Paroxetine Induced Toxic Hepatitis: Case Report

Paroksetinin Neden Olduğu Toksik Hepatit

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ABSTRACT Paroxetine is an antidepressant agent, which affects via selective inhibition of serotonin reuptake. It is widely used for the treatment of depression, obsessive compulsive disorder, panic disorder and anxiety disorder. Although it has low side effects and a high safety profile, some cases of severe toxic hepatitis associated with paroxetine have been reported. Hepatotoxicity can be hepatocellular, cholestatic or mixed type. It is generally idiosyncratic and unpredictable, however patients with high risk such as coexisting liver disease and use of other potential hepatotoxic drugs, should be monitored carefully for hepatotoxicity while using this drug. Here we report a case of severe toxic hepatitis related to use of paroxetine. The patient recoverd completely after the the drug was stopped.

Key Words: Paroxetine; hepatitis, toxic

ÖZET Paroksetin serotonin geri alımının seçici olarak inhibisyonu üzerinden etki eden antidepresan bir ilaçtır. Depresyon, obsesif kompulsif bozukluk, panik bozukluk ve anksiyete bozukluğunun tedavisinde yaygın olarak kullanılır. Yan etkileri az ve güvenlik profili yüksek bir ilaç olmasına rağmen, paroksetinle ilişkili ciddi toksik hepatit olguları bildirilmiştir. Hepatotoksisite hepatosellüler, kolestatik ve karma tipte olabilir. Genellikle idiyosenkraziktir ve öngörülemez; fakat eşlik eden karaciğer hastalığı olanlar ve potansiyel hepatotoksik ilaç kullananlar gibi yüksek riskli hastalar, bu ilacın kullanımı sırasında hepatotoksisite yönünden dikkatle izlenmelidir. Burada, paroksetin kullanımına bağlı ağır bir toksik hepatit olgusu sunulmuştur. İlaç kesildikten sonra tam düzelme gözlenmiştir.

Anahtar Kelimeler: Paroksetin; hepatit, toksik

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Paroxetine is an antidepressant agent, which affects via selective inhibition of serotonin reuptake. It is effective for the treatment of depression, obsessive compulsive disorder, panic disorder and anxiety disorder. These agents are widely preferred because of their favourable side effects and safety profiles.[1,2] Severe hepatotoxicity associated with paroxetine is a rare condition and only a few cases have been reported in the literature. Clinical and laboratory improvement was observed in all of cases after the cessation of the drug.[3-10]

Here we report a case who was treated with paroxetine because of depressive symptoms and developed a severe hepatocellular toxic hepatitis, which completely recovered after the cessation of the drug.

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CASE REPORT

A 34-year-old woman was admitted to our clinic because of weakness that persisted for 1 month. In her history, she had no diseases except type 2 diabetes for 1 year. She did not use alcohol or any herbal medicine. She has used paroxetine 20 mg daily for 1 month, because of depression. Laboratory findings were as follows: serum alanine aminotransferase (ALT) 1340 U/L (0-34 U/L), aspartam aminotransferase (AST) 1124 U/L (0-31 U/L), gamma glutamyl transferase (GGT) 36 U/L (0-38 U/L), alkaline phosphatase (ALP) 268 U/L (30-120 U/L), total bilirubin 1,6 mg/dL, direct bilirubin 0,4 mg/dL, albumin 3,6 g/dL, prothrombin time 13 sec, Hbs Ag and anti-Hbc IgM negative, anti-HBs positive, anti-Hepatitis C Virus (HCV) antibody and anti-hepatitis A virus (HAV) IgM antibody negative. Abdominal ultrasonography revealed no pathologic findings except for mild hepatomegaly. The patient was hospitalized with the diagnosis of acute hepatitis and paroxetine was stopped. The laboratory findings to investigate other possible etiologic factors for the hepatitis were as follows: anti-Epstein Barr Virus IgM antibodies, anti-cytomegalovirus IgM antibodies, antinuclear antibody (ANA), anti-smooth muscle antibody (ASMA), anti liver-kidney microsomal (LKM) antibodies and anti-mitochondrial antibody (AMA) negative, serum alpha 1-antitrypsin level 220 mg/dL (78-200 mg/dL), ceruloplasmin 49 mg/dL (25-63 mg/dL), 24-hour urine copper 43 microgram/day (2-80 microgram/L), serum ferritin level 2 ng/mL, and transferrin saturation 2%. Serum aminotranspherase levels gradually decreased within days; serum ALT level was 20 U/L and AST level was 30 U/L 4 weeks after the cessation of paroxetine. Liver enzymes were normal within 4 months of follow-up.

DISCUSSION

Paroxetine is a selective serotonin reuptake inhibitor and a popular choice for depression therapy worldwide. It has a low side-effect profile, even at high doses.[1]

Altough transient mild elevations of liver enzymes have been observed with use of paroxetine,[11,12] severe hepatoxicity is a rare condition and only ten cases were reported in the literature. Hepatotoxicity can be hepatocellular, cholestatic or mixed type.[3-10] Diagnosis of toxic hepatitis was supported by liver biopsy in some of these cases, while it was considered unnecessary in the others because of improvement within days after the cessation of the drug. In cases reported in the literature, liver enzymes completely improved in a follow-up period ranging from 1 week to 6 months and all cases showed favourable outcome.

Paroxetine is metabolized by two major liver enzymes. Lack of cytochrome P450 2D6 enzyme activity was detected in the patients with poor metabolization of this drug.[13,14] In addition, elderly patients achive higher plasma paroxetine concentrations than younger cases using similar doses.[15] The hepatocellular damage of paroxetine seems to be an idiosyncratic reaction rather than a dose-dependent effect.[4,6] It is unpredictable and usually does not require the monitorization of liver enzymes. However, in the presence of risk factors such as pre-existing cirrhosis and use of other hepatotoxic drugs, patients should be monitored carefully.[6]

In our case, severe elevations of liver enzymes, which were hepatocellular type, were detected 1 month after the initiation of paroxetine. Liver enzymes gradually decreased within days and completely improved at 4 weeks after the cessation of the drug. Liver biopsy was considered unnecessary because of the exclusion of other possible etiologic factors for hepatitis and the rapid improvement of transaminase levels. Considering the findings and no use of any other hepatotoxic drug, this clinical condition was diagnosed as paroxetine induced hepatocellular toxic hepatitis.

In conclusion, hepatotoxicity associated with paroxetine is a rare condition, but it can occur. Severe liver injury can develop with the use of these drugs and especially patients with high risk should be monitored for hepatotoxicity during the treatment period.

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