Colchicine induced rhabdomyolysis

I Chattopadhyay, H G M Shetty, P A Routledge, J Jeffery

Abstract
A case of colchicine induced rhabdomyolysis is reported. A 73 year old man with ischaemic heart disease, atrial fibrillation, chronic congestive cardiac failure, and chronic gout presented with diffuse muscle pain. He had been taking an increased dose of colchicine (1.5 mg daily) for an exacerbation of gout for six weeks before the presentation. Investigations confirmed the diagnosis of rhabdomyolysis and discontinuation of colchicine resulted in resolution of clinical and biochemical features of rhabdomyolysis. Although neuromuscular adverse effects of colchicine are well recognised, rhabdomyolysis is rare and this is only the fourth reported case of colchicine induced rhabdomyolysis in the literature.

Keywords: colchicine; rhabdomyolysis; gout

Colchicine is a unique anti-inflammatory agent that has been therapeutically used in acute gout for over 230 years. The adverse effects of the drug range from nausea, vomiting, diarrhoea, and abdominal pain to agranulocytosis, aplastic anaemia, and alopecia. Colchicine has been reported to cause myoneuropathy and myotonia, and rarely, rhabdomyolysis and discontinuation of colchicine resulted in biochemical features of rhabdomyolysis. Colchicine induced myotoxicity may occur in presence of normal renal function. Cautious dosing of colchicine is important especially in presence of renal impairment. Any patient on colchicine should be monitored for neuromuscular adverse effects.

Key points
- Colchicine may cause myoneuropathy, myotonia and, rarely, rhabdomyolysis.
- Cautious dosing of colchicine is important especially in presence of renal impairment.
- Any patient on colchicine should be monitored for neuromuscular adverse effects.

Figure 1   Plasma creatine kinase and creatinine concentrations after withdrawal of colchicine.
myocardial infarction and the echocardiogram confirmed moderate left ventricular dysfunction. Ultrasound scan of the kidneys was normal. A muscle biopsy was not performed as the patient was on warfarin and had an international normalised ratio of 2.5. Rhabdomyolysis was diagnosed on clinical and biochemical grounds. Colchicine was thought to be a factor in the genesis of the rhabdomyolysis because of the rapid onset of symptoms shortly after an increase in the dose of the drug and the lack of any alternative explanations for myotoxicity.

Colchicine was withdrawn and frusemide and lisinopril doses were reduced because of the renal impairment. By day 3, his muscle pain and tenderness had improved but he required assistance to walk. By day 4, his renal functions began to improve and the creatine kinase had fallen to 5294 U/l. By day 7 his muscle power had improved significantly and by day 20, his renal function had improved further and creatine kinase was normal (urea 6.5 mmol/l, creatinine 116 µmol/l, creatine kinase 161 U/l) (fig 1).

Fourteen days after colchicine withdrawal, his muscle pain and tenderness had improved but he required assistance to walk. By day 4, his renal functions began to improve and the creatine kinase had fallen to 5294 U/l. By day 7 his muscle power had returned to normal and he was mobilising independently.

Discussion
Neuromuscular adverse effects of colchicine in the form of myoneuropathy and myotonia are well recognised. Rhabdomyolysis induced by colchicine is, however, rare with only three reports in the literature. One case each of myositis and polymyositis had previously been reported to the Committee on Safety of Medicines (CSM). This is the first case of colchicine induced rhabdomyolysis reported to the CSM. Although patients with impaired renal function appear to be at a higher risk for colchicine induced neuromuscular adverse effects, the drug can be myotoxic even in presence of normal renal function as in our case. In some renal and cardiac transplant cases drug interaction with cyclosporin has been suggested to be the precipitating factor for colchicine myopathy.

The dosage and duration of colchicine ingestion does not seem to be clearly related to the risk of developing muscle toxicity. On an average most patients reported with myopathy consumed 1 mg or more of the drug for more than six months.

Rhabdomyolysis has been reported in a case of familial Mediterranean fever after ingestion of 1 mg of colchicine daily for one year. Our patient had consumed 1.5 mg of the drug daily for six weeks, similar to a previously described case of rhabdomyolysis.

The pathogenesis of colchicine myopathy may be related to disruption of a cytoskeletal microtubular network that interacts with lysosomes. Although an electromyogram in colchicine myopathy shows non-specific myopathic changes, a muscle biopsy specimen shows a characteristic vacuolar myopathy in the absence of necrosis. Complete recovery is the rule and occurs, as in our case, within weeks of stopping colchicine. Corticosteroids have been used to hasten recovery in certain cases.

This case highlights a rare but serious and potentially life threatening neuromuscular adverse effect of colchicine. Since pre-existent renal impairment is a predisposing factor for neuromuscular toxicity, cautious dosing of colchicine is warranted in the presence of renal impairment. Cautious dosing of colchicine is warranted in the presence of abnormal baseline renal function. It is important to note, however, that colchicine may be myotoxic even in presence of normal renal function, as illustrated in our case. Hence any patient on the drug should be carefully monitored for symptoms of myotoxicity with measurement of creatine kinase when clinically indicated.

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