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 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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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].

<table>
<thead>
<tr>
<th>Table 1: Laboratory Parameters.</th>
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<tbody>
<tr>
<td>Lab Parameter</td>
<td>Value</td>
<td>Lab Parameter</td>
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<tr>
<td>Chemistry profile</td>
<td>Sodium 136 mmol/L</td>
<td>White Blood Cell</td>
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<td></td>
<td>Potassium 4.8 mmol/L</td>
<td>Red Blood Cell</td>
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<td></td>
<td>Chloride 91 mmol/L</td>
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<td></td>
<td>Bicarbonate 27 mmol/L</td>
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<td></td>
<td>Blood Urea Nitrogen 55 mg/dL</td>
<td>Mean Cell Volume</td>
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<tr>
<td></td>
<td>Creatinine 10.25 mg/dL</td>
<td>Mean Cell Hgb</td>
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<td></td>
<td>Glucose 147 mg/dL</td>
<td>Mean Cell Hgb Conc</td>
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<td>Anion Gap 18 mmol/L</td>
<td>Red Cell Dist Width</td>
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<td>Osmolality, Cal 300 mosm/kg</td>
<td>Platelet Count</td>
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<tr>
<td></td>
<td>Vitamin D 25 Hydroxy 19.1 ng/mL</td>
<td>Hemoglobin A1c</td>
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<td>Calcium 8.0 mg/dL</td>
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<td>Phosphorus 1.3 mg/dL</td>
<td>DS DNS Ab</td>
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<td></td>
<td>Albumin 2.3 g/dL</td>
<td>SSA Auto antibody</td>
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<tr>
<td></td>
<td>Alkaline Phosphatase 287 U/L</td>
<td>SSB Auto antibody</td>
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<td></td>
<td>CK 141 U/L</td>
<td>Histone antibody</td>
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<td></td>
<td>Vitamin B12 825 pg/ml</td>
<td>Centromere antibody</td>
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<td>Parathyroid Hormone 255 pg/mL</td>
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<td>Inflammatory markers</td>
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<td></td>
<td>C Reactive Protein 234.3 mg/L</td>
<td>RNP Autoantibody</td>
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<tr>
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<td>Sed Rate - ESR 62 mm/hr</td>
<td>SCL-70 Autoantibody</td>
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Figure 1: Hyperpigmented, lace-like rash on the right leg on admission.

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 endomyosial compartment; (B) H&E stained section at 400 × total
magnification demonstrating fibre size variation and a perivascular
collection of lymphocytes; (C) Gomori trichrome stained section 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
stroke at 100 × total magnification demonstrating rare myophagocytosis as
well as endomyosial 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].

References
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2. Al-Said YA, Al-Rached HS, Al-Qahtani HA, Jan MM. Severe proximal
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