Quinidine hypersensitivity: a side effect of a forgotten antiarrhythmic

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Case report

Quinidine hypersensitivity: a side effect of a forgotten antiarrhythmic

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SUMMARY
Quinidine is one of the oldest antiarrhythmics known. Over the years, its use has decreased along with its side effects. Our case describes a 69-year-old woman with recurrent resistant ventricular tachycardia on Quinidine and Amiodarone who presented with acute liver toxicity. Drug-induced liver toxicity was at the top of our differential diagnosis list. Taking multiple factors into consideration, a decision was made to discontinue Quinidine, the patient’s symptoms and lab abnormalities resolved within 1 week, yielding the diagnosis of Quinidine hypersensitivity.

BACKGROUND
Quinidine is a natural cinchona alkaloid with potent antiarrhythmic activity. It was Food and Drug Administration approved in 1950 to treat atrial and ventricular arrhythmias. Many studies have shown that treatment with Quinidine increases mortality, therefore its use has declined significantly as well as the rate of its side effects.1 The most frequently described side effects are gastrointestinal, including nausea, diarrhoea, abdominal bloating and discomfort.2 Quinidine hypersensitivity is another side effect that occurs in up to 2% of treated patients and can present with fever, mild jaundice and an apparent liver injury.1 Hypersensitivity is well described in the literature, most of these cases were reported from the 1970s and 1980s when Quinidine’s use was prevalent.

Patients with complicated medical comorbidities are often placed on multiple medications with overlapping side effects. In the setting of suspected drug-induced injury, a timeline of the patient’s illness in relation to medication initiation is crucial for identifying the causative agent.

CASE PRESENTATION
A 69-year-old woman presented to the hospital with a 3-day history of nausea and vomiting unresponsive to antiemetics. Her past medical history includes hypertension, type 2 diabetes mellitus, chronic kidney disease stage III, non-ischaemic cardiomyopathy s/p Biventricular Intracardiac Defibrillator, atrial fibrillation and recurrent ventricular tachycardia (VT) s/p ablation on Amiodarone and Quinidine. Review of systems was remarkable for nausea, vomiting, epigastric abdominal pain, indigestion and lightheadedness. Vital signs were significant for a blood pressure of 100/70, heart rate 82 bpm and oxygen saturation of 93% on room air. Physical examination was remarkable for epigastric tenderness on abdominal palpation.

On further review of history, it was found that the patient’s VT was refractory to multiple antiarrhythmics including sotalol and mexiletine. She also has a history of multiple admissions for Implantable Cardioverter Defibrillator (ICD) firing, the last being 4 weeks prior to this presentation. At that time, she was placed on Quinidine in addition to her home Amiodarone. Of note, the patient was on Quinidine years prior to this presentation but it was discontinued due to severe diarrhoea. A list of the patient’s medications on admission are shown in table 1.

INVESTIGATIONS
Initial laboratory studies showed unremarkable complete blood count (CBC), elevated creatinine to 1.49 (from a baseline of 1.1–1.2) and an abnormal liver function test (LFT) including aspartate transaminase 214, alanine transaminase 155, alkaline phosphatase 268; and a normal bilirubin (table 2). Further studies showed a negative viral hepatitis panel. Abdominal ultrasound (US) showed chronic mild extrahepatic bile duct dilatation with changes consistent with cholecystectomy. CT of abdomen and pelvis revealed increased attenuation of the liver suggestive of amiodarone-induced liver toxicity (figure 1).

DIFFERENTIAL DIAGNOSIS
Our initial differential diagnosis included infectious, obstructive and drug-induced liver injury (DILI). The infectious aetiology was ruled out given no history of sick contacts, absence of fever, normal CBC and a negative viral hepatitis panel.
Obstructive biliary disease was ruled out by the patient’s history of a cholecystectomy as well as no evidence of choledocholithiasis or strictures on imaging. DILI was at the top of our differential diagnosis list given the patient’s extensive medication history and liver attenuation findings on CT suggestive of amiodarone-induced toxicity. On thorough review of the patient’s medication list, Amiodarone and Quinidine were the two most likely to cause liver injury. Despite imaging findings, the decision was made to discontinue Quinidine given the fact that the patient was started on it 4 weeks prior to admission in addition to her being on Amiodarone for several years without any side effects, as well as a known history of intolerability to Quinidine. Electrophysiology agreed to discontinuing the Quinidine. The patient was taken off the medication with resolution of her symptoms over the next week, and normalisation of LFT’s over the next 7–10 days (table 3).

TREATMENT

On admission, the patient was started on intravenous fluids, intravenous proton pump inhibitors and antiemetics with no improvement of her symptoms. During her admission, supportive management was continued, and her diet was advanced as tolerated. However, the main treatment modality was discontinuing the offending agent.

OUTCOME AND FOLLOW-UP

The patient was discharged home after resolution of her symptoms and lab abnormalities. She was advised to follow-up with her primary care physician (PCP) and electrophysiologist for monitoring of her VT and initiation of a new antiarrhythmic.

DAILY LAB VALUES

The patient was discharged home after resolution of her symptoms and lab abnormalities. She was advised to follow-up with her primary care physician (PCP) and electrophysiologist for monitoring of her VT and initiation of a new antiarrhythmic.

Learning points

- Physicians should always remember that patients with complex medical conditions are usually on multiple medications with overlapping side effects.
- The chronological relationship between medication administration and the development of signs and symptoms of drug-induced liver injury (DILI) should be established.
- Forgotten medications often have forgotten side effects.
- Quinidine hypersensitivity is a form of DILI that is reversible by medication discontinuation.
- Imaging can oftentimes be non-specific and should be added into clinical decision-making with consideration of other factors including the patient’s history and medication list.
discontinuation of the medication. The patient was given a chance to improve without this invasive diagnostic test as it was delayed given that she was on anticoagulation for other various reasons.

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