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Case Report

# Hepatic Hyperattenuation on CT Caused by Using Amiodarone: Report of a Case

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**Abstract**

Amiodarone is a class III antiarrhythmic agent and has the broadest spectrum for use of treatment and prevention of ventricular tachycardia, Wolf-Parkinson-White syndrome, atrial fibrillation and cardiac arrest. It blocks potassium, sodium, calcium channels and alfa/beta receptors but dominantly potassium channels. It has numerous side effects including hepatotoxicity and elevation of liver enzymes. We report a patient who has hyper density of liver on abdominal CT scans. The most important finding of using amiodarone on abdominal CT scans is the increase of liver attenuation.

## INTRODUCTION

Amiodarone is an iodinated benzofuran form and an analogue of thyroxine, used for the various cardiac dysrhythmia. That molecular structure and lipophilic feature can possibly **cause** easily pass through the cells and acts like thyroxine and the other lypofilic hormones. It dominantly blocks potassium channels but can also block the other channels and receptors (e.g. sodium, calcium channels and adrenergic receptors). It is the most effective drug for ventricular dysrhythmia. It is a negative chronotrope for the heart can repress atrioventricular node and can change the function of the sinoatrial node. Amiodarone is used for acute myocardial infarction and cardiac arrest with ventricular tachycardia, prevention of ventricular tachycardia, fibrillation, Wolf-Parkinson-Whites syndrome, supraventricular tachycardia, chemical cardioversion and atrial fibrillation. It is metabolized by the liver and excreted with bile, so the toxic effect of amiodarone can be detected mostly in the liver [1]. It has numerous side effects including interstitial lung diseases, pulmonary fibrosis, corneal micro deposits, and prolongation of QT interval, optic neuritis, bradycardia, hypo/hyperthyroidism, and peripheral neuropathy, discoloration of skin, hepatotoxicity and elevation of liver enzymes [2]. The main toxic effects to the liver are caused by desethylamiodarone, which is a metabolite of Amiodarone. On CT scans of the patients who have hepatic enzyme elevation and and use amiodarone can be detect hepatic hyperattenuation.Elevation of enzymes like AST and ALT show damage of liver.There is correlation with level of hepatic hyperattenuation and blood desethylamiodarone levels with chronic amiodarone usage.This shows there is a correlation with hepatic damage and amiodarone usage [3].

Intravenous form of amiodarone can be used in emergencies and tablet form can be used for the prevention of dysrhythmias. The patients can use the drug for long and short periods. Intravenous high doses are used for induction and oral doses are used for maintenance of treatment [4]. Liver toxicity is usually observed on high dose usage and long duration treatments [5].

Figure 1 we report a 66 year old woman who has hyperdensity of liver on abdominal computerized tomography (CT) scans and usage of amiodarone for 6 years for prevention of ventricular tachycardia. She had not the other risk factors for hyperattenuation of liver.The cause of the hyperattenuation was chronic usage of amiodarone.

## CASE PRESENTATION

The patient is a 66 year old woman, who used amiodarone about 6years for the prevention of ventricular tachycardia. She has used 400mg amiodarone in tablet form per day. She also has atherosclerosis, mild heart failure and hypertension (about 140-150 mmHg). She had no known illnesses except listed above. She also used Beta-blocker, metoprolol 50 mg/day for treatment of hypertension and 100 mg/day acetylsalicylic acid for atherosclerosis. On her blood tests, her HCV-HBV and the other infective parameters were normal. She did not consume alcohol and there were no risk factors for liver diseases. Her weight was higher than normal (body mass index was 31). Her body mass index higher then normal but on her blood tests she did not have very abnormal or much increased elevate lipid profile. Increasing of liver density excluded liver hepatosteatozis,because the density is decreasing in hepatosteatozis [6]. Average of total colesterol was 217 mg/dL (borderline level), LDL was 138 mg/dL (borderline level).

Patient who are prescribed or taking amiodarone must

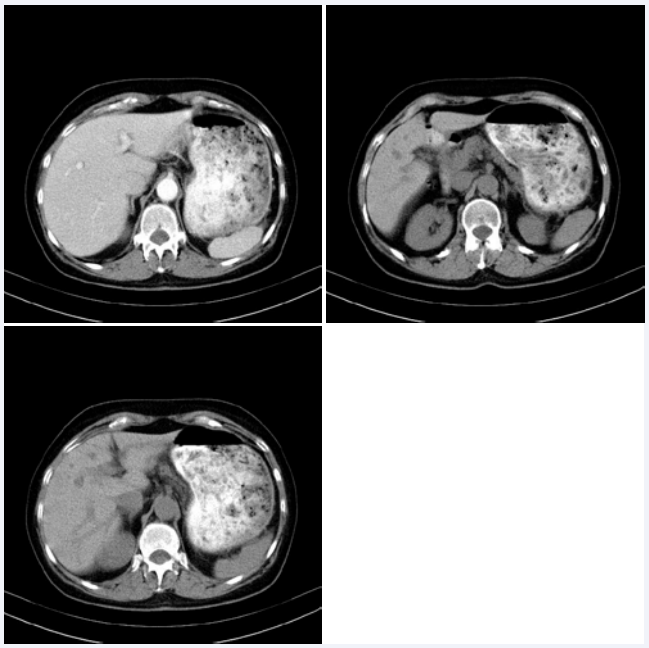

**Figure 1** Axial computed tomography (CT) scans of the upper abdomen after oral contrast agent, with and without IV contrast agent administration; at the upper (A) and lower (B) part of the liver show an increase in liver density with normal attenuation of the other organs. On the axial CT scan with IV contrast agent (C); Hyperdense liver parenchyma can be seen.

