Acute liver failure due to fluconazole and ornidazole usage

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To the Editor,

24-year-old female patient was admitted with jaundice, itching and abdominal distention. The patient was puted on fluconazole 150 mg/day, ornidazol 1500 mg/day therapy with the diagnosis of vaginitis. On the fifth day of the treatment the patient stopped treatment because of nausea and vomiting. 15 days after the ongoing complaints, jaundice, pruritus and abdominal swelling was developed and the patients was hospitalized. Physical examination revealed icterus, ascites. There was no hepatosplenomegaly. Laboratory exams revealed, Leukocyte : 6000 mm^3, Hemoglobin : 11,5 g/dl, Hematocrit : 33%, Platelet : 189.000 mm^3, ALT : 918 U/L, AST : 1569 U/L, ALP : 207 U/L, GGT : 72 U/L, Total bilirubin : 17 mg/dl, Direct bilirubin : 13,9 mg/dl, Albumin : 2.4 gr/dl, INR : 1.74, PT : 20,9 sec, PTT : 47 sec, Sedimentation rate : 2 mm/hr and C-reactive protein : 4 mg/dl, respectively. During etiological investigations of the patient diagnosed as acute hepatitis ; viral markers and autoimmune antibody were negative. Kayser Fleischer ring was not found in ophthalmologic examination. Ceruloplasmin level, and 24-hour urine copper levels were within normal limits. Transferrin saturation and alpha-1 antitrypsin level was normal. No pathology was found in abdominal computed tomography and angiography other than common intraabdominal fluid. All the reasons for the etiology of acute hepatitis were ruled out. Ornidazole and fluconazole was considered to be toxic to the liver. Supportive therapy was started to the patient whose couagulation tests was deteriorated (INR 3.3), emerging massive ascites but there was no encephalopathy. In follow-ups, liver enzymes and bilirubin levels began to decline, and coagulation tests became to normal. After 3 months of the admission, biochemistry values were completely normal.

Ornidazole, synthetic nitroimidazole derivatives are used in the treatment of infections caused by anaerobic bacteria and protozoa. The drugs are generally well tolerated. The most common side effect are metallic taste, nausea, vomiting, abdominal pain and diarrhea (1). Hepatotoxicity is a rare side effect and few cases have been reported (2).

Drug-related liver injuries are rare. These are usually mild and subclinical. Serious consequences and even death may ocur rarely. Drug reactions are divided into two basic types. Type A reactions, which are predictable, common and related to the pharmacologic action of the drug ; and type B reactions, which are unpredictable, non-dose-dependent, uncommon and generally not related to any pharmacologic action, with several subclassifications (2). Drug-induced liver injury has three characteristics : absence of baseline liver abnormality, temporal relationship to the use of the drug and improvement upon withdrawal. Recurrence with incidental rechallenge confirms the diagnosis ; however, it is unethical to be intentional (3). Liver injury may be cytolytic, cholestatic or mixed. Our patient had cholestatic laboratory findings. The drugs may trigger an autoimmune hepatitis as previously described by Kosar *et al*. (4). In conclusion, ornidazole and fluconazole may cause hepatotoxic damage resembling acute severe cholestatic hepatitis and acute liver failure. Early recognition and withdrawal of the drug may prevent further damage.

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