Man with Methadone-Induced Polymorphic Ventricular Tachycardia

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Case Presentation

A 55 yr old male with past medical history significant for end stage liver disease, intravenous drug abuse and hypertension presents to the ED with complaints of bright red blood per rectum for the past 3 days and non-specific chest discomfort. Medications on admission were amlodipine, valsartan /HCTZ, xanax, terazosin, and high dose methadone maintenance therapy.

On admission, temperature was 98º F, heart rate was 50, respiratory rate was 18, blood pressure was 122/75, and oxygen saturation was 99% on room air. Physical examination was normal. No bright red blood per rectum was noticed and stool was heme-negative. Initial laboratory values including a complete blood count and chemistry panel were within normal limits inclucing a hemoglobin of 14.6, calcium of 9.6, potassium of 3.9, and magnesium of 1.8. The patient was ruled out for myocardial infarction with three negative troponins. The admission EKG is presented below (Figure 1).

While in the ED on the day of admission, the patient was noticed to have ventricular tachycardia on telemetry. He was asymptomatic during the episode and his vital signs were stable. The telemetry strip at that time is shown below (Figure 2).

The patient was given 2 grams magnesium in the and the patient was admitted to the CCU. QT interval prolongation from high dose methadone therapy was the most likely cause of his episode of polymorphic ventricular tachycardia. Electrophysiology consultation recommended that his methadone dose be decreased so that his QT interval would be within normal limits. Prior to discharge, his methadone dose had been lowered without any symptoms of methadone withdrawal and his EKG on discharge is shown below (Figure 3).

Discussion

The long QT syndrome is a disorder of myocardial repolarization characterized by a prolonged QT interval on the electrocardiogram. This syndrome is associated with an increased risk of a characteristic life threatening cardiac arrhythmia known as Torsades de pointes. Torsade de pointes is a form of polymorphic ventricular tachycardia that occurs in the setting of acquired or congenital QT interval prolongation. Polymorphic ventricular tachycardia is defined as a ventricular rhythm faster than 100 beats/min with frequent variations of the QRS axis, morphology or both. The peaks of the QRS complexes appear to twist around the isoelectric line of recording; the name literally translates to "twisting of the points."

The most common causes of acquired long QT interval syndrome are either medication-induced or electrolyte abnormalities. Some medications known to cause QT interval prolongation are anti-arrhythmics such as quinidine, procainamide, disopyramide, amiodarone, dofetilide, and ibutilide; antibiotics including erythromycin, clarithromycin, and fluoroquinolones; antihistamines such as terfinadine and astemizole; the antipsychotic agents chlorpromazine, haloperidol, and thioridazine; and high dose methadone. Caution should be used when prescribing a drug that prolongs QT interval in patients with risk factors; a baseline EKG and daily EKGs should be obtained during the course of therapy. There are various risk factors for drug induced torsades including female sex, hypokalemia, hypomagnesemia, bradycardia, rapid rate of intravenous infusion with a QT interval prolonging drug, congestive heart failure, baseline QT interval prolongation; sub clinical long QT interval prolongation, and ion channel polymorphisms.

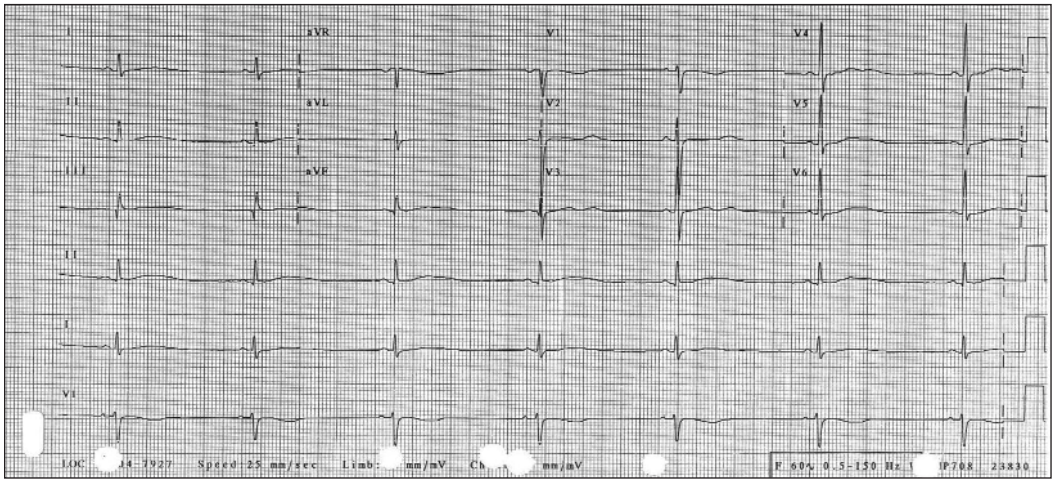

Figure 1.

