These patients are often misdiagnosed as having liver problems that can lead to inappropriate discontinuation of medications, further unnecessary testing, or referral to a specialist.[3]

With the increased awareness of the importance of exercise and strength training, psychiatrists may encounter patients whose LFTs are elevated owing to muscle injury.

When evaluating patients with elevated LFTs, it is important to assess exercise habits and CK in addition to inquiring about medications and supplements that may cause liver or muscle injury or both.

In the case of exercise-induced muscle injury, CK is also transiently elevated but returns to normal levels along with transaminase levels after the discontinuation of strenuous exercise.[3,4]

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