

Torsades de pointes following concurrent amiodarone and levofloxacin therapy

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A case of torsades de pointes is reported following administration of amiodarone concurrent with the fluoroquinolone levofloxacin. Prolongation of the QTc interval has occurred with the fluoroquinolone class of antibiotics. The incidence of torsades has been considered rare with amiodarone. Caution is warranted when these two agents are administered concurrently.

A number of drugs can prolong the QTc interval, including the macrolides, some antipsychotics and antidepressants, migraine serotonin receptor agonists, cardiovascular antiarrhythmics, and fluoroquinolones. A very significant drug-drug interaction can occur when a quinolone is coadministered with an agent in one of these classes. We report a case of torsades de pointes that developed when amiodarone, a class III antiarrhythmic, was added to a drug regimen that included the fluoroquinolone levofloxacin.

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A 67-year-old white woman was admitted to the hospital for mitral valve repair. She had a history of hypothyroidism, non-insulin-dependent diabetes mellitus, obesity, chronic atrial fibrillation, hypertension, and heart failure. Before admission, she took the following oral medications each day: aspirin 325 mg, ramipril 2.5 mg, levothyroxine 0.175 mg, warfarin 5 mg, and citalopram 20 mg. After mitral valve repair, her postoperative medications included nesiritide 0.01 mcg/kg/min for 2 days, milrinone 0.5 mcg/kg/min for 4 days, vancomycin 1 gm intravenously every 12 hours for 4 days, epinephrine 0.07 mcg/kg/min for 1 day, famotidine 20 mg intravenously every 12 hours, and enteric-coated aspirin 325 mg orally daily. Amiodarone 1 mg/min for 6 hours and then 0.5 mg/min was administered to maintain sinus rhythm.

On the second day following her operation, the patient remained on a ventilator due to respiratory difficulties. Bumetanide 2 mg intravenously every 8 hours was ordered. The third day after the operation, levofloxacin 250 mg intravenously daily was begun for an elevated white blood cell count with a left shift in the white blood cell differential and pulmonary infiltrates. Warfarin 5 mg via nasogastric tube was given. Levothyroxine 0.175 mg and ramipril 2.5 mg orally daily were also started. The amiodarone was changed to 400 mg via nasogas-



Figure 1. The patient's electrocardiogram while taking levofloxacin and amiodarone, with a QTc interval of 0.64 seconds.

tric tube every 8 hours. She continued to have a stable sinus rhythm with a prolonged PR interval and a QTc interval of 0.64 seconds (*Figure 1*). She was extubated on day 4. The dose of levofloxacin was increased to 500 mg daily due to a further elevation in the white blood cell count and possible pneumonia. Pantoprazole 40 mg orally daily was started, and the famotidine was discontinued.

The patient continued to progress satisfactorily, and early on the sixth day following her operation she was transferred to the telemetry unit. She continued to receive amiodarone orally and levofloxacin intravenously. The next day the patient had two runs of nonsustained ventricular tachycardia (VT). Her serum potassium was within normal range at 3.5 mEq/L but less than our desired postoperative value of 4.0 mEq/L. Amiodarone 150 mg as an intravenous bolus was given. Later she had sustained VT, requiring cardiopulmonary resuscitation and defibrillation. Her heart rate went into junctional and then sinus rhythm. She was transferred back to the intensive care unit, intubated, and sedated. Sinus tachycardia was noted and then sinus rhythm with first atrioventricular block. The amiodarone was converted to a drip running at 0.5 mg/min and was later increased to 1 mg/min. Propofol was initiated for sedation. Two additional 150-mg boluses of intravenous amiodarone were given for recurrent VT. After the second bolus, torsades de pointes was evident on her electrocardiogram (*Figure 2*). The QTc interval

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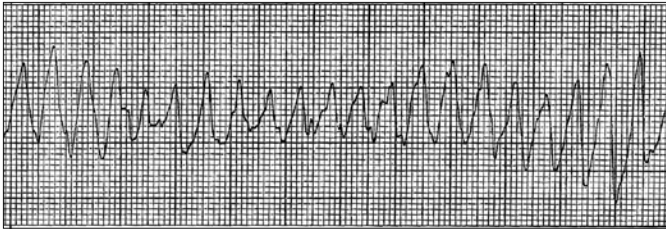


Figure 2. The patient's electrocardiogram showing torsades.



Figure 3. The patient's electrocardiogram after discontinuation of the drugs, with a QTc interval of 0.32 seconds.

was prolonged with a slower sinus rhythm. Ventricular pacing was initiated. Amiodarone and levofloxacin were immediately discontinued.

No further events occurred. She remained in sinus rhythm, and the QTc interval was noted to be much shorter at 0.32 seconds after discontinuation of the amiodarone and levofloxacin (Figure 3). Over the next 3 days, the patient continued to improve. Her QTc interval was 0.12 seconds. She reverted to atrial fibrillation with a heart rate of 90 to 100 beats per minute but showed no further signs of VT. An adverse drug reaction report was completed, with a Naranjo analysis score of 5. She was discharged to a skilled nursing facility.

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Arrhythmias with levofloxacin are an unusual adverse effect, with an estimated incidence of 0.1% to 0.9%. The administration of levofloxacin when significant bradycardia, hypokalemia, or a class Ia or III antiarrhythmic agent is present increases the risk of cardiotoxicity (1). Frothingham conducted a retrospective analysis of the incidence of torsades de pointes as-

sociated with the use of ciprofloxacin, ofloxacin, gatifloxacin, levofloxacin, and moxifloxacin. The results indicated that the rate of torsades was highest with levofloxacin and gatifloxacin (2). The exact mechanism by which proarrhythmic effects are seen with the fluoroquinolones is unknown but may be related to the blockade of the rapid component of the delayed rectifier potassium current, which leads to QTc interval prolongation and torsades (3).

Utilization of amiodarone is on the rise. Amiodarone is a preferred antiarrhythmic because it has fewer proarrhythmic effects than other agents. The incidence of torsades following amiodarone is considered rare but has been reported (4, 5). Our patient's electrocardiogram distinctly showed torsades de pointes after the administration of an amiodarone 150 mg bolus. Her hospital course was uneventful after discontinuation of levofloxacin and amiodarone. When levofloxacin is given in combination with other drugs that have the potential to induce QTc prolongation, the risk of life-threatening arrhythmias increases.

Acknowledgments

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