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# A Case of Amiodarone Hepatotoxicity in Patient with Atrial Fibrillation

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## Abstract

Amiodarone has an important drug in treatment for arrhythmia, but cannot be overlooked in practical medicine. Among the side effects associated with iodine contained in amiodarone, thyroid dysfunction is well known, but steatohepatitis is rarely reported. We described a 65-year-old female, with history of amiodarone treatment for atrial fibrillation, presenting with dyspnea and hand-tremor. Computed tomography (CT) revealed a high-density of liver parenchyma on non-enhanced imaging which was compatible with the hepatotoxicity as of iodine accumulation. Thus, we report an unusual but important presentation of amiodarone hepatotoxicity.

**Key Words :** Amiodarone, Atrial fibrillation, Hepatotoxicity

## Introduction

Amiodarone, an iodine-containing compound, is a class III antiarrhythmic drug which is used in the treatment of cardiac arrhythmias. However, therapy is restrictive frequently because of development of serious and harmful adverse reactions. Amiodarone toxicity is frequently associated with long-term or high dose of administration. Occasionally it may develop early during intravenous administration or late several months after discontinuation of the drug [1].

Amiodarone is related with side effects including thyroid dysfunction, lung fibrosis, skin discoloration, neuropathy, electrocardiographic changes and hepatotoxicity. Although the elevation of liver enzyme would be frequently encountered in clinical practice (15%), hepatitis or cirrhosis is rarely reported (less than 3%) [2].

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Our case showed the side effects of hand tremor and mildly elevated liver enzymes associated with amiodarone treatment. In addition, we incidentally found steatohepatitis on chest CT, and reported to our case.

## Case Report

A 65-year-old woman who had a past history of hypertension and Atrial fibrillation (AF), presented with worsening dyspnea for a month. She had been treated with amiodarone for maintaining normal sinus rhythm for 18 months and thus, maintained on 200 mg twicea day. She was also receiving bisoprolol and lacidipine (1.25 mg and 4 mg once a day, respectively) for hypertension. However, in recent six months, the blood pressure could not be controlled adequately because of poor compliances of medication. On physical examination, heart rate was 41 beat per minutes, blood pressure was 166/80 mmHg, breath sounds decreased and she showed both hand-tremor.

Initial laboratory test showed: AST/ALT 51/43 IU/L, ALP 369 IU/L and total bilirubin 0.4 mg/dL. The complete blood cell count was normal. Her electrocardiography (ECG) revealed sinus bradycardia and 491 ms of QTc interval (Fig. 1A). Chest radiography showed the existence of both pleural effusions. For the further evaluation of elevated liver enzyme, we performed an abdominal computed tomography (CT). It showed that hepatic contour was round and there were no gross abnormalities in biliary trees, pancreas, both kidney, and visible bowel loops. However, there was the great increased density of liver with attenuation values ranging from 105 to 120 house field unit (HU), compared with kidney or nearby muscle on non-enhanced CT (Fig. 1B).

We then concluded that CT findings were suggestive of iodine accumulation in liver parenchyma caused by amiodarone toxicity, which was also evidenced by both hands tremor. Thus, for evaluation additional amiodarone side effects, we performed thyroid function test. However, we could not find out any abnormalities.

With those findings, we stopped the amiodarone therapy and started conservative treatment with diuretics. After one week of withdrawal of amiodarone, both hands tremor was relieved and the patients was discharged with no persisting symptoms.

## Discussion

Amiodarone is easily used for treatment of cardiac arrhythmias, despite of various adverse reaction. Amiodarone toxicity has been reported to show variable side-effects such as QT prolongation, liver toxicity, pulmonary fibrosis, thyroid dysfunction and optic neuritis. In addition, tremor and ataxia are most common neuropsychiatric side effects (3-35%) which is associated with the demyelination of peripheral nerves, although the definite pathophysiology is still unknown [2,3].

With respect to amiodarone hepatotoxicity, the toxicity usually develops more commonly in patients receiving higher dose or long-term administration with amiodarone. However, it appears that serious adverse reactions are uncommon. According to recent study, the incidence of elevated enzyme levels is 15-30%, hepatitis and cirrhosis less than 3%, respectively [2].

