CASE REPORT

Thiocolchicoside-induced liver injury

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TO THE EDITOR

Drug-induced liver injury (DILI) is an important cause of mortality and morbidity in the general population. Patients suffering from DILI may present with symptoms ranging from minor, nonspecific changes in hepatic structure and function to fulminant hepatic failure or chronic hepatitis.[1] Thiocolchicoside is widely used as a muscle relaxant. The primary side effects of thiocolchicoside are nausea, somnolence, allergy and vasovagal reaction.[2] Epileptic seizures following thiocolchicoside ingestion have been reported in a few cases[3], but other systemic side effects, such as cardiotoxicity, nephrotoxicity or hepatotoxicity, have not been reported. Here, we report the case of a patient whose hepatic and cholestatic enzyme levels were elevated during thiocolchicoside therapy and returned to normal after thiocolchicoside was discontinued. Resolution of the hepatotoxicity was observed after discontinuation of the drug and the initiation of conservative treatment measures. An objective causality assessment, based on a Naranjo score[4] of **6**, suggests that the liver injury was related to the thiocolchicoside treatment.

A 58-year-old man was admitted to the emergency clinic with abdominal discomfort, nausea and a yellowish discoloration of the sclera. Complete blood count and hemostasis parameters were normal. The patient's biochemical test results were as follows: blood urea nitrogen 30 mg/dl (normal: 0 to 40 mg/dl), creatinine 0.9 mg/dl (normal: 0.6 to 1.3 mg/dl), **albumin 3.7 mg/dl (normal: 3.5 to 4.5 mg/dl)**, lactic dehydrogenase 320 IU/L (normal: 0 to 125 IU/L), total bilirubin 3.5 mg/dl (normal: 0.6 to 1.2 mg/dl) with **direct bilirubin 3 mg/dL (normal: 0.2 to 0.4 mg/dl) and indirect bilirubin 0.4 mg/dl** (normal: 0.4 to 0.8 mg/dl), alkaline phosphatase 280 IU/L (normal: 64 to 160 IU/L), gamma glutamyl transpeptidase 204 IU/L (normal: 20 to 64 IU/L), alanine aminotransferase 368 IU/L (normal: 0 to 54 IU/L), aspartate aminotransferase 346 IU/L (normal: 0 to 34 IU/L), serum amylase 280 IU/L (normal: 0 to 250 IU/L). The patient was taking no drugs other than thiocolchicoside and was not consuming alcohol at the time. **Viral serologies (hepatitis A, B and C; cytomegalovirus; Epstein-Barr; herpes simplex; and HIV) and all of the tests for autoantibodies typical of autoimmune liver diseases were negative**. Abdominal ultrasonography and **magnetic resonance cholangiopancreatography** revealed no pathology. Thiocolchicoside was discontinued, and liver and cholestatic enzymes began to decrease, but complete normalization of biochemical parameters was not achieved until 12 days later.

DISCUSSION

DILI can be defined as a liver injury induced by drugs or herbal medicines that leads to liver enzyme abnormalities. The diagnosis of DILI is based on the exclusion of other possible causes of hepatic dysfunction and on a close association between drug administration and the onset of liver disease. Due to methodological difficulties, the true prevalence of DILI is not known, but an occurrence of approximately 14 cases per 100,000 population per year has been reported. Antibiotics, analgesics and NSAIDs are the most common causes of DILI.[1] Thiocolchicoside is a semi-synthetic derivative of colchicoside that exhibits selective affinity for gamma-aminobutyric acid and glycinergic receptors.[5] Thiocolchicoside is used as a muscle relaxant in the treatment of symptomatic spasms and contractures in muscular, rheumatic and neurologic disorders. Adverse events from the use of thiocolchicoside are rarely reported. The main side effects of thiocolchicoside are nausea, somnolence, asthenia, allergy and vasovagal reactions.[2,5] Colchicine, an analog of colchicoside, is also a commonly used drug, especially for rheumatic diseases. Crocenzi et al.[6] demonstrated that in experimental models, colchicine-induced hepatotoxicity depended on the magnitude and composition of the bile salt flux traversing the liver. Ataş et al.[7] reported the cases of four children who presented with gastrointestinal symptoms, hepatotoxicity, cardiotoxicity and bone marrow suppression after colchicine poisoning. However, no cases of hepatotoxicity resulting from therapeutic doses of either thiocolchicoside or colchicine have been reported. In our patient, serum AST and ALT levels were increased when oral thiocolchicoside was administered at 8 mg/day. Two weeks after discontinuing thiocolchicoside therapy, lever enzymes had decreased to normal levels. Because of the increase in the serum aminotransferase levels upon the initiation of thiocolchicoside and their return to normal levels when the drug was discontinued, the negative serology for acute viral infection, the negative tests for autoantibody markers and the exclusion of other drugs or potentially hepatotoxic agents, we believe that thiocolchicoside at therapeutic doses may cause liver injury in some patients. To our knowledge, this is first case of thiocolchicoside-induced hepatotoxicity that has been reported. Although this toxicity occurs only

infrequently, thiocolchicoside should be considered to be a rare hepatotoxic agent in clinical practice.

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