Case Report

THAI J GASTROENTEROL 2014
Vol. 15 No. 2
May - Aug. 2014
105

Fatal Acute-on-Chronic Liver Failure from Amiodarone Toxicity

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ABSTRACT

Background: Drug induced liver injury is common problem in clinical practice. Amiodarone hepatotoxicity has various clinical presentations from asymptomatic elevation of aminotransferase to acute liver failure.

Objective: To investigate the clinicopathological characteristics of acute-on-chronic liver failure from amiodarone toxicity.

Material and Method: One case of amiodarone toxicity was reported in a review of literature. The clinical and histopathological features were described.

Results: We report a 62-year-old female patient with prolong administration of amiodarone. She developed clinical of acute-on-chronic liver failure. Liver pathology reported cholestatic hepatitis with extensive Mallory's body with pericellular fibrosis. Amiodarone induce hepatotoxicity was diagnosed.

Conclusion: This report suggests that amiodarone toxicity should be considered as one possibly cause of acute-on-chronic liver failure.

Key words : Amiodarone, drug toxicity, acute-on-chronic liver failure, fatal, ascites.

[Thai J Gastroenterol 2014; 15(2):109-113.]

INTRODUCTION

Amiodarone, an iodine-containing benzofuran derivative, has been widely available. The drug has potent anti-arrhythmic properties and has proved effective against a variety of supraventricular and ventricular cardiac arrhythmias. Asymptomatic rise of liver transaminases in approximately 25% of patients, less than 3% develop symptomatic hepatotoxicity[1].

Amiodarone induced hepatotoxicity has various clinical presentations from asymptomatic elevation of aminotransferase, acute hepatitis to acute liver failure[2,3]. However, amiodarone-induced hepatitis can progress to cirrhosis, resulting in decompensated hepatic failure, although this rarely happens[4].

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Table 1. Results of liver function tests and platelet count.

Laboratory data	*4 weeks earlier*	*2 weeks earlier*	*On admission*
TB (mg/dL)	1.7	4.1	7.4
DB (mg/dL)	1.3	3.9	6.5
Albumin (U/L)	2.6	2.3	1.7
Globulin (U/L)	-	5.2	5.1
AST (U/L)	334	378	278
ALT (U/L)	104	96	93
ALP (U/L)	190	180	146
INR	1.19	1.29	1.6
Platelet count	403,000	-	289,000

TB: total bilirubin, DB: direct bilirubin, AST: aspartate transaminase, ALT: alanine transaminase, ALP: alkaline phosphatase, INR: international normalized ratio.

Case Report

A 62-year-old Thai female patient, who lives in Samutprakan, presented with progressive abdominal distension for 3 months. She had underlying of dilated cardiomyopathy and paroxysmal ventricular tachycardia. She was treated with amiodarone 200 mg/day for sixteen years. She denied having any history of alcohol, herbal use or other medication. Patient had been evaluated in out-patients clinic of King Chulalongkorn memorial hospital. In last 2 weeks, she complained rapidly progressive abdominal distension and icteric sclera. Laboratory data showed progressive elevation of aminotransferase and serum bilirubin, prolongation of INR and serum albumin decrease (Table 1). The physical examination revealed that the subject was markedly distended abdomen with ascites, liver enlargement with firm consistency. Chronic liver stigmata included spider nevi and palmar erythema was observed. The temperature was 36.8˚C, the blood pressure 90/60 mmHg, the pulse 80 beats per minute, the respiratory rate 20 breaths per minute. Neither neck vein engorgement nor abdominal superficial vein dilatation were detected. Laboratory data showed impair of liver function and negative possible etiologies determined by serological tests (Table 2). Computer tomography showed hepatomegaly with diffuse slightly high attenuation of liver parenchyma, gastric varices and ascites (Figure 1). Tran-jugular liver biopsy was performed due to limitation of percutaneous liver biopsy by ascites and coagulopathy. Pathological reported cholestatic hepatitis with extensive Mallory's body with pericellular fibrosis (Figure 2). This finding was exactly similar to alcoholic liver disease. Without history of alcohol intake, amiodarone induce hepatotoxicity was diagnosed. Despite of amiodarone cessation, patient still had progressive of liver deterioration and developed kidney dysfunction. Two weeks after admission patients was passed away due to multi-organ failure.

Table 2. Results of serological tests, thyroid functions test and serum iron study.