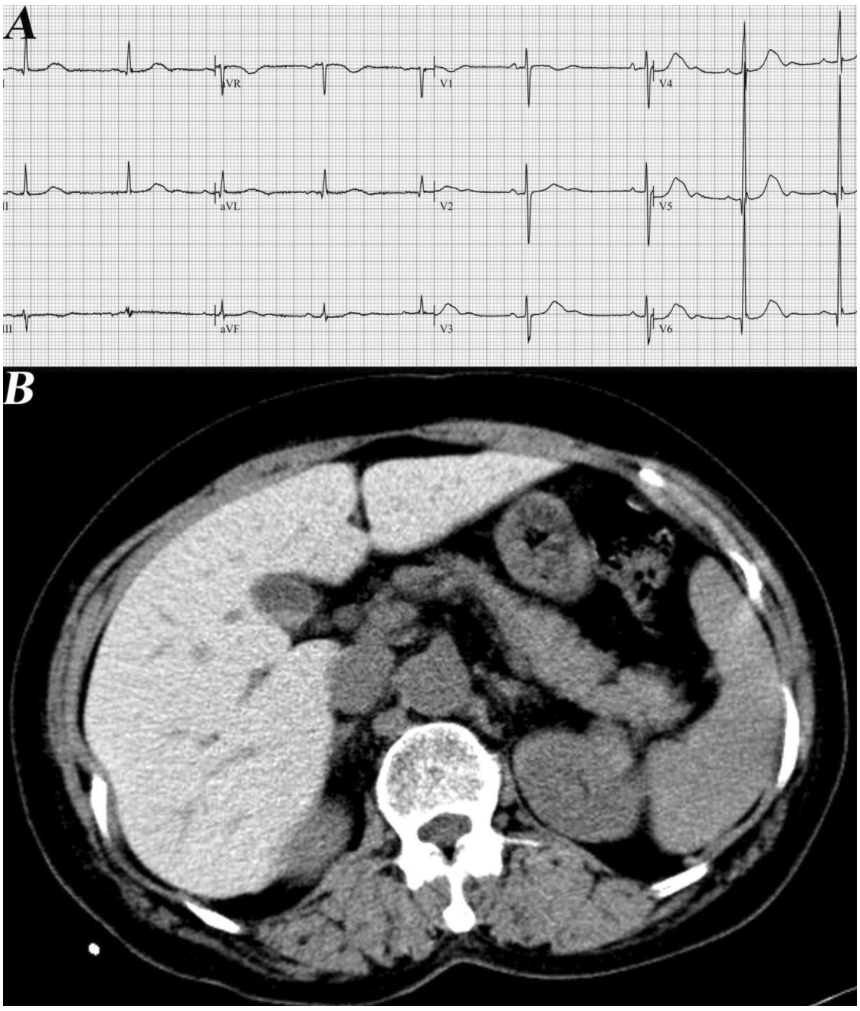


**Fig. 1.** A Bradycardia (52 bpm) and prolonged QTc intervals (491 ms) were noted on ECG. B Non-enhanced CT finding reveals a high density of liver parenchyma with an attenuation value of mean 110 HU, compared with those of nearby kidney and muscle.

From the consensus of the North American Society of Pacing and Electrophysiology (NASPE), the lowest possible efficacious dose of amiodarone is recommended, and regular follow-up is also suggested with monitoring of liver enzymes at baseline, 3-monthly for the first year and 6-monthly after starting therapy [4,5]. In particular, persistent ALT elevation is the best indicator of amiodarone liver injury. Thus, drug discontinuation is recommended once an ALT of more than 2 times the upper limit of normal. However, ALT is not specific and sensitive for hepatic toxicity, although ALT level could be increased in the case of a more serious hepatic lesion such as liver cirrhosis [6]. In our case, ALT is within the upper limit of reference range, thus we didn't consider for detection of early phase of hepatotoxicity.

As regards the side-effects associated with iodine accumulation, thyroid dysfunction is usually well known. There were limited

data or reports about iodine accumulation into liver parenchyma. However, in the lung parenchyma, deposition of iodine had been reported previously, and thus, this similar finding could be probably consistent with high attenuation of non enhanced CT imaging [7]. In our case, CT showed liver has a greatly increased density compared with kidney or muscle [8]. This is because of the increased attenuation in the liver due to the accumulation of the iodinated drug (desethylamiodarone (DA)), that was metabolite form of amiodarone, in tissue macrophage on CT scan which would correlate with plasma drug concentrations [9]. However, unfortunately, there remains no effective specific treatment for the amiodarone hepatotoxicity. Previous studies recommend the considering of discontinuation of amiodarone in the case of hepatotoxicity or elevated liver enzyme levels three times higher than normal [10].

This patient report showed two related side effects linked to amiodarone; hands tremor as neuropsychiatric aspect, and steatohepatitis, even though ALT level was normal. Although the incidence of hepatotoxicity was low and insignificant as for low dose amiodarone (mean 150 to 330 mg per day) compared with placebo in previous studies, careful concerns for hepatic side effects should be needed in the presence of any abnormalities associated with toxicity because of its irreversibility [11].

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