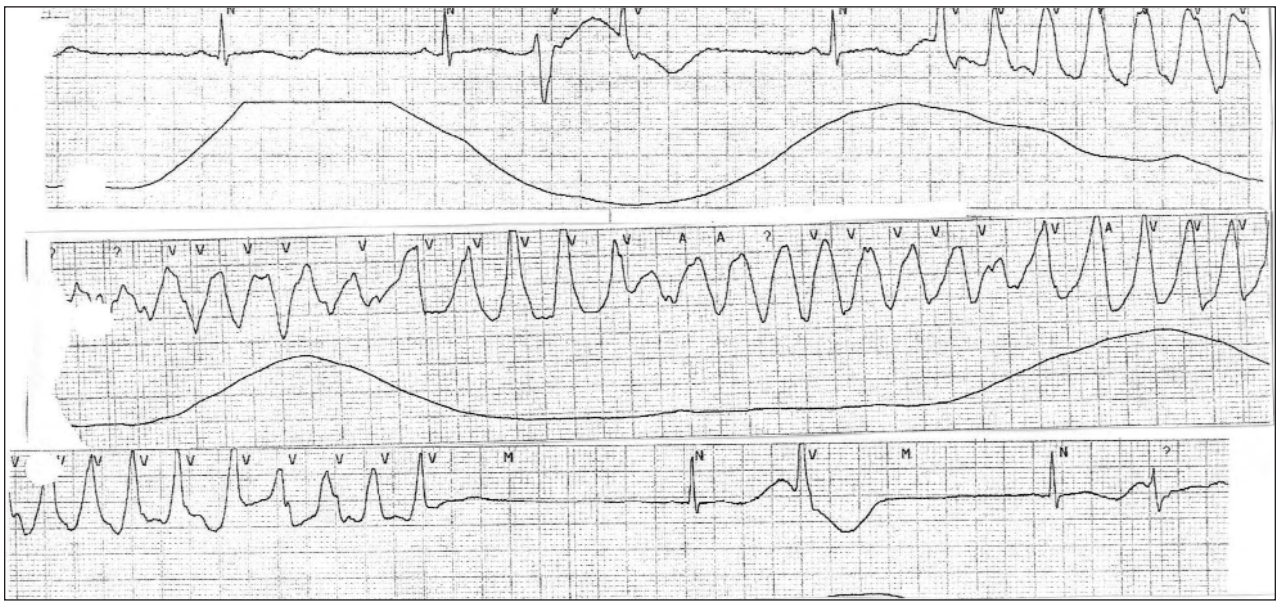

Figure 2.

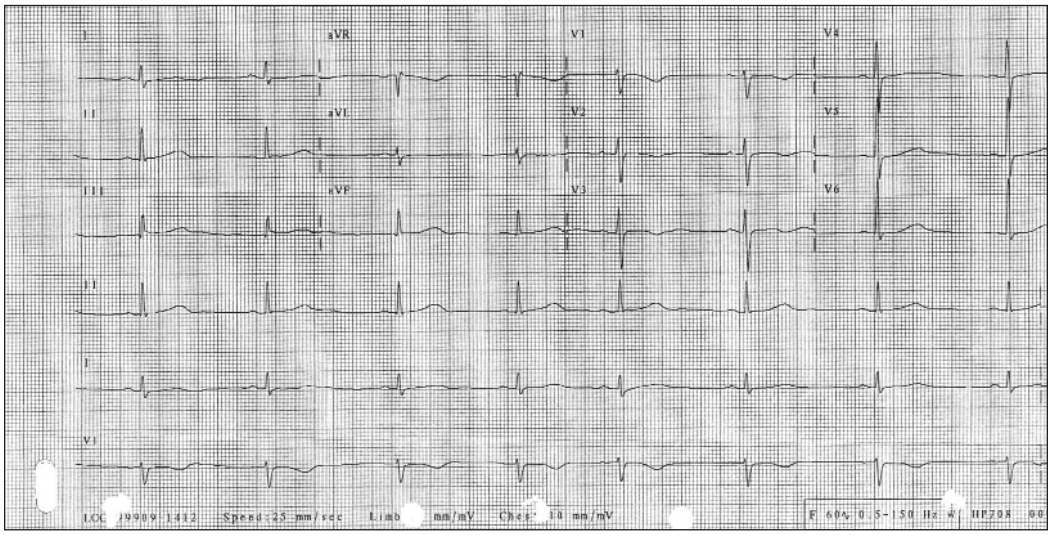

Figure 3.

QT prolongation and torsade de pointes have been reported in patients on high doses (100 to 400 mg) of methadone. Methadone has a long plasma elimination half life and is metabolized by the CYP3A4 enzyme system in the liver, so any drug which inhibits the CYP3A4 enzyme system can increase methadone levels in the blood. CYP3A4 inhibitors include antimicrobials, antifungals, statins, and acetaminophen. Two mechanisms can explain the association between methadone and torsade de pointes, synthetic opoids cause bradycardia and they can inhibit the outward potassium current during phase 3 of action potential.

In a retrospective analysis of reports of adverse events associated with methadone from 1969 to 2002 found that out of a total of 5,503 adverse events associated with methadone, 43 (0.78%) were reported to be torsades de pointes and an additional 16 were noted to have QT prolongation. The dose reported was 410+/-349 mg/day (median 345 mg, range 29-1680) while only 10 cases were within the recommended range for methadone maintenance (60-100mg). Female gender, interacting medications, hypokalemia, hypomagnesemia and structural heart disease were found in 44 (75%) cases. Most adverse events required hospitalization (28/59) and death resulted in 5 cases. ■

References

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