Laboratory data	
HBsAg	Negative
Anti-HBc	Negative
Anti-HBs	Negative
Anti-HAV IgM	Negative
Anti-HCV	Negative
Anti-nuclear antibody	Negative
Anti-mitochondrial antibody	Negative
Anti-smooth muscle antibody	Weakly positive
Free T4 (0.8-1.8 ng/dL)	1.83
Free T3 (1.6-4.0 pg/dL)	1.88
TSH (0.3-4.1 mU/mL)	3.47
Ferritin (15-50 ng/mL)	161
Serum iron (37-145 µg/dL)	26
TIBC (37-145 µg/dL)	218

Discussion and conclusion

Drugs known to be capable of inducing steatosis and steatohepatitis can be divided into three broad groups: those that cause steatosis and steatohepatitis

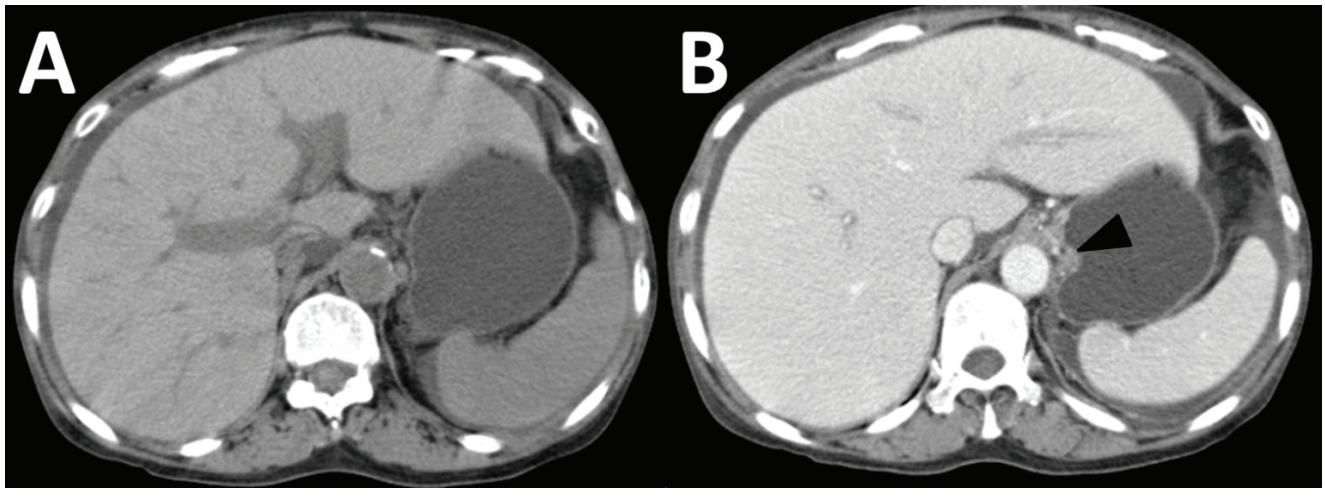

Figure 1. Non-contrast CT scan upper abdomen showed hepatomegaly with diffuse slightly high attenuation (73-83 HU) of liver parenchyma (A). Contrast-enhance CT scan upper abdomen showed diffuse enlargement of the liver amount of ascites and evidence of gastric varices (Black arrow) (B).

