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LETTER TO EDITOR

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Venlafaxine-Induced Hepatotoxicity in a Patient with Ulcerative Colitis

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DEAR EDITOR:

Venlafaxine-induced hepatotoxicity with notably high levels of cholestasis enzymes has rarely been described.[1] Presence of increased cholestasis parameters in a patient with ulcerative colitis (UC) may mimic primary sclerosing cholangitis (PSC). We present here the first case of hepatotoxicity with a prominent increase in the cholestatic enzyme serum level in a patient with UC after Venlafaxine administration.

A 55-year-old man who had a history of UC, pancolitis type, was admitted to our hospital with complaints of appetite loss, malaise and abdominal pain, on February 15, 2006. He has been treated with mesalazine in different doses of 2 to 3 g/day for the last three years. Venlafaxine 150 mg/day which was started after psychiatric consultation two months ago while the serum transaminase levels were normal. He has had two attacks and has been treated with steroids. He has no alcohol consumption and no history of liver disease in his family. Laboratory tests were as follows: alanine aminotransferase level, 192 U/L (ULN, 40 U/L), aspartate aminotransferase level, 157 U/L (ULN, 40 U/L), alkaline phosphatase (ALP) level, 419 U/L (ULN, 141 U/L), and γ-glutamyltransferase (GGT) level, 985 U/L (ULN, 50 U/L). Total and direct bilirubin levels were normal. Viral hepatitis (including HCV RNA-PCR), autoimmune hepatitis, Wilson's disease, hemochromatosis and alpha-1-antitrypsin deficiency were excluded. P-ANCA was negative. Abdominal ultrasonographic examination and magnetic resonance cholangiography were normal.

Venlafaxine was discontinued because of probable adverse reaction. On the 15th day, transaminase levels were normal, but ALP and GGT levels were 696 U/L and 1,635 U/L, respectively. These test results progressively improved 18 days after cessation and all test results were normal on April 9, 2006. The Naranjo probability scale indicated to a probable adverse reaction.

Incidence of PSC in UC patients is about one to four percent.[2] Laboratory, radiological and histological examinations are essential for the diagnosis of PSC. Prognosis of UC worsens with presence of PSC and increases frequency of malignancy. Thus diagnosis of PSC is critical. Increased ALP and GGT levels are signs of concurrent PSC. Inflammatory bowel diseases are frequently associated with psychological disorders. Venlafaxine is generally preferred for treatment of depression due to low incidence of adverse effects like nausea, headache, appetite loss, anxiety, and insomnia. Moreover, it was reported that Venlafaxine may cause acute hepatitis.[3] In our case, increase of ALP and GGT was more remarkable than that of transaminases and no other pathology was determined. ALP and GGT are known as a predictive indicator for liver cholestasis. The presence of increased levels of bilirubin conjugates is indicative of an impaired hepatic clearance. We did not find an increase in bilirubin levels. This maybe related to early stage of drug hepatotoxicity. Cholestasis parameters started to improve three weeks after cessation of Venlafaxine treatment, and returned to normal levels at the end of two months. In two other cases reported in the literature similar to our case increase of cholestasis parameters is higher compared to that of transaminases.[1,4] Although liver biopsy was not

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performed, unexplained increase of ALP and GGT, and reduction of the enzyme levels after discontinuation of the drug suggested drug toxicity. This is the first reported Venlafaxine-induced hepatotoxicity in a patient with UC.

As a conclusion, it is crucial to be cautious in the treatment and follow-up of toxicity due to drugs that can cause laboratory abnormalities which mimic sclerosing cholangitis in ulcerative colitis patients.

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