have regular blood tests to detect hepatoxicity. On the routine blood tests, elevation of liver enzymes including AST and ALT was detected with our patient. (AST: 220 IU/L, ALT: 189 IU/L). The elevation of these two enzymes indicates liver damage and hepatotoxicity. Other enzymes levels (e.g. cholestasis) and other blood parameters were normal, GGT was 22, ALP was 63 U/L. Physical examinations was also normal and she was asymptomatic, the ventricular dysrhythmia was non-existent.

The patient has been referred to our radiology clinic for abdominal ultra sonography (USG). We did not detect any abnormality except hepatomegaly. After USG, the abdominal CT scans were obtained with and without I.V. contrast agent administration. Multi slice helical computed tomography was performed on a 128 slice CT scanner (Somatom Sensation 128, Siemens, AG, Erlanger, Germany). Gantry rotation time was 0.5s. A tube voltage of 130kVp and tube current of 53m. As (effective) was used. Slice thickness was 5 mm and there was no slice interval. On the CT scan, liver attenuation was found high with contrast and without contrast series.We measured HU values in three different locations of liver and spleen. Average Hounsfield Unit (HU) value of the liver was 90(normal 50-65) and liver/spleen relative CT density was 1.7 which is an increase value (normal 1.0 to 1.3) [3]. Hepatomegaly was also found, nearly 170 mm on the craniocaudal axis. There were no additional lesions found. After these findings, considering the toxicity of amiodarone, the drug has been withdrawn.After cessation of the drug, the levels of the liver enzymes backed to normal in three months.The last AST level was 30 U/L, ALT was 47 U/L.The patient did not want another CT scan after stopping of the drug for detection situation of hyperattenuation of liver. The patient allowed to share all information about CT scans, medical background and blood tests except her name and the other personal information without medication.

## DISCUSSION

Amiodarone is used for acute and chronic cardiac dysrhythmias. This drug is preferred due to it'sbroad spectrum for dysrhythmias. It accumulates in the spleen, reticuloendothelial system and muscles but mostly in the liver [7]. When the liver is damaged, we can detect elevation of liver enzymes. The radiological appearance of these effects is non-specific, most common finding on abdominal CT scans is hepatic hyper attenuation [8].

Amiodarone (2-butyl-3-benzofuranyl 4-[2-(diethylamino)-ethoxy]-3, 5-diiodophenyl ketone hydrochloride) and its toxic metabolite "desethylamiodarone" are responsible for the damage of hepatocytes. The mechanism of toxicity is not clear. There are two known effects of the drug; one of them is the reduction of the macrophages lysosomal phospholipase activity with accumulation of phospholipases in macrophages.This reduction give rise to phospholipids and a new formation of drug-lipid complexes.Its name is amiodarone-related phospholipidosis,may be detect granular depositions in the macrophages of liver biopsy [9,10]. The other more important effect is the inhibition of mitochondrial ß -oxidation of hepatocyte cells and activation of oxygen radicals. It causes apoptosis of the hepatocytes, steatohepatitis and cirrhosis [2]. Also amiodarone and its metabolites (iodine is 37% of the molecular weight of the drug) is a derivative of iodine benzofuran. It imitates iodine accumulation in hepatic cells and increases the density of the liver. On the other hand,some reporters believe chronic oral amiodaron usage direct damage the lipid blayers and the disturbance mitochondrial and lysosomal function,acute IV usage due to some different mechanism like hypersenstivity reaction and hypotension in hepatocytes causes liver damage. There is average HU density value of the liver on CT scans [3]. Normally the density of the liver on CT is similar to that of the spleen [9].

We also researched other reasons of hyperattenuation of the liver: certain metal deposition diseases (e.g. hemochromatosis, hemosiderosis, and Wilson disease), Glycogen storage diseases, gold therapy and exposure of thorotrast [11,12]. We excluded other possible reasons by profiling and background screening of the patient.

We searched about connection of amiodarone and liver in literature. There are few clinical reports about using amiodarone and hyperattenuation of liver on CT. Kojima et al., [13], Jones WP et al., [14], Cumpaet et al., [15] reported correlation hepatic hyperattenuation and used amiodarone in their case reports. Hirakawa et al., reported a practice about 13 patients using amiodarone. They found hepatic hyperattenuation at all of these patients. They reported that there is not correlation with cumulative doses of amiodarone and liver density on CT scans but significantly correlation level of blood desethylamiodarone and hyperattenuation of liver [16].

In conclusion we can say that, amiodarone usage can cause hyperattenuation of the liver more frequently than any other

reason.In differential diagnosis of hepatic hyperattenuation on CT scans, amiodarone usage should be one of the first reason to consider.

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