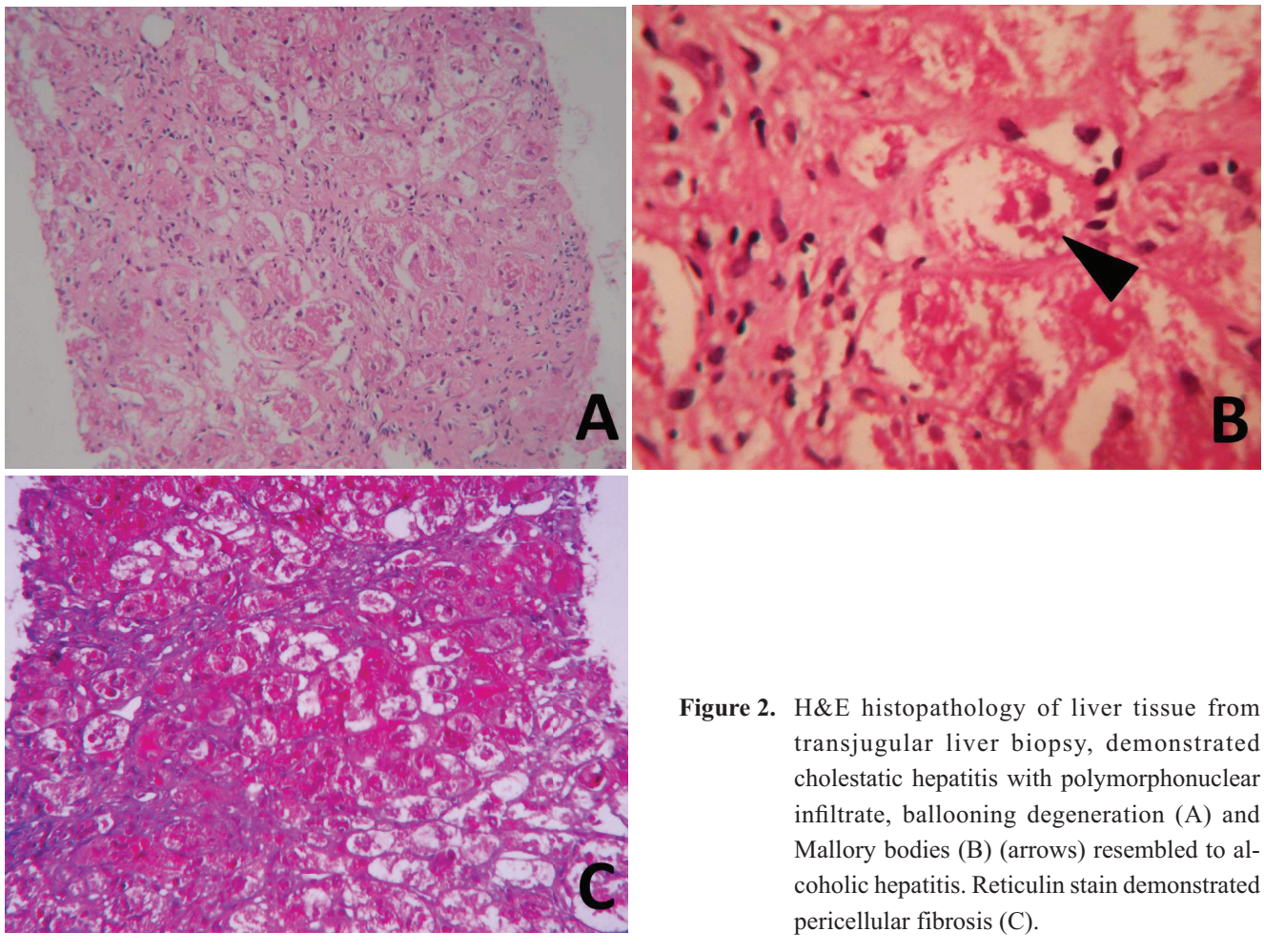

Figure 2. H&E histopathology of liver tissue from transjugular liver biopsy, demonstrated cholestatic hepatitis with polymorphonuclear infiltrate, ballooning degeneration (A) and Mallory bodies (B) (arrows) resembled to alcoholic hepatitis. Reticulin stain demonstrated pericellular fibrosis (C).

