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Case Report

Cardiopulmonary Exercise Testing and Metabolic Myopathy as a Cause of Dyspnea: A Case Report

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Abstract

Clinical presentation of Mitochondrial disease is wide due to different organs involved in it. When skeletal muscle is affected, the term mitochondrial myopathy is used. Exercise limitation is among symptoms affecting patients with myopathy. In approaching dyspnea Establishing an accurate diagnosis is essential because treatment depends on the underlying condition. The case we report is a patient with chronic dyspnea in whom evaluated through cardiopulmonary exercise test and metabolic myopathy was identified.

Keywords: Mitochondrial Disease; Dyspnea; Cardiopulmonary Exercise Test (CPET)

Introduction

Sustained exercise requires tight integration of multiple physiologic systems including cardiac, neuromuscular, and respiratory system. Disease affecting any of these systems can manifest as dyspnea or exercise limitation [1]. There are different modalities for assessment of patients with these complaints. We can asses exercise responses by using cardiopulmonary exercise test (CPET) systemically and identify the system in which is contributing the most. Muscular system as a major part of systems involved in exercise can be assessed through CPET.

Case Presentation

A 24 years old woman was referred to our center to perform CPET due to unexplained dyspnea.

She was complaining of dyspnea and fatigue since about 10 years ago.

Dyspnea was at both rest and activity. There was no history of fever or cough. No family member had similar problem. She denied keeping pet at home.

Heart and lung exams were unremarkable.

There was a normal lung ct scan in Patient's medical records. In our center an echocardiography was performed that showed normal cardiac structure and function.

Spirometry and body plethysmography showed restrictive pattern with air trapping.

(FVC =57%TLC=70% RV =140%)

ECG was normal.

Exercise testing was performed on a cycle ergometer beginning with 2 minutes of cycling at 60 rpm without added load, then followed by continuous increase in work rate by 10 W per minute to 6 minutes. She ended exercise with generalized fatigue and palpitation. There was no significant ECG changes, except sinus tachycardia.

CPET data are shown in table 1.

		Pred	Rest	AT	MAX load	MAX/pre	AT/Ref
Load	W	113		22	43	38%	19%
Vo2	l/min	1.77	0.35	0.39	0.40	23%	22%
Vo2/Kg	ml/kg/min	39.3	7.7	8.6	8.9	23%	22%
Vco2	l/min	1.94	0.44	0.49	0.53	27%	25%
RER			1.26	1.26	1.31		
Circulation							
HR	1/min	196	150	166	160	82%	85%
O2pulse	ml/beat	9.4	2.3	2.3	2.5	27%	25%
BPsys	mmHg		115	145	145		
BPdia	mmHg		76	78	78		
Ventilation							
VE	l/min	60.06	31.54	34.02	37.89	63%	57%
VT	L	1.62	0.65	0.64	0.71	44%	39%
f-ergo	1/min	36	49	53	53	147%	146%
BR	%	47	43	37			
VD//VT		0.53	0.49	0.48			
Gs exchange							
EQo2		84	81	88			
EQco2		66	65	67			
PETo2	mmHg	109.0	110.4	112.8			
PETco2	mmHg	23	22.2	21.2			

Table 1: CPET data.

As it is necessary to know patient's effort for the accurate interpretation of a CPET , in the first step patient's effort was evaluated. R was more than 1.15 and so poor effort was excluded.

As it is shown in the table 1. Peak $\mathring{V}o_2$ is very low and $\Delta\mathring{V}o_2/\Delta WR$ is markedly reduced.

Progressive rise in R throughout exercise is consistent with early onset of lactic acidosis and lack of oxygen consumption by cells. This is compatible with ABG results.

Figure 1: vo2/vco2 plotted as a function of time.

Figure 2: VT plotted as a function of VE.

According to ATS/ACCP statement on CPET increased HRR and normal BR and decreased AT with normal o_2 saturation, all together result in 3 differential diagnosis; deconditioning, cardiovascular and mithochondrial myopathy.

Reduced $\Delta\mathring{V}o_2/\Delta WR$ is in contrast with deconditioning.

