Colchicine-Induced Myopathy with Normal Creatine Phosphokinase Level in a Renal Transplant Patient

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Abstract

A case of a renal transplant recipient with colchicine-induced myopathy is presented. He was on colchicine therapy for 10 months. He was hospitalized for investigation of fatigue, severe myalgia in the lower extremities and elevated serum aminotransferase levels. His viral markers and other factors that may cause myalgia and that may increase the serum aminotransferase levels were either normal or negative. Creatine phosphokinase (CK) levels were normal. Electrophysiological findings indicated myopathy and muscle biopsy was consistent with vacuolar myopathy. After withdrawal of colchicine, the symptoms disappeared gradually and serum aminotransferase levels were normalized. We suggest that colchicine myopathy should be taken into account in patients who have been on colchicine therapy and had unexplained myalgia as well as elevated aminotransferase levels even with normal CK levels.

Introduction

Drug-induced myopathy is an important cause of muscle disease. Its precise incidence is not known. Myopathy has been reported as an important side effect of colchicine administration especially in patients with renal failure [1]. It is generally believed that colchicine-induced myopathy is associated with rather high creatine phosphokinase (CK) levels. The present report describes a renal transplant recipient with normal serum creatinine and CK levels who developed colchicine-induced myopathy.

Case Report

A 47-year-old man was admitted to the hospital in June 1999, because of weakness, fatigue and diffuse muscle pain in the distal extremities. He received a cadaveric kidney allograft in 1996 for end-stage renal failure due to amyloidosis secondary to familial Mediterranean fever (FMF). Prior to the kidney transplantation he had undergone hemodialysis for 14 months. The patient was in good health until 1 week before admission. The immunosuppressive regimen consisted of cyclosporine (200 mg daily), azathioprine (100 mg daily) and prednisolone (10 mg daily). Colchicine (0.6 mg b.i.d.) has been given since September 1998 when he developed an FMF attack.

On admission, his blood pressure was 120/70 mm Hg, pulse rate was 70 bpm and respiratory rate was 22/min. Cardiovascular, respiratory and abdominal examinations were unremarkable. Neurologi-
cal examination showed normal cranial nerve functions, moderate proximal limb weakness, normal sensation, severe tenderness on palpation and hyporeflexia in both lower extremities. Laboratory results revealed normal white blood cell, hematocrit, hemoglobin, and platelet levels. Serum electrolytes were normal. Serum creatinine was: 1.8 mg/dl (normal: 0.5–1.3 mg/dl), urea: 45 mg/dl (normal: 15–44 mg/dl), serum albumin: 3.8 g/dl (normal: 3.5–5.5 mg/dl), aspartate aminotransferase (AST): 103 U/l (normal: 8–40 U/l), alanine aminotransferase (ALT): 73 U/l (normal: 5–40 U/l), CK:165 U/l (normal: 31–221 U/l), lactic dehydrogenase (LDH) 261U/l (normal: 91–232 U/l), and blood cyclosporine level: 431 ng/ml. Chest X-ray and ECG were normal. Cyclosporine was discontinued for 5 days and then restarted at a dose of 100 mg/day. After this application blood cyclosporine level was reduced to 165 ng/ml and serum creatinine level reduced to 1.4 and then to 1.2 mg/dl. On the other hand, AST and ALT levels were increased to 390 and 273 U/l, respectively, within this period. CK levels were also repeated and normal results were obtained. In this period his symptoms were increased. Liver ultrasonography was found as normal. Antinuclear antibodies, anti-DNA, serum complements, antineutrophilic cytoplasmic antibody, antimitochondrial antibody and anti-Sm antibody were either negative or normal. Cytomegalovirus, Ebstein-Barr virus and herpes simplex virus IgM levels were normal. Hepatitis-B surface antigen, anti-HCV, anti-HAV-IgM, HBV-DNA, HCV-RNA, CMV-DNA and anti-HIV were negative.

Nerve conduction study was normal. Needle EMG of distal and proximal muscles revealed motor unit potentials characterized by short duration and low amplitude with early recruitment. There were no fibrillation potentials and positive sharp waves. These electrophysiological findings were indicative of myopathy. Muscle biopsy examined in frozen section revealed vacuolar myopathy, which is highly suggestive of colchicine myopathy (fig. 1). These vacuolar changes were also present in paraffin sections.

From these findings, the patient was diagnosed as having colchicine-induced myopathy, and this drug was discontinued. After colchicine had been stopped, his symptoms gradually disappeared within 2 weeks and AST, ALT levels were reduced to 39 and 30 U/l, respectively.

Discussion

There are insufficient data about muscle disease in renal transplant recipients. Ducloux et al. found that 50% of renal transplant recipients on both cyclosporine and colchicine exhibited muscular symptoms characterized by short duration and low amplitude with early recruitment. There were no fibrillation potentials and positive sharp waves. These electrophysiological findings were indicative of myopathy. Muscle biopsy examined in frozen section revealed vacuolar myopathy, which is highly suggestive of colchicine myopathy (fig. 1). These vacuolar changes were also present in paraffin sections.

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brillation potentials appear 2 weeks later after the initiating factor. Since EMG was performed within this period, the lack of the features of peripheral neuropathy was not unusual. We speculated that it is possible for this patient to have CK inhibitors, which has also been suggested by Kagen et al. [6]. To our knowledge, this patient is the first reported case of colchicine myopathy with normal CK levels in a renal transplant recipient.

In conclusion, renal transplant recipients receiving colchicine therapy should be followed cautiously. In patients who are on colchicine therapy and suffer from fatigue, malaise, and myalgia with elevated aminotransferase levels, colchicine myopathy must be taken into account even with normal CK levels.

References