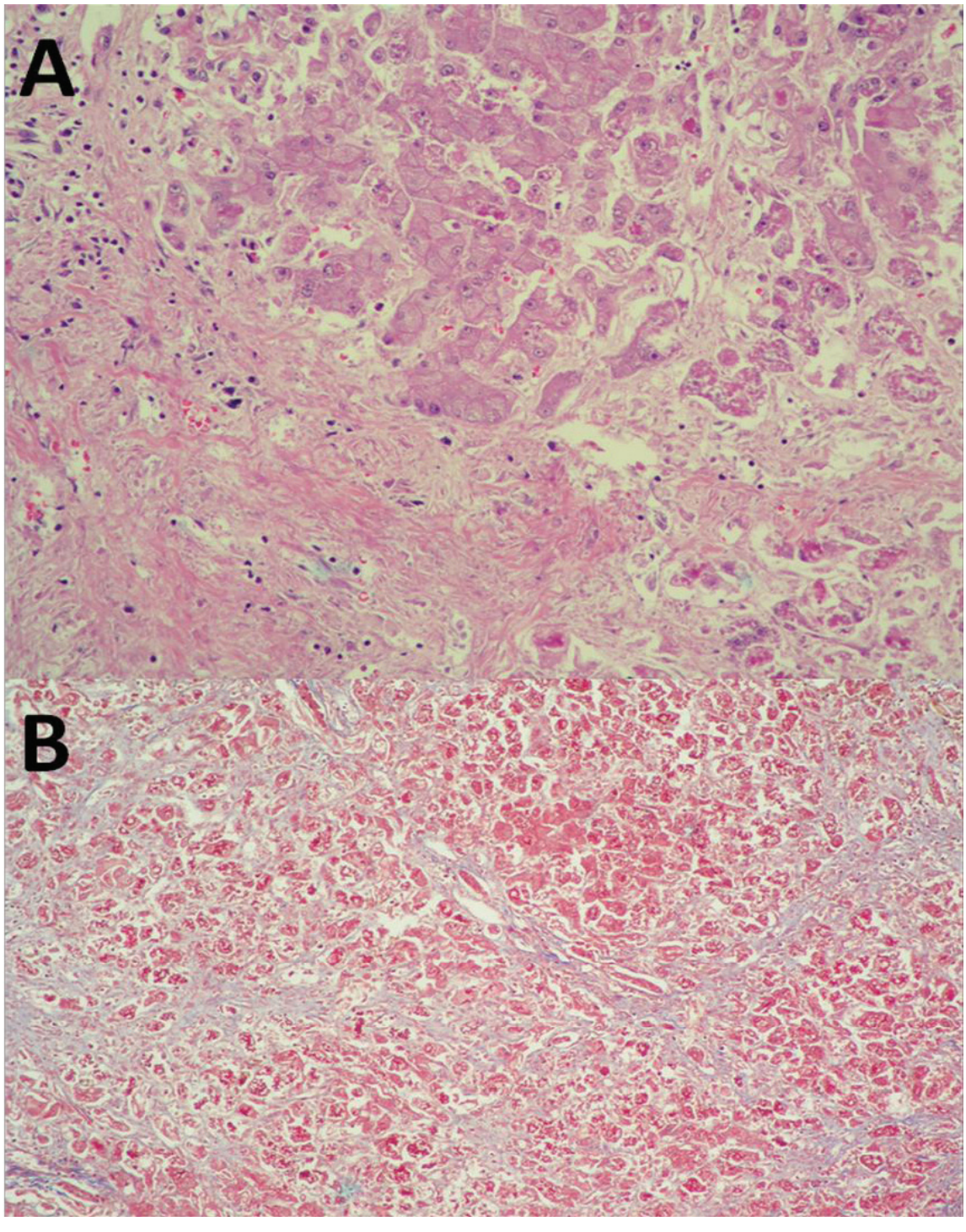

Figure 3. H&E histopathology of liver tissue from autopsy, demonstrated cirrhosis with polymorphonuclear infiltration, Mallory bodies, and ballooning degeneration (A), focal area of hepatic necrosis (B).

independently (e.g., amiodarone, perhexiline maleate); drugs which can precipitate latent NASH (e.g., tamoxifen); drugs which can induce sporadic events of steatosis/steatohepatitis (e.g., carbamazepine)[5].

Amiodarone, one of the cationic amphiphilic drugs (CADs), is a lipophilic drug that concentrates in the liver and can cause phospholipidosis in liver[6]. This inhibits the mitochondrial beta-oxidation of fatty acids and produces microvesicular steatosis of the liver[7]. Over a period of time, the drug can leads to toxicity related to drug accumulation. There is marked histological similarity between amiodarone-induced liver disease and alcoholic and nonalcoholic steatohepatitis[8]. The cytotoxic pseudoalcoholic

changes, both macrovesicular and microvesicular, was the most frequent histopathologic feature. Ballooning of hepatocytes, Mallory bodies, and fibrosis were also common[9,10].

While amiodarone mostly associated with long-term oral administration of the drug, toxicity has also been reported early during intravenous administration and months after discontinuation of therapy[11]. In the majority of patients, it is discovered incidentally during routine testing of liver biochemistry and rarely do the hepatic effects develop into symptomatic liver injury or failure[12].

In summary, this case suggests that amiodarone toxicity should be considered as one possibly cause of acute-on-chronic liver failure.

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