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Case Report
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Metabolic Myopathy Caused by Vitamin D Deficiency in the Setting of End-Stage Renal Disease

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Abstract

Metabolic myopathies from vitamin D deficiency are quite rare and potentially challenging with respect to management due to their presentation. They often mimic other forms of myopathies which lead to delay in diagnosis and appropriate treatment.

Introduction

We discuss a case of metabolic myopathy from vitamin D deficiency in the setting of End-Stage Renal Disease (ESRD). We will highlight some of the challenges faced while making the correct diagnosis; key features that help differentiate from other types of myopathies, and finally a discussion on the approach to proper management.

Case Presentation

A 38-year-old man with a history of type 1 diabetes mellitus, ESRD on hemodialysis, presented with progressive right thigh swelling, pain and hyperpigmented, brown, lace-like rash that began on his knee and gradually progressed proximally to cover his anterior thigh over a 3-month period (Figure 1). He denied any previous injury or trauma to his leg. He presented to the hospital on several occasions, in the 3-month period, with worsening leg pain, fever, and leukocytosis and treated with antibiotics for presumed cellulitis with no improvement. On examination, his right thigh was tender on palpation. There was significant pain with active and passive range of motion. Sensation, motor function, and tendon reflexes were normal. Left leg and upper extremities were unaffected. The patient was unable to bear weight on his right leg due to extreme pain. CT and MRI studies demonstrated vascular calcifications, demineralization of leg bones, mild degenerative changes in the knee joint, which were out of proportion to the patient's age, and moderate muscle edema concerning for myositis. He remained afebrile; however, laboratory evaluation demonstrated leukocytosis, elevated ESR, CRP, LDH, PTH, and alkaline phosphatase. Phosphorus and calcium levels were low. CK, Lyme antibody titers, and auto-immune markers were negative (Table 1). Skin biopsy demonstrated focal chronic inflammation with no calciphylaxis, vasculitis or neoplasia. Muscle biopsy was diagnostic for non-infectious myopathy which was not definitive for one subtype of inflammatory or metabolic myopathy (Figure 2). Given concern for inflammatory myopathy, he was started on prednisone therapy with no improvement.

Discussion

Vitamin D deficiency is an important treatable cause of osteomalacic myopathy, defined as a 25-hydroxy vitamin D level less than 20 ng/ml [1]. In most cases, the myopathy is generalized; however, in about 30%, it can be localized and can present solely in the proximal muscles of a single muscle group [2]. Skeletal muscle contains vitamin D receptors, which are responsible for transcription factors within muscle cells to mediate muscle cell proliferation and differentiation into mature type II muscle fibers. Furthermore, vitamin D plays an essential role in the transportation of calcium into the sarcoplasmic reticulum, necessary for muscular contraction.

Measuring a serum 25-hydroxy vitamin D level is a reliable test to help diagnose and prevent metabolic myopathy in individuals at risk. Low levels can be present even before other laboratory abnormalities are seen. Creatinine Kinase (CK) levels are often normal in cases of metabolic myopathies, whereas in inflammatory myopathies they are elevated, except in Inclusion Body Myositis (IBM) [3]. Muscle biopsy is not usually indicated; however, if the presentation is non-

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Table 1: Laboratory Parameters.

Lab Parameter	Value		Lab Parameter	Value	
Chemistry profile			**Complete Blood Count**		
Sodium	136 mmol/L		White Blood Cell	15.0 10*3/uL	high
Potassium	4.8 mmol/L		Red Blood Cell	2.39 10*6/uL	low
Chloride	91 mmol/L	low	Hemoglobin	7.0g/dL	low
Bicarbonate	27 mmol/L		Hematocrit	20.7%	low
Blood Urea Nitrogen	55 mg/dL	high	Mean Cell Volume	86.4 fL	
Creatinine	10.25 mg/dL	high	Mean Cell Hgb	29.4 pg	
Glucose	147 mg/dL	high	Mean Cell Hgb Conc	34.0 9/dL	
Anion Gap	18 mmol/L	high	Red Cell Dist Width	15.1%	high
Osmolality, Cal	300 mosm/kg		Platelet Count	421 10*3/uL	high
Vitamin D 25 Hydroxy	19.1 ng/mL	low	Hemoglobin A1c	8.3%	high
Calcium	8.0 mg/dL	low	**Autoimmune panel**		
Phosphorus	1.3 mg/dL	low	DS DNS Ab	42 [AU]/mlL	
Albumin	2.3 g/dL	low	SSA Auto antibody	7 [AU]/mlL	
Alkaline Phosphatase	287 U/L	high	SSB Auto antibody	18 [AU]/mlL	
CK	141 U/L		Histone antibody	21 [AU]/mlL	
Vitamin B12	825 pg/ml		Centromore antibody	18 [AU]/mlL	
Parathyroid Hormone	255 pg/mL	high	Smith Autoantibody	7 [AU]/mlL	
Inflammatory markers			RNP Autoantibody	63 [AU]/mlL	
C Reactive Protein	234.3 mg/L	high	SCL-70 Autoantibody	9 [AU]/mlL	
Sed Rate - ESR	62 mm/hr	high	JO-1 Autoantibody	11 [AU]/mlL	

