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Single Case

Amiodarone-Induced Acute Liver Injury

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Keywords

Amiodarone · Acute liver injury · Elevated bilirubin · Atrial fibrillation · Shortness of breath · Lactate dehydrogenase

Abstract

Amiodarone is a lipophilic structure with a half-life of 25–100 days. Long-term oral amiodarone is associated with photosensitivity, thyroid dysfunction, and pulmonary and hepatic toxicity. Intravenous amiodarone can lead to sweating, heating sensation, nausea, phlebitis at the injection site, and rarely acute hepatitis. This is a compelling case of a 60-year-old male who developed acute liver injury 24–36 h after starting amiodarone. All the possible causes of acute liver injury were ruled out, and his liver enzymes improved after discontinuing amiodarone.

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Introduction

Amiodarone is a lipophilic structure with a half-life of 25–100 days. Long-term oral amiodarone is associated with photosensitivity, thyroid dysfunction, and pulmonary and hepatic toxicity. Hepatic toxicity varies from an asymptomatic and transient rise of serum amino-

transferases that resolves after dose reduction or withdrawal, to severe liver disease [1]. Intravenous amiodarone can lead to sweating, heating sensation, nausea, and phlebitis at the injection site. Acute hepatotoxicity is a rare but potentially fatal complication of intravenous amiodarone use and has been rarely reported [2].

Case Report

A 60-year-old male with a past medical history of hypertension and atrial fibrillation was admitted for shortness of breath. He was taking Lopressor 25 mg twice a day and apixaban 5 mg twice a day at home. On physical examination, blood pressure was 130/70 mm Hg, saturation 92% on room air, respiratory rate 13, and heart rate 145, which was irregular. ECG showed atrial fibrillation with a rapid ventricular rate. He was treated with diltiazem bolus and infusion but became hypotensive, so diltiazem infusion was discontinued. Amiodarone 150 mg bolus was given, followed by continuous amiodarone infusion of 900 mg over 24 h. Blood work performed 24 h later showed a sudden rise in aminotransferases (aspartate aminotransferase 3,254 U/L, alanine aminotransferase 1,643 U/L), lactate dehydrogenase (2,234 U/L), direct bilirubin (5.12 mg/dL), and international normalized ratio (2.53). Gamma-GT and alkaline phosphatase were normal. Extensive workup like abdominal ultrasonography, viral hepatitis serologies (hepatitis B and C, cytomegalovirus, Epstein-Barr, HIV, and herpes zoster viruses), and autoimmune markers (antinuclear antibody, anti-smooth muscle antibody, anti-liver/kidney microsomal antibody type 1) were unremarkable. The retrospective review did not reveal use of alcohol or any other hepatotoxic drug besides amiodarone.

Amiodarone-induced liver injury was the primary diagnostic hypothesis, so amiodarone was discontinued about 50 h after its beginning. Since then, he improved gradually with progressive improvement of hepatic liver enzyme and normalization in 7 days. His heart rate was controlled with oral Lopressor and diltiazem.

Discussion

Acute liver failure can be caused by multiple etiologies which includes (1) viral hepatitis such as hepatitis A–E, herpes simplex virus, varicella-zoster virus, Epstein-Barr virus, adenovirus, and cytomegalovirus; (2) drug-induced liver failure such as Tylenol, amiodarone, and many other drugs like dapsone; (3) hypoperfusion due to cardiac dysfunction, sepsis, or drugs; (4) autoimmune causes.

American College of Gastroenterology guidelines recommend that the causality assessment in patients with drug-induced hepatic injury should rely primarily on consensus expert opinion following a thorough evaluation for competing etiologies [3]. The causal relationship between intravenous amiodarone exposure and acute hepatitis was established based on the following principles: (1) sudden hepatic test abnormalities within 24 h after starting amiodarone administration; (2) presence of a pattern of hepatocellular injury with peak aminotransferase levels of more than 50 times the upper limit of normal; (3) rapid improvement after amiodarone withdrawal; and (4) exclusion of other causes.

Acute intravenous amiodarone-induced hepatotoxicity is a rare but potentially lethal side effect, so physicians should be aware of it and check for its occurrence by performing serial liver tests. The exact mechanism of this adverse effect is still unclear. Different potential mechanisms have been proposed, including an immunologically mediated mechanism [4], a free

radical mechanism, in which formation of free radicals leads to peroxidative injury of membrane lipids and necrosis [5], and a mechanism based on increased expression of the PPAR α gene secondary to disrupted hepatic lipid homeostasis [6]. The mechanism of oral amiodarone-induced hepatotoxicity seems to be different from that induced by intravenous amiodarone. Some reports showed that introduction of oral amiodarone in these patients did not result in any additional liver injury. Based on this observation, Rhodes et al. [7] proposed that polysorbate 80, the solvent of an intravenous formulation of amiodarone, could be involved in this adverse effect since it is present in the intravenous but not in the oral form of amiodarone. Gough et al. [8] mentioned that the hypotensive effect attributable to polysorbate 80 present in intravenous amiodarone is a compelling hypothesis. A case-control retrospective study by Gluck et al. [9] in 2011 including 22 cases of intravenous amiodarone-induced hepatitis and 25 cases of ischemic hepatitis concluded indistinguishable features between the groups and provided support for the hypothesis of a hypotensive effect.

Treatment is mainly supportive. A recent study has shown evidence in favor of the use of *N*-acetylcysteine in acute liver injury beyond acetaminophen intoxication [10]. The liver injury does not recur upon reintroduction of amiodarone by the oral route; yet in this case, it was decided for a rate-control strategy.

In conclusion, acute hepatotoxicity is a rare, but potentially fatal, adverse effect of intravenous amiodarone. Physicians should carefully monitor hepatic function during amiodarone infusion. In patients with hepatic injury, intravenous amiodarone should be stopped immediately and not be reintroduced again. If there is no alternative and amiodarone is still needed clinically, an oral form may be used with a lower dose.

Statement of Ethics

Consent was obtained from the patient for publication. Ethics approval was not needed for this paper.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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Author Contributions

Rajesh Essrani, Shri Jai Kirshan Ravi, Shehriyar Mehershahi, Rajesh Kumar Essrani, Sajeer Bhura, Anuraj Sudhakaran, Muhammad Hossain, and Asif Mehmood contributed to the writing of this case report. All authors read and approved the final manuscript.

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