High RER and no rising $\mathring{V}o_2$ and Abnormalities of o_2 pulse as shown in the table and reduced $\Delta\mathring{V}o_2/\Delta WR$ are striking and are indicative of severe abnormalities in o_2 delivery and or muscle o_2 extraction.

Given these findings and considering lack of any evidence for cardiovascular disorders, impaired skeletal muscle oxygen utilization was suspected.

In order to evaluate muscle disorder CPK and LDH ordered and EMG and NCV and muscle biopsy was performed.

Discussion

Mitochondrial diseases result from failures of the mitochondria, specialized compartments present in every cell of the body (except red blood cells).

Mitochondria are responsible for creating more than 90% of the energy needed by the body to sustain life and support organ function. When they fail, less and less energy is generated within the cell.

The parts of the body, such as the heart, brain, muscles and lungs, requiring the greatest amounts of energy are the most affected. Mitochondrial disease is difficult to diagnose, because it affects each individual differently. Symptoms can include seizures, strokes, severe developmental delays, inability to walk, talk, see, and digest food combined with a host of other complications. Although mitochondrial disease primarily affects children, adult onset is becoming more common [2]. Two studies have estimated the prevalence of mitochondrial disease in adults to be 5.7 [3] and 22.9 [4] in 100,000, although myopathy was present in only 60 to 80%. The main symptoms of mitochondrial myopathy are exercise intolerance with fatigue, dyspnea, and muscle cramps. Serum creatine kinase is normal or only slightly elevated in most, although some mutations show significant elevations [5,6].

Cardiopulmonary exercise testing (CPET) is increasingly being used for the evaluation of undiagnosed exercise intolerance, exercise-related symptoms, and, uniquely, for the objective determination of functional capacity and impairment. In CPET we measure respiratory gas exchange: oxygen uptake ($\dot{V}o_2$), carbon dioxide output ($\dot{V}co_2$), and minute ventilation ($\dot{V}E$), in addition we monitor patient's electrocardiography, blood pressure, and pulse oximetry, typically during a symptom-limited maximal progressive exercise tolerance test.

CPET provides a global assessment of the integrative exercise response involving the pulmonary, cardiovascular, hematopoietic, neuropsychologic, and skeletal muscle systems that is not adequately reflected through the measurement of individual organ system function [7].

Significantly reduced peak work rate and peak $\dot{V}o_2$ are seen during CPET in mitochondrial myopathy; as in our case which showed peak $\dot{V}o_2$ of 23%. Besides, there is early lactic acidosis in mitochondrial myopathies during exercise, as there is increased reliance on anaerobic metabolism to produce ATP. Early lactic acidosis is reflected, it self in early gas exchange lactic acidosis threshold.

In the case we presented here, there is marked elevation in both $\mathring{V}E/\dot{V}o_2$ and $\mathring{V}E/\mathring{v}co_2$ (88 and 67 respectively). This is consistent with findings of heinicke and colleagues [8] that reported responses to exercise in five patients with mitochondrial myopathy. They found marked elevations in both $V.E/V.o_2$ and $V.E/V.co_2$ at peak exercise.

There is a hyperdynamic circulatory response in patients with mitochondrial myopathy [9]. As in our patient that showed high HR at start of CPET and Some studies indicate that Peak exercise cardiac output is similar to that seen in normal subjects [9].

Measurement of blood lactate and cpk and LDH provided useful additional information about the patient (46, 382 U//L and 757 U/L respectively). Serum creatine kinase is normal or only slightly elevated in most, although some mutations show significant elevations [5,6].

Muscle biopsy obtained by open technique from left quadriceps revealed mitochondrial myopathy pathologically. It was in consistent with EMG finding that showed myopathy.

Finally the etiology of dyspnea in the young woman was identified.

What was interesting in the case presented here was the way through diagnosis was made.

Although there is not enough data about CPET in mitochondrial disease, but the case presented highlights the potential of cardiopulmonary exercise testing in combination with other modalities such as peripheral venous lactate an Jr d creatine kinase measurements to identify metabolic myopathies.

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