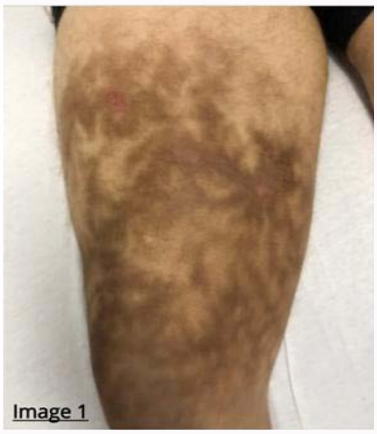

Figure 1: Hyperpigmented, lace-like rash on the right leg on admission.

specific or atypical, then it can be considered. A caveat to performing a muscle biopsy is that, in metabolic myopathies, it can demonstrate non-specific inflammation which may lead to an alternate diagnosis such as Idiopathic Inflammatory Myopathies (IIM). Physicians would then be inclined to order auto-antibody markers such as ANA, Rheumatoid factor, and anti-JO-1 antibodies, which delay the diagnosis and management, such as in our patient. Both IIM and Metabolic Myopathies demonstrate macrophage predominant inflammatory infiltrates into the muscle fibers. Lack of elevation in CK helps to exclude DM and PM. With respect to IBM, microscopy demonstrates focal invasion of CD8+ T cells into non-necrotic muscle fibers that express MHC-I complexes. The CD8/MHC-1 complex predominance is a distinctive feature of IBM, whereas in our patient, CD4 predominance in the muscle fibers along with perivascular T-lymphocytes was observed. Lastly, IBM demonstrates rimmed vacuoles within muscle tissues whereas they were not rimmed in our case and not found in other Metabolic Myopathies [4].

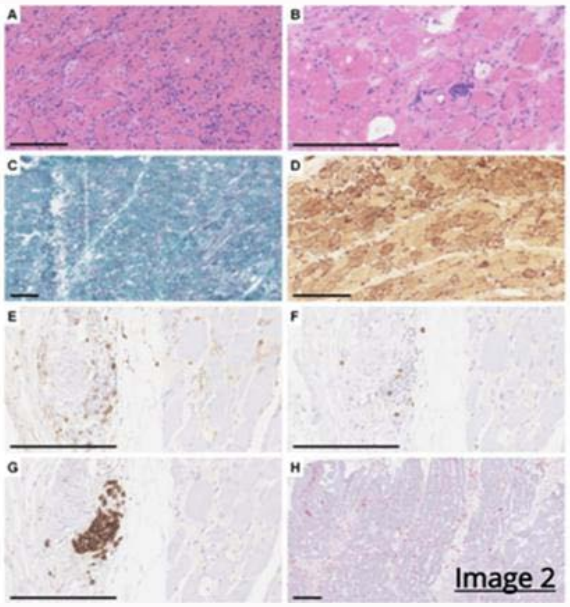

Figure 2: Representative images from a muscle biopsy H&E stained section at 200 × total magnification demonstrating myopathic changes including fiber size variation, as well as increased numbers of lymphocytes in the endomysial compartment; (B) H&E stained section at 400 × total magnification demonstrating fibre size variation and a perivascular collection of lympgocytes; (C) Gomori trichrome stained sction at 100 × total magnification demonstrating lack of ragged red fibers or red-rimmed vacuoles; (D) non-specific esterase stained section at 200 × total magnification highlighting degenerating and regenerating fibers as well as rare angulated, denervated fibers; (E) CD4 immunohistochemical stain at 400 × total magnification demonstrating perivascular T-lymphocytes; (F) CD8 immunohistochemical stain at 400 × total magnification demonstrating perivascular T-lymphocytes; (G) CD20 stain at 400 × total magnification demonstrating perivascular T-lymphocytes; (H) CD68 immunohistochemical stain at 100 × total magnification demonstrating rare myophagocytosis as well as endomysial and perifascicular histocytes. All scale bars = 200 µm.

All causes of myopathy were worked up and ruled out. With a history of Vitamin D deficiency and non-compliance to oral vitamin D therapy, a diagnosis of vitamin D induced myopathy was made. Other supportive parameters include elevated alkaline phosphatase, PTH, and hypophosphatemia. Based on our literature review, one treatment option is the administration of 50,000 International Units (IU) of vitamin D2 or D3, orally, once per week, for six to eight weeks followed by 800 IU of vitamin D3 daily, with monitoring of the vitamin D levels. Treatment response is dramatic, and most patients experience a prompt reversal of the symptoms with a complete or near-complete restoration of muscle strength within 4-6 weeks of starting treatment [5].

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