Acute Myopathy Induced by Colchicine in a Cyclosporine-treated Renal Transplant Recipient

- A Case Report and Review of the Literature -

We report a case of colchicine-induced myopathy related to short-term, customary administration of colchicine. A 49-year-old male was admitted because of muscle weakness and myalgia that had developed 10 days previously. He had received renal transplantation 5 years previously and took cyclosporine as an immunosuppressant. Two weeks before admission, gout was developed and he took colchicine (1.2 mg b.i.d) by himself for three days. Colchicine-induced myopathy was clinically suspected, and colchicine intake was stopped immediately. After that, clinical symptoms gradually improved and serum muscle enzyme returned to normal. In this case, mild renal dysfunction and drug interaction between cyclosporine and colchicine were suggested to be the precipitating factors of colchicine-induced myopathy.

(JKMS 1997;12:160~1)

Key Words : *Colchicine, Cyclosporine, Myopathy*

Bo In Lee, M.D.,[1] Seok Jun Shin, M.D.,[1] Sung No Yoon, M.D.,[1] Yeong Jin Choi, M.D.,[2] Chul Woo Yang, M.D.,[1] Byung Kee Bang, M.D.[1]

Departments of Internal Medicine[1] and Clinical Pathology[2], Kangnam St. Mary's Hospital, Catholic Medical College, Seoul, Korea

Received : July 18, 1996
Accepted : January 14, 1997

Address for correspondence
Byung Kee Bang, Department of Internal Medicine, Kangnam St. Mary's Hospital, Catholic University Medical College, 505 Banpo-dong, Seocho-ku, Seoul 137-040, Korea.
Tel : (02) 590-1422, Fax : (02) 599-3589

* This report was supported in part by the Clinical Research Foundation of the Catholic Medical Center.

INTRODUCTION

The principal pharmacological effect of colchicine is antigout activity, and this drug has been used therapeutically for more than 200 years. In spite of its usefulness, many adverse effects of colchicine (e.g. myopathy and neuropathy) have been reported. Of these, colchicine-induced myopathy was mainly related to the long-term use (1~4) or acute intoxication due to bizarre self-dosing (5). We recently experienced a case of acute myopathy developed after a routine short term dosage of colchicine in a cyclosporine-treated renal transplant patient.

CASE REPORT

A 49-year-old male presented with weakness and myalgia in the lower extremities which had developed 10 days earlier. He had received a renal transplantation and bilateral nephrectomy due to chronic pyelonephritis with bilateral renal stones 5 years ago and was taking cyclosporine A 125 mg twice daily. He had taken colchicine infrequently because of gouty arthritis, which had developed 3 years before. Again, a painful swelling developed on the right great toe 2 weeks before the admission, so he took colchicine 1.2 mg twice daily for 3 days by himself.

On admission, vital signs were stable and physical examinations showed mild muscle weakness in the lower extremities. Blood chemistry were as follows ; BUN 37.9 mg/dl (16.9 mg/dl, 3 months ago), creatinine 2.7 mg/dl (1.6 mg/dl, 3months ago), sodium 141 mEq/L, potassium 5.2 mEq/L, total calcium 9.6 mg/dl, phosphate 3.2 mg/dl, magnesium 1.9 mg/dl, uric acid 8.6 mg/dl (6.8 mg/dl, 3 months ago), creatinine phosphokinase 14,958 IU/L (CK-MM type), aspartate aminotransferase 561 IU/L, lactic dehydrogenase 1102 IU/L (increased with isomorphic pattern), alanine aminotransferase 403 IU/L, serum myoglobin over 300 ng/ml, serum aldolase 23.5 U/ml. Whole blood cyclosporine A level was 267 ng/ml. 24 hour urine volume was 2,000 ml/day and Ccr was 48.6 ml/min.

HBsAg/Ab were negative/positive, HBeAg/Ab were negative/positive, IgG/IgM antiHBc were positive/negative and anti-HCV was negative. Hepatic scintigraphy showed no definite abnormality and thyroid function was normal.

Tc^{99}-MDP bone scan showed diffuse muscular uptake, suggesting muscular destruction. Electromyography demonstrated a myopathy as evidenced by positive sharp waves at rest and decreased numbers of multiple unit

action potentials in proximal and distal limb muscles. Nerve conduction studies showed normal values. Muscle biopsy, performed at the quadriceps on the 4th hospital day, showed a loss of cross striation and centralization of nuclei, consistent with degenerative changes of muscle fibers (Fig. 1).

