CLINICAL VIGNETTE

An Adult with Atomoxetine-Induced Hepatitis: A Report of a Rare Case

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Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is the most common childhood neurobehavioral disorder in the world, with a prevalence of 6-8%.[1] This disorder often persists into adulthood, and current prevalence in the US is estimated to be 4.4%.[2] Because ADHD is associated with a significant impairment in social, occupational, and academic settings, pharmacotherapy is of the ultimate importance. While stimulants are the most tested and commonly prescribed treatments and demonstrate the greatest efficacy in ADHD non-stimulants, including atomoxetine, are often preferred due to less potential for abuse and an overall safer side effect profile. We report a rare adverse effect in an adult likely caused by a new prescription of atomoxetine for ADHD.

Case Report

A 59-year-old Caucasian male with ADHD presented to his primary care provider after developing abdominal pain, decreased appetite, fatigue, and jaundice over a seven-day period. He also had an abscess on his right hand that had developed over the past several days. He had no prior history of liver disease but had been exposed to Hepatitis C with undetectable viral loads and to Hepatitis B with subsequent immunity. The patient was taking hydrochlorothiazide for hypertension and mirtazapine for depression. He had been started on atomoxetine for his ADHD three weeks prior to presentation. He was not taking any other medications, including acetaminophen, non-steroidal anti-inflammatory medications, over-the-counter drugs, or herbals. The patient was abusing heroin several times per week, both intravenously and intramuscularly, using clean needles and not sharing. He was smoking a half-pack of cigarettes daily but denied any alcohol use. His vital signs were normal. Examination was significant for generalized jaundice, conjunctival icterus, and mild right upper quadrant tenderness. There was no rash and no hepatosplenomegaly. Blood tests were drawn, and the patient was instructed to stop taking atomoxetine. He was prescribed oral cephalexin for the abscess on his right hand and informed he would be called with his laboratory test results.

Three days later, the lab tests returned significant for a total bilirubin of 14.3 mg/dL (direct 7.1) and marked elevations in serum aminotransferase levels (ALT 3566 and AST 2934) with minimal increase in serum alkaline phosphatase (269 U/L). The patient was contacted and referred to the emergency department for further evaluation of abnormal liver tests. In the emergency room later that day, the patient had the same physical complaints as before but stated that the abdominal pain had slightly improved. His vital signs and physical exam were unchanged. Labs were significant for WBC 5.9 k/uL, platelets 110 k/uL, PT 15.3 seconds, PTT 39.7 seconds, INR 1.4, total bilirubin of 13.4 mg/dL (direct 7.5), ALT 2306 U/L, AST 881 U/L, and alkaline phosphatase 214 U/L. Urine toxicology demonstrated opiates. Serum acetaminophen and ethanol levels were undetectable. Abdominal ultrasound showed no evidence of hepatic vein thrombosis or ischemic process. Tests for antibodies to Hepatitis A and B confirmed immunity; hepatitis C RNA was undetectable.

Atomoxetine was discontinued, and the patient was monitored on supportive measures only. An incision and drainage was performed on the abscess, and the patient continued oral minocycline for two doses with transition to cephalexin. He markedly improved over the next several days with resolution of his jaundice and abdominal pain and improvement of his laboratory values. Upon discharge, the patient had a total bilirubin of 5.2 mg/dL, ALT 850 U/L, AST 161 U/L, and alkaline phosphatase 199 U/L.

It was felt the patient had an acute hepatitis secondary to atomoxetine. Because of the risk of recurrence with re-exposure, the patient was instructed to avoid atomoxetine in the future and follow up with psychiatry as an outpatient. Several months after his initial presentation, the patient's acute hepatitis has completely resolved, and his liver function tests normalized.

Discussion

We described a case of acute hepatitis in an adult occurring after initiation of atomoxetine therapy with a combination of jaundice and high serum aminotransferase levels, signaling hepatocellular injury. Upon discontinuation of this medication, the patient's jaundice resolved, and the laboratory levels normalized.

Atomoxetine, a selective norepinephrine reuptake inhibitor, was the first non-stimulant approved for ADHD in children and adults. This medication is generally considered both safe

and effective and is associated with only a few adverse effects–primarily anti-cholinergic–as well as dyspepsia, nausea, vomiting, fatigue, rash, decreased appetite, and weight loss.[3] Because it is rare, hepatotoxicity is an under-reported side effect. When it does occur, it is usually transient and related to liver injury, not failure.[4] A PubMed literature search found only four reported cases of this medication inducing liver injury since atomoxetine was approved for use in 2002.[5-7] Out of these four, all but one were in children, and all but one resolved after discontinuation of the medication and did not pose a serious risk. However, our case occurred in an adult and demonstrated a serious potential to lead to acute liver failure.

Due to its efficacy, relatively safe side effect profile, and low potential for abuse, atomoxetine is becoming an increasingly popular treatment choice for both children and adults with ADHD. Perhaps because it is such a rare adverse effect, liver injury is often under-recognized, but it can lead to liver failure if not identified early. Therefore, our case emphasizes the importance of providers and patients being aware of symptoms stemming from adverse reactions associated with atomoxetine therapy.

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