Amiodarone-induced hepatotoxicity

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DESCRIPTION
A male patient in his 50s presented to our hospital with generalised malaise that had started a few days before. He had been on oral amiodarone for 3 years, and had implantable cardioverter defibrillator implantation for ventricular fibrillation 3 years earlier. He had no history of alcohol consumption or injection drug abuse. Vital signs were within the normal range, except for hypotension (87/49 mm Hg). Physical findings were normal. Laboratory tests showed abnormal liver function parameters: total bilirubin, 1.7 mg/dL; aspartate aminotransferase, 861 U/L; alanine aminotransferase, 1601 U/L; γ-glutamyl transpeptidase, 100 U/L. CT revealed a high-density (95–100 Hounsfield units) area (figure 1) that was not found in the liver 16 months before (figure 2). The patient was diagnosed with amiodarone-induced hepatotoxicity. Additional laboratory tests revealed a blood concentration of amiodarone at 649 ng/mL, within the therapeutic range (500–1000 ng/mL). However, there was an elevated level of the amiodarone metabolite, desethyl-amiodarone, at 1199 ng/mL, resulting in a desethyl-amiodarone/amiodarone ratio of 1.84 (base: 0.8). Oral administration of amiodarone was discontinued, and the symptoms and CT findings showed prompt improvement (figure 3). Liver biopsy was performed approximately 1 month after discontinuation of amiodarone. Histopathologically, in cases of amiodarone-induced hepatic changes, the presence of lipid droplets of varying sizes is generally observed. However, due to the liver biopsy being performed post-therapeutic intervention, a significant presence of fatty liver was not observed. However, within the hepatic lobules, lymphocytic cellular infiltration, primarily lymphocytic in nature, was prominently noted within the hepatic sinusoids. In certain hepatocytes, hepatocyte necrosis was observed, while the remaining hepatocytes exhibited enlargement, vacuolisation and nuclear hypertrophy.

Amiodarone is trapped in lysosomes due to its pH gradient, and forms strong hydrophobic and electrostatic bonds with polar lipids. As a result, it interferes with the normal enzymatic action of phospholipase. Therefore, the half-life of amiodarone is relatively long, at 2–4 months. Hepatic deposition of amiodarone results in elevated CT density of the liver, as amiodarone includes about 37 mg of iodine per 100 mg. Differential diagnoses that show similar images are glycogen storage diseases, drug toxicity including gold, haemochromatosis, Wilson’s disease and fulminant hepatitis. Medical history is important for distinguishing these diagnoses. The continued use of amiodarone could lead to progression into liver cirrhosis.

With rapid advances in diagnostic imaging technology, opportunities for patients with heart disease to undergo coronary CT examinations are increasing. The part of the liver near the heart may be imaged by coronary CT.
Therefore, clinicians should be aware of the characteristic findings of amiodarone-induced hepatotoxicity.

Learning points

► Amiodarone liver should be the differential diagnosis when CT shows high-dense areas of liver.
► Clinicians should be aware of the characteristic findings of amiodarone-induced hepatotoxicity.
► Liver function in amiodarone liver often improves with discontinuation of the medication.

Contributors

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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