Colchicine was discontinued immediately under the presumptive diagnosis of colchicine-induced myopathy. After that, clinical symptoms gradually improved and the serum muscle enzyme levels returned to normal. On the 14th hospital day, serum creatinine was decreased to 1.5 mg/dl. He was discharged on the 17th hospital day with an improved condition.

DISCUSSION

Colchicine-induced myopathy was strongly suggested in this case since the clinical symptoms and signs of myopathy developed just after colchicine ingestion and improved dramatically after withdrawal from the drug. Although many other possible causes (cyclosporine, myopathy-inducing drugs, electrolyte imbalances, endocrine abnormalities or infections) of myopathy were considered, they could be excluded on the basis of the following facts.

First, cyclosporine doesn't seem to be directly associated with the muscle damage since the whole blood cyclosporine level was normal and the myopathy improved in spite of continuous administration of this drug. Second, other myopathy inducing drugs (glucocorticoid, lovastatin, bezafibrate, gemfibrozil, cimetidine, and sulfonamide etc.) or alcohol abuse were excluded by clinical history. Third, electrolyte imbalances like hyperkalemia, hypophosphatemia or hypomagnesemia were not present. Fourth, there was no clinical evidence of endocrine abnormalities including hypothyroidism. Finally, infection-associated myopathy was excluded on the basis of clinical history and laboratory findings.

The known predisposing factors of colchicine-induced myopathy are chronic use of colchicine or acute intoxication by bizzare dosage. This case is distinguished from previous reports by the fact that short-term (only three days), customary dose (1.2 mg b.i.d.) of colchicine could induce myopathy. Easy accumulation of colchicine by renal insufficieny (2) and interference with the hepatic metabolism or renal clearance of this drug by cyclosporine (1) was suggested as the main pathogenesis of myopathy in this case.

Colchicine-induced myopathy is characterized by vacuolar changes in myocytes. This finding represents an accumulation of lysosomes and autophagic vacuoles and is related to the disruptions of microtubule-dependent cytoskeletal network. But, a muscle biopsy in our case revealed only degenerative changes. This minor changes seemed to be related to the short clinical course, and extraction or distortion of vacuoles during paraffin-embedding (4).

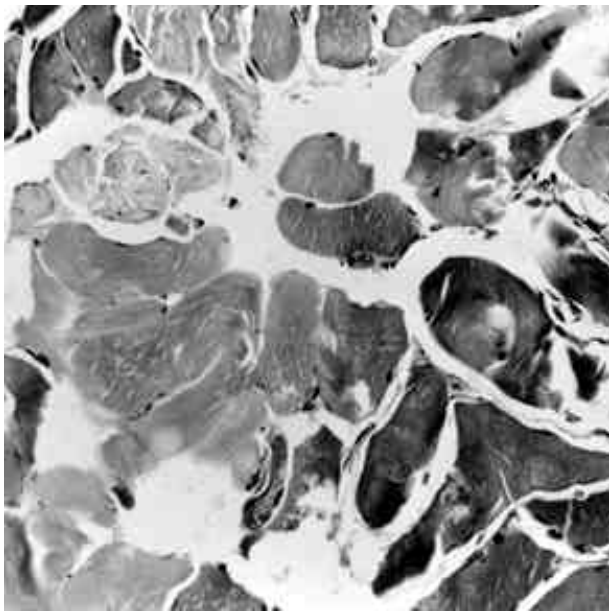

Fig. 1. Muscle biopsy shows loss of cross-striation and centralization of nuclei, suggestive of muscular degeneration.

In summary, this case shows that even short term administration of a routine dose of colchicine can cause myopahty in cyclosporine-treated renal transplant patients.

REFERENCES

1. Rieger EH, Halasz NA, Wahlstrom HE. *Colchicine neuropathy after renal transplantation. Transplantation 1990 ; 49 : 1196-8.*
2. Kuncl RW, Duncan G, Watson D, Alderson K, Rogawski MA, Pepper M. *Colchicine myopathy and neuropathy. N Engl J Med 1987 ; 316 : 1562-8.*
3. Younger DS, Mayer SA, Weimer LH, Alderson LM, Seplowitz AH, Lovelace RE. *Colchicine-induced myopathy and neuropathy. Neurology 1991 ; 41 : 943.*
4. Kuncl RW, Duncan G. *Chronic human colchicine myopathy and neuropathy. Arch Neurol 1988 ; 45 : 245-6.*
5. Riggs JE, Schochet SS, Gutmann L, Crosby TW, DiBartolomeo AG. *Chronic human colchicine neuropahty and myopathy. Arch Neurol 1986 ; 43 : 521-3.*