A suspected case of carbimazole-associated torsades de pointes

Chiranjib Bagchi, Dhurjati Prasad Sinha\(^1\), Santanu Kumar Tripathi

Introduction

Torsades de pointes (TdP) or polymorphic ventricular tachycardia owing to drug-induced QT prolongation is a common cause of withdrawal of marketed drugs and has caused increasing concern in the recent past. Carbimazole, the common antithyroid drug, is not a very well-known offender to cause QT prolongation and TdP. Only a few cases of carbimazole-induced TdP have been reported so far. We report a 53-year-old woman who was on tab. carbimazole (10 mg) twice daily for one month and who presented with respiratory distress, palpitation and syncope attack. Her surface electrocardiogram (ECG) was showing the evidence of TdP and subsequently hypokalemia was also detected. She received conservative management including potassium supplementation. However, QT prolongation persisted even after normalization of serum potassium level. Carbimazole was withdrawn and the patient was discharged as she remained stable and symptom free. This study highlights a possible association between carbimazole and TdP.

KEY WORDS: Carbimazole, QT prolongation, torsades de pointes
day indicated the presence of hypokalemia and hyponatremia with serum potassium and sodium levels at 2.6 mmol/L (normal 3.5–5 mmol/L) and 133 mmol/L (normal 135–145 mmol/L), respectively. Inj. frusemide was then replaced with combination of tab. frusemide plus spironolactone. Normal saline (NS) infusion started with inj. potassium chloride (20 meq) added to each bottle of NS. Serum sodium and potassium levels were normalized within 24 hours. Her thyroid profile showed euthyroid state with normal serum T3 148.2 ng/dL (normal 70–190 ng/dL) and T4 11.06 µg/dL (normal 5–12 µg/dL) with low serum TSH 0.13 µU/mL (normal 0.4-0.5 µU/mL). QT prolongation, however, persisted even after normalization of serum potassium level. The patient was treated conservatively and tab. carbimazole was withdrawn. She remained stable and symptom-free and was discharged with instruction to attend the outpatient department regularly.

The patient was admitted in the same hospital 3 months ago on August 01, 2008 for ventricular ectopics, but there was no evidence of prolonged QT interval. Although carbimazole is not well known to prolong QT interval, there are few reports of its association with TdP.[4,5] Caro.[4] In the present study, the thyroid profile was normal during her hospital stay while she was on carbimazole.

A suspected drug interaction between carbimazole and erythromycin taken orally thereby increasing the serum concentration of the later and producing TdP has been reported. Carbimazole has recently been known as a hepatic microsomal enzyme inhibitor.[5] In the present case, the only concomitant medication the patient was receiving was tab. ramipril (1.25 mg) once daily which is not known to either prolong QT or cause TdP. The association between carbimazole and TdP was evaluated using both Naranjo’s Causality Assessment Scale[6] and World Health Organisation (WHO) Uppsala Monitoring Centre (UMC) Causality Assessment Criteria.[7] Naranjo’s scale revealed a score of 3, signifying a possible association. The WHO-UMC scale also indicated a possible association. In conclusion, this case report suggests a possible association between carbimazole therapy and occurrence of TdP.

As QT prolongation persisted even after termination of TdP and normalization of serum potassium level, TdP could have been precipitated by hypokalemia interacting with carbimazole.

Frusemide is known to cause hypokalemia. However, in this case TdP manifested before the administration of frusemide. Therefore, an association between frusemide and TdP does not exist. At best frusemide-induced hypokalemia if any, might have aggravated the condition. Frusemide was given initially as the patient had the symptoms of pulmonary edema possibly caused by the impairment of left ventricular ejection due to VT.

There may be a probability of hereditary long QT syndrome. However, during her previous hospital admission and subsequent follow-up visits, there was no evidence of prolonged QT interval. Although carbimazole is not well known to prolong QT interval, there are few reports of its association with TdP.[4,5] In a patient of thyrotoxicosis with bradycardia owing to atrioventricular conduction block, occurrence of hypothyroidism owing to overtreatment with carbimazole was proposed to initiate the TdP.[4] In the present study, the thyroid profile was normal during her hospital stay while she was on carbimazole.

Discussion

Considering the causes of TdP, the probabilities in this case were analyzed. Hypokalemia is well known to cause QT prolongation and TdP, but in this study QT prolongation persisted even after normalization of serum potassium level.

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