Colchicine-Induced Hepatotoxicity

Altuğ Şenol Assoc. Prof. MD[1], Mehmet İşler Prof. MD[1], Muhammed Cem Koçkar Assoc. Prof. MD[1], Erkan Cüre MD[2], Yıldıran Songür Prof. MD[1]

[1]Süleyman Demirel University, Medical Faculty, Department of Gastroenterology, Isparta, TURKEY

[2]Safranbolu State Hospital, Department of Internal Medicine, Safranbolu, TURKEY

ABSTRACT

Colchicine is an agent that is used for the treatment of inflammatory disease such as Familial Mediterranean Fever (FMF) and acute gouty arthritis. Therapeutic oral doses of colchicine therapy are associated with numerous adverse effects. Gastrointestinal symptoms due to increased peristaltic activity are common. However, no cases of colchicine induced hepatotoxicity have been reported in the literature with the therapeutic oral doses. We report a case of colchicine induced hepatotoxicity in a 38 year old patient with FMF.

• ***Key Words:*** *Colchicine, hepatotoxicity, Familial Mediterranean Fever (FMF).* ***Nobel Med 2009; 5(2): 72-74***

ÖZET

KOLŞİSİN KULLANIMINA BAĞLI GELİŞEN HEPATOTOKSİSİTE

Kolşisin akut gut artriti ve ailevi akdeniz ateşi (AAA) gibi inflamatuvar hastalıkların tedavisinde kullanılan bir ajandır. Kolşisin tedavisinin terapötik oral dozlarında çeşitli yan etkiler görülebilir. Peristaltik activite artışından dolayı gastrointestinal semptomlar sıktır. Bununla birlikte, literatürde kolşisinin terapötik dozlarında oluşan hepatotoksisite vakası bildirilmemiştir.

AAA'li 38 yaşındaki bir hastada kolşisine bağlı gelişen hepatotoksisite vakası sunulacaktır.

• **Anahtar Kelimeler:** Kolşisin, hepatotoksisite, Ailevi Akdeniz Ateşi (AAA). **Nobel Med 2009; 5(2): 72-74**

INTRODUCTION

Drugs are important causes of the liver injury. The severity of injury may vary from minor non-specific changes in hepatic structure and function to fulminant hepatic failure and chronic hepatitis. Colchicine induced hepatotoxicity is a rare condition in clinical practice.

Colchicine is derived from the corms of colchicum autumnale and is used primarily to treat familial Mediterranean fever (FMF) attacks and FMF-associated amyloidosis, as well as for the treatment of acute gouty arthritis and prophylaxis of recurrent attacks. In here, we report a case of colchicine induced hepatotoxicity in a 38 year old patient with FMF.

CASE REPORT

A 38 year old man was admitted to emergency department with acute attack of intermittent abdominal pain which has been started when he was 10 years old. His abdominal pain was appearing from right hypochondriac region and was expanding to all abdomens. Fever was usually accompanying to pain and both were lasting two or three days. At the beginning of pain attack was seen in monthly, but in recent it became weekly. On admission he had no constipation, vomiting and nausea. Physical examination was normal except abdominal tenderness. Erythrocyte sedimentation rate (ESR) was 73 mm/h, C reactive protein (CRP) was 55 mg/l (normal: 0-5 mg/l), fibrinogen was 4/L (normal: 2.0-4.0, g/dl), white blood cell count (WBC) was 5.700/ml, hemoglobin was 13.2 g/dl, blood glucose, creatine, aspartate aminotransferase (AST), alanine aminotransferase (ALT) were normal, alkaline phosphates (ALP) was 215 (normal: 53-28 U/L).

Upper gastrointestinal endoscopy showed antral gastritis. His abdominal pain was disappeared three days later. At day 5, ESR was 51 mm/hour, WBC was 5.900/mL, CRP was 22,7 mg/L, fibrinogen was 2.87/L. Familial Mediterranean fever gene mutation test revealed M680I (G/C) homozygote mutation. Colchicine 0.5 mg t.i.d has been started. Abdominal pain has not occurred during one month. Routine laboratory control showed AST of 101U/L and ALT of 193 U/L, one month later. He was taking no drug except colchicine and no alcohol at that time. Liver parenchyma echogenicity and liver size were normal ultrasonographically. Serum albumin, prothrombin time, ALP and thyroid stimulating hormone levels were in normal ranges. Anti-HAV IgG was positive, anti-HAV IgM, HbsAg, anti-HBc IgM, anti-HCV, HCV-RNA and anti-HIV were negative. Antinuclear antibody, anti-smooth muscle antibody, and anti-liver-kidney microsomal type I antibody were also within normal ranges. Thereafter dose of colchicum was decreased to 0.5 mg b.i.d. Fifteen days later, AST was 98 U/L and ALT was 245 U/L. So colchicum was stopped. One month later, AST was 20 U/L and ALT was 29 U/L. However, about two weeks later he had abdominal pain again. So colchicine was started again. One month later AST was 49 U/L and ALT was 151 U/L, so colchicum was stopped again. Twenty days later AST and ALT levels were detected as normal. Afterwards abdominal pain attack was recurred, and so azathioprine was started. Now, he has no abdominal pain and transaminase levels are still normal in one year follow up.

DISCUSSION

The diagnosis of drug-induced hepatotoxicity is based on exclusion of other possible causes of hepatic dysfunction and on close to association between drug administration and the onset of liver disease while liver biopsy may allow a correct diagnosis.[1-3] In literature, there are few case reports of hepatoxicity associated with colchicine poisoning,[4-6] but no case of hepatotoxicity induced by therapeutic doses colchicine has been reported. Ataş et al. reported to findings of colchicine poisoning such as gastrointestinal symptoms, hepatotoxicity, cardiotoxicity, bone marrow suppression, hypocalcaemia, hair loss and died.[4]

Crocenzi et al. reported that colchicine-induced hepatotoxicity in experimental models depends on the magnitude and composition of the bile salt flux traversing the liver.[7] Colchicine significantly impairs hepatocyte integrity argue for caution in interpreting previous data obtained using microtubule-disrupting agents as a tool to assess vesicular transport in the liver.[7]

Colchicine is effective in a dose of 0.015 mg/kg, toxic in dose greater than 0.1 mg/kg, and lethal in a dose of 0.8 mg/kg. Thus, therapeutic range of colchicine level is narrow.[1, 8] In our patient, serum AST and ALT levels were increased 5 times when oral colchicine was used 1.5 mg/day. So colchicine was discontinued. After 2 weeks of discontinuation of colchicine therapy, liver function tests were decreased to normal levels.

As the abdominal pain was recurred after drug therapy was discontinued, so colchicine was started again. At follow up, liver function tests were increased 4 or 5 times again. We could not examine serum colchicine levels in our patient. Because of the increase in the serum aminotransferase levels with the beginning of colchicine and come to the normal levels when the drug stopped and also with the negative serology →

for acute viral infection, negative autoantibody markers and exclusion of other drugs or potentially hepatotoxic agents, we believed that when the colchicine is used in the therapeutic doses it causes hepatotoxicity. In conclusion, patients treated with colchicine need control of liver function tests.

C CORRESPONDING AUTHOR: Erkan Cüre MD, Safranbolu State Hospital, Department of Internal Medicine, Safranbolu, TURKEY erkancure@yahoo.com

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