Exercise Induced Fatigue: Unfit or Unwell?

Abstract:

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Abstract
This case report outlines the diagnoses of a rare myophosphorylase deficiency (McArdle Syndrome) in a unique way. A set of characteristic values from a Cardiopulmonary Exercise Test (CPET) combined with a typical patient history pointed to a failure of the glycolytic pathway in the skeletal muscle. McArdle Syndrome was confirmed with a skeletal muscle biopsy. There is no evidence of such a diagnostic method in the literature.

Case Report
A 20 year old man presented to the cardiology service complaining of an inability to engage in moderate exercise. He described a lifelong problem with muscle fatigue after a short period of sustained exertion. There was no background medical or family history.His physical examination was normal. Routine blood tests (full blood count and renal profile) were normal. His creatinine kinase was not checked. Normal echocardiography, holter monitoring and exercise stress testing suggested a cardiac aetiology was unlikely. He was sent for Cardiopulmonary Exercise Testing (CPET) to differentiate between poor aerobic conditioning or a possible pathological aetiology. â Cardiopulmonary exercise testing (CPET) provides a global assessment of the integrative exercise responses involving the pulmonary, cardiovascular, hematopoietic, neuropsychological, and skeletal muscle systems, which are not adequately reflected through the measurement of individual organ system functionâ [1].

The key figures in CPET are represented by VO_2 (oxygen uptake â aerobic metabolism), VCO_2 (CO_2 output), and RER (respiratory exchange ratio - VCO_2/ VO_2). In a healthy individual, V O2 should rise linearly with exercise and plateau at VO_2 max. VCO_2 normally continues to rise in anaerobic respiration. Therefore, RER should normally be about 1 at the start of aerobic exercise. However, as testing continues and oxygen delivery to the muscles reduces, anaerobic respiration takes over and CO_2 levels rise, leading to an RER > 1. If the subject has a poor level of fitness, the VO_2 max will be reduced. As a consequence of poor oxygen availability, the muscles are forced to switch to anaerobic metabolism earlier and as such, we get an earlier rise in VCO2 and an early RER > 1.

The patient exercised for six minutes (limited by muscle fatigue), achieving an early rise in VO_2 consistent with aerobic metabolism but had a significantly reduced VO_2 max of 51%. This would suggest an early failure in the aerobic metabolic pathway. Generally, in response to this failure, the anaerobic pathway becomes active earlier with a corresponding rise in the VCO_2. However, in this case, the VCO_2 failed to rise in any significant way throughout the entire test and his RER never increases above 1 at any stage, with a maximum value of 0.96. These values signal a concurrent failure of the anaerobic pathway.

Discussion
The test results raise the important question: what condition could cause an early failure of the aerobic metabolic pathway without an anaerobic response? The answer is a deficiency in the common denominator of both pathways: glucose. The supply of glucose to both pathways is regulated by a series of important enzymes. Two of these enzymes are vital to the supply of glucose to skeletal muscles. When we consider the CPET results and the fact that the symptoms are

entirely confined to the skeletal muscle system, we can confidently assume that one of these enzymes is deficient. The first enzyme is called glycogen phosphorylase, with a muscle isozyme called myophoshorylase. It degrades glycogen in the first step of gluconeogenesis. Its deficiency is commonly called McArdle Syndrome. The second enzyme is phosphofructokinase. The deficiency of this enzyme is extremely rare, with more severe side effects and commonly, the individual presents before puberty. As such, McArdle Syndrome appeared to be the most likely diagnosis. This clinical diagnosis was confirmed on a muscle biopsy of the left thigh, with intense glycogen staining and the complete absence of enzyme on myophosphorylase staining.

McArdle Syndrome was suspected on the basis of characteristic symptoms and values on CPET. The diagnosis was later confirmed on muscle biopsy. On review of the literature, the possibility of using CPET as an adjuctive diagnostic test for McArdle Syndrome is explored but there are no recorded cases of such a diagnosis [2]. The diagnoses of McArdle Syndrome may be aided with CPET, and identify patients for skeletal muscle biopsy.

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