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Acute Severe Hepatotoxicity Associated with Clomipramine

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ÖZET:

Klomipramine bağlı akut ve ciddi hepatotoksisite

Bayan Y, irritabilite, depresif duygudurum, istenç yokluğu, ilgi-istek azalması, iştah azalması ve iki ay içinde 10 kg'a varan kilo kaybı, amenore, dismorfofobi, ve psikoomotor retardasyon bulgu ve yakınmalarıyla başvurdu. Psikiyatrik değerlendirme major depresif epizot varlığını ortaya koydu. Hastaya 25 mg/gün klomipramin ve beraberinde bilişsel davranışçı tedavi başlandı. Aspartat aminotransferaz düzeyi 212 IU/lt ve alanin aminotransferaz düzeyi de 474 IU/lt idi. Bunun üzerine klomipramin hemen kesildi. Bir ay sonra enzim düzeyleri normale dönmüştü. Hekimler, klomipraminin akut hepatotoksisiteye yol açabilme ihtimali karşısında uyanık olmalı ve şüphelenildiğinde kesmelidirler.

Anahtar sözcükler: Klomipramin, hepatotoksisite, aspartat

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ABSTRACT:

Acute severe hepatotoxicity associated with clomipramine

Miss Y. presented with complaints of irritability, depressed mood, avolition, anhedonia, markedly decreased appetite and around 10 kg weight loss within two months, amenorrhea, dysmorphophobia, and psychomotor retardation. The psychiatric evaluation revealed major depressive episode. She was given a prescription for 25 mg/day of clomipramine for her depression, and also cognitive behavioral therapy was started. Her level of aspartate aminotransferase was 212 IU/liter, and her alanine aminotransferase level was 474 IU/liter. Therefore, clomipramine was stopped urgently. After one month, the enzymes returned to normal values. Physicians should be alert to the possibility that clomipramine can cause acute hepatotoxicity and consider early discontinuation of an antidepressant if the condition is suspected.

Key words: Clomipramine, hepatotoxicity, aspartate

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INTRODUCTION

Clomipramine, classified as a tricyclic antidepressant with serotonin reuptake inhibiting properties, is effective in treating various psychiatric disorders, including depressive and anxiety disorders and particularly obsessive-compulsive disorder. It has a wide range of transient side effects, particularly anticholinergic ones. Drug-induced hepatotoxicity is a rare but obviously serious and life-threatening side effect of the antidepressant agents. Only isolated cases of liver injury in association with clomipramine have previously been reported (1). To our knowledge, the following case is the first reported instance of significant liver damage related to clomipramine. In the present paper, we report the case of a patient with depressive disorder who developed acute and severe hepatotoxicity while on clomipramine.

CASE REPORT

Miss Y, female, 18 years-old, single.

Miss Y. and her parents applied to our outpatient clinic at Firat University School of Medicine because of complaints of irritability, depressive mood, avolition, anhedonia, markedly decreased appetite and around 10 kg weight loss within two months, amenorrhea, dysmorphophobia, and psychomotor retardation. Psychiatric evaluation revealed a major depressive episode according to the DSM-IV. In addition, The Structured Clinical Interview for DSM-IV–Patient Version (SCID-I) in Turkish version (2) was conducted to assess Axis I psychiatric comorbidity and showed there was no comorbid disorder. Her complaints had started about one year ago. She had been admitted to a inpatient medicine unit of a local general hospital one month ago because of marked

weight loss. Her admission lasted for two weeks and no organic etiology had been detected. Afterwards she was referred and admitted to our inpatient unit. For routine medical evaluation, blood samples for biochemical tests, posterior-anterior lung radiography and electrocardiography were requested. All of the results were within normal limits. The Hamilton Depression Rating Scale (HDRS) (3) score was determined to be 26 at baseline. She was given a prescription for 25 mg/day of clomipramine for her depression, and cognitive behavioral therapy was started for her depression. The clomipramine dose was increased to 75 mg/day by day 4. At day 7 of the treatment, she complained of significant weakness. When we performed a physical examination, the results were normal; however, after a stat biochemical investigation, some important data were obtained. Her level of aspartate aminotransferase was 212 IU/liter, and her alanine aminotransferase level was 474 IU/liter. Bilirubin and alkaline phosphatase levels were normal. There was no abnormality in the complete blood count. Abdominal ultrasonography and serologic examinations were normal. All investigations on autoantibodies were evaluated as normal. Therefore, clomipramine was stopped urgently. Three days later, aspartate transaminase had decreased to 168 IU/liter, and alanine aminotransferase level to 364 IU/liter. Six days later, both enzymes had decreased to below half the day 7 values. After one month, it was observed that the enzymes returned to normal values.

DISCUSSION

This is one of several clomipramine-induced acute hepatotoxicity cases in the literature. Clomipramine is classified as a tricyclic antidepressant with serotonin reuptake inhibiting properties. It is effective in treating several psychiatric disorders, including depression, panic disorder, and obsessive-compulsive disorder. Clomipramine, in common with other tricyclic antidepressants, has some side effects particularly anticholinergic ones, which decrease treatment adherence. In the present case, a causal association between clomipramine and hepatotoxicity can be proposed because of the following reasons; (a) the patient had no history of hepatic illness, as informed by herself and her first-degree relatives, (b) routine biochemical examination was evaluated as completely normal at the beginning of therapy, (c) there was a temporal relationship between the administration of the drug and the onset of hepatic abnormalities, and (d) a rapid recovery was observed after stopping the clomipramine. In the literature, there is only one hepatitis case associated directly with clomipramine. Alderman et al. (1) reported a case at 67-year-old man who developed concurrent severe agranulocytosis and hepatitis as a result of treatment with clomipramine. Apart from this, we could not find any report about direct clomipramine-induced acute hepatotoxicity. Therefore, individual genetic factors may be playing an important role. Meanwhile it should also be taken into consideration that there may be cross-hepatotoxicity between tricyclic antidepressants (4).

Given the high prevalence of depression and the widespread use of antidepressants including clomipramine, physicians should be alert to the possibility that these medications can cause acute hepatotoxicity and consider early discontinuation of an antidepressant if the condition is suspected.

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