First report of metronidazole-induced QT interval prolongation

Sir,

We report marked QT interval prolongation appearing on an electrocardiogram (ECG) of a 90-year-old female receiving metronidazole as treatment for aspiration pneumonia. To the best of our knowledge, no previous reports of metronidazole-induced QT interval prolongation exist, excluding cases of drug–drug interactions. We believe that metronidazole might be arrhythmogenic, as are other azole derivatives, particularly in patients at high risk for arrhythmias.

A 90-year-old female with a history of Parkinson’s disease and osteoporosis was hospitalised due to aspiration pneumonia. She had no known structural heart disease. She was started on intravenous ceftriaxone (1 g once daily) and metronidazole (500 mg three times a day). Her regular medication included levodopa and calcium preparations. An ECG performed on admission demonstrated a QTc interval of 324 ms. The following day her ECG showed a prolonged QTc interval of 703 ms (Fig. 1). Metronidazole treatment was immediately withdrawn. Physical examination and chest radiography were unremarkable. Laboratory tests, including serum potassium and magnesium levels, were within normal limits. Renal function and liver enzymes were also normal. Over the following days her QTc interval gradually decreased to its initial value without any clinically significant arrhythmias and the patient was discharged from the department in good condition. We recommended that she avoid any medication known to cause QT interval prolongation.

A variety of commonly prescribed non-cardiovascular drugs, including antimicrobials, psychotropic agents and certain histamine H1-receptor antagonists, can prolong cardiac repolarisation and might trigger a polymorphic ventricular tachycardia called Torsade de Pointes (TdP) [1]. Azole derivatives such as ketoconazole, itraconazole and fluconazole can trigger TdP mainly by interacting with other QT prolonging agents, but also due to their own QT prolongation effect [2]. Metronidazole, a widely used azole derivative with antibacterial and antiparasitic properties, is a potent inhibitor of CYP3A4 and CYP2C9 isoenzymes. Its mechanism of action may cause QT prolongation and TdP through its interaction with other QT-prolonging agents [3–5]. However, as our patient presented a strong temporal relationship between metronidazole administration and the development of QT prolongation, metronidazole itself might have caused the QT prolongation in her case, similar to the effect of other azole derivatives [2]. Since our patient did not suffer from any known structural heart disease or electrolyte imbalances, she might have been the carrier of a silent mutation in one of the congenital long QT syndrome-associated genes. These patients are at high risk for developing TdP when exposed to cardiac as well as non-cardiac-related drugs whose mechanism is based on potassium channel blocking [6]. In light of all this, we believe the arrhythmogenic properties of metronidazole should be studied in vitro and, in the meantime, metronidazole should be prescribed cautiously to patients at high risk for drug-induced TdP, such as elderly women with structural heart disease, renal failure or impaired liver function [7].

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References

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