

# Gitelman Syndrome Presenting as Torsades De Pointes

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## Abstract

Acquired long QT syndrome is often caused by metabolic disorders and can degenerate into a polymorphic ventricular tachycardia, known as Torsades de Pointes. It has been demonstrated that in patients with either hypokalemia or hypomagnesemia, the ones at greatest risk of developing Torsades de Pointes are those on antiarrhythmic medical therapy.<sup>1</sup> Here, we present and discuss a case of Torsades de Pointes in a patient with Gitelman Syndrome on sotalol therapy.

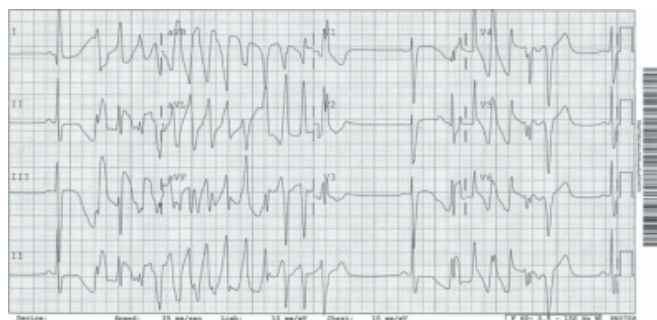
## CASE REPORT

In September 2008, a 55-year-old African American woman presented with recurrent episodes of syncope over the past 17 years. During these episodes that occurred at rest, she became lightheaded, dizzy, and briefly lost consciousness. She denied any chest pain, dyspnea, vomiting, diarrhea, or urinary incontinence. She was not on diuretics, did not consume licorice and had no family history of similar problems. Review of systems was positive for generalized fatigue, muscle cramps, and polyuria.

Five months prior to admission, she was treated for a similar episode at an outside facility for nonsustained ventricular tachycardia. At that hospitalization, a cardiac catheterization revealed normal coronary arteries. The patient recalled being diagnosed with ventricular arrhythmias in the past and therefore was discharged on amiodarone. In spite of this, the patient had persistent symptoms and was switched to sotalol a few weeks prior to the current admission.

On admission, the initial electrocardiogram (ECG) revealed nonsustained polymorphic ventricular tachycardia with a rate of 184 beats/min and features consistent with Torsades de Pointes (Figure 1). The sotalol was discontinued and she was treated emergently with intravenous magnesium, calcium gluconate, and amiodarone. Subsequent ECGs displayed normal sinus rhythm with rates ranging from 60-80 beats/min, but a prolonged QT interval corrected for heart rate (QTc) as high as 584 milliseconds.

Figure 1



Initial serum chemistries revealed a potassium level of 2.8 mEq/L (normal range, 3.4 to 5.1 mEq/L) and a magnesium level of 1.3 mEq/L (normal range, 1.2 to 2.1 mEq/L). Even while receiving intravenous/oral repletion of potassium and magnesium daily, the serum potassium and magnesium levels persistently decreased throughout each day. Subsequent analysis of 24-hour urine chemistries revealed renal wasting of potassium, with a transtubular potassium gradient (TTKG) of approximately 12 (TTKG>7 indicates renal loss). The patient was also found to have persistently elevated serum bicarbonate of 28-30 mEq/L (normal, 22 to 32 mEq/L). A transthoracic echocardiogram done on admission revealed an ejection fraction of 55%. The renin and aldosterone levels were within normal on serum assays, essentially ruling out hyperaldosteronism. Given the combination of hypokalemia, hypomagnesemia, and metabolic alkalosis, the patient was given the diagnosis of acquired long QT syndrome secondary to a metabolic disorder, most likely Gitelman Syndrome.

The patient did not have any further episodes of ventricular

tachycardia and her QTc interval narrowed to 484 milliseconds on discharge after several days of aggressive electrolyte repletion. The patient received an implantable cardioverter defibrillator and was discharged on daily oral potassium and magnesium supplements. A genetic analysis was not performed to further investigate the diagnosis of Gitelman Syndrome as it would not have affected our management. Even though the patient denies any family history of similar symptoms, she was urged to notify her family members of this possible genetic defect as they may also be at risk for fatal arrhythmias.

### DISCUSSION

Gitelman Syndrome is a disorder that causes a defect in the sodium-chloride cotransporter in the renal distal convoluted tubule, causing hypokalemia, hypomagnesemia, and metabolic alkalosis. The prevalence of Gitelman Syndrome is estimated at approximately 1 per 40,000.<sup>2</sup> It is an autosomal recessive disorder which may not be diagnosed until adulthood, with common complaints of cramps, fatigue, dizziness and polyuria. Diagnosis is often one of exclusion, ruling out other causes of hypokalemia and metabolic alkalosis, such as vomiting and diuretic use. However, diagnosis can also be made with the following laboratory findings: hypokalemia due to renal losses, metabolic alkalosis, hypomagnesemia due to renal losses, elevated urinary chloride excretion, and a decrease in urinary calcium excretion.<sup>3</sup>

The laboratory values in this patient explicitly satisfied all of the above criteria for the diagnosis of Gitelman Syndrome, except elevated urinary chloride excretion and a decrease in urinary calcium excretion (which were not assayed for in the urine). However, the 24-hour urinary sodium excretion was >300 meq/L (normal, 10-300 meq/L), which is consistent with the defect in the thiazide sensitive sodium-chloride cotransporter seen in Gitelman Syndrome. In addition, the serum calcium was slightly elevated at 10.0 mg/dl (normal, 8.9 to 10.3 mg/dl), which would be consistent with the decreased urinary calcium excretion seen in Gitelman

Syndrome.

Hypokalemia and hypomagnesemia can prolong the QT interval and increase the susceptibility of the heart towards fatal ventricular arrhythmias. It has been demonstrated that there is a tendency for prolonged QT intervals in patients with Gitelman Syndrome, one study showing the prevalence of more than 40%.<sup>4</sup> The recent addition of sotalol most likely triggered the episode of Torsades de Pointes. Sotalol is a class III antiarrhythmic drug that prolongs the action potential and lengthens the effective refractory period in the cardiac myocytes and conduction pathways, showing efficacy in preventing recurrence of sustained ventricular tachycardia or ventricular fibrillation. However, these actions can also lead sotalol to become proarrhythmogenic by prolonging the QT interval. It has been estimated that rate of Torsades de Pointes is approximately 2.5% after nearly 6 months of treatment with sotalol, with increased rates seen in female patients and higher doses.<sup>5</sup>

Gitelman Syndrome was the most likely predisposing condition that lead to the episodes of recurrent syncope and ventricular arrhythmias in this patient. Before starting patients on antiarrhythmic therapy for recurrent syncope due to arrhythmias, metabolic causes, such as hypokalemia and hypomagnesemia should be fully evaluated.

### References

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