Azithromycin-Induced Torsade De Pointes

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Although erythromycin frequently induces long QT interval and torsade de pointes, the newer drug, azithromycin, has rarely been reported to be associated with torsade de pointes. We report here the occurrence of a significant typical QT prolongation within a few hours after taking azithromycin which lead to torsade de pointes. (PACE 2007; 30:1579–1582)

macrolides, azithromycin, long QT syndrome, torsade de pointes

Introduction

Macrolides are effective and popular antibiotics for upper and lower respiratory tract infections. Because of the side effects observed with erythromycin, involving long QT intervals and torsade de pointes (TdP), newer macrolides have been developed for the treatment of atypical organisms involved in respiratory tract infections. Azithromycin is a very effective agent for pneumonia due to atypical organisms and has a good safety profile. Only one patient developed torsade de pointes during the post market surveillance.[1] There were some reports of QT prolongation when azithromycin was used in combination with amiodarone.[2] Other reports have also described the occurrence of ventricular tachycardia when it was used in combination with disopyramide[3] or in congenital long QT syndrome.[4] This is a report describing the occurrence of a significant typical QT prolongation within a few hours after taking azithromycin which leads to torsade de pointes.

Case report

The patient was a 90-year-old woman with hypertension and an old cerebrovascular accident (stroke), who was being cared for at a chronic care center. The patient had a fever and shortness of breath, and was sent to our hospital's emergency department. The patient's chest X-ray revealed that she was suffering from interstitial pneumonia and respiratory failure. Therefore, an intratracheal intubation was performed and ventilator support was initiated in the medical intensive care unit. The antibiotics, penicillin + sulbactam (375 mg three times a day) and azithromycin (500 mg a day), were given during that day. Within four hours after taking the medication, a pronounced QT prolongation observed on the 12-lead electrocardiogram (EKG) was noted (Fig. 1A). After a few minutes the patient lost consciousness transiently due to polymorphic ventricular tachycardia (PMVT). Initiation of the PMVT with a short-long-short cycle with repetitive attacks confirmed the diagnosis of torsade de pointes (Fig. 2A and B). An electrolyte evaluation revealed that the levels were within normal limits. One gram of magnesium sulfate was given slowly intravenously, but the tachycardia still persisted (Fig. 2B). Then, 100 mg of lidocaine was slowly given intravenously. After the tachycardia terminated, a continuous intravenous administration of lidocaine was given at a dose of 2 mg/min. However, the QT interval was still prolonged. After stopping the azithromycin for one day, the QT interval returned to normal and no more tachycardia was noted (Fig.1B). After the next day, the patient's condition improved and the endotracheal tube was removed, and the patient was transferred to an ordinary ward. After close monitoring of the heart rate, no more prolonged QT intervals or TdP were noted. The patient's baseline EKG was normal and no long QT syndrome was noted. There was also no family history of sudden death. The patient currently has not been taking any medications that may prolong the QT interval (e.g. amiodarone, sotalol, procainamide, etc.).

Discussion

Very rare case reports on azithromycin associated with long QT syndrome and TdP have been published. Azithromycin is a member of the macrolide family, which is a group of antibiotics used to treat respiratory tract infections, especially caused by an atypical organism. Erythromycin is the prototype. Another member includes clarithromycin which is effectively used in the treatment of Helicobacter infections associated with peptic ulcer diseases.

An experimental study showed that these three drugs exhibited different interference mechanisms with the repolarization and had a different incidence of TdP. Azithromycin was associated with the least incidence of TdP.[5] In that study, the authors showed that all three macrolides lead to a similar increase in the QT interval and monophasic action potential (MAP) duration in

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Received April 4, 2007; revised May 27, 2007; accepted June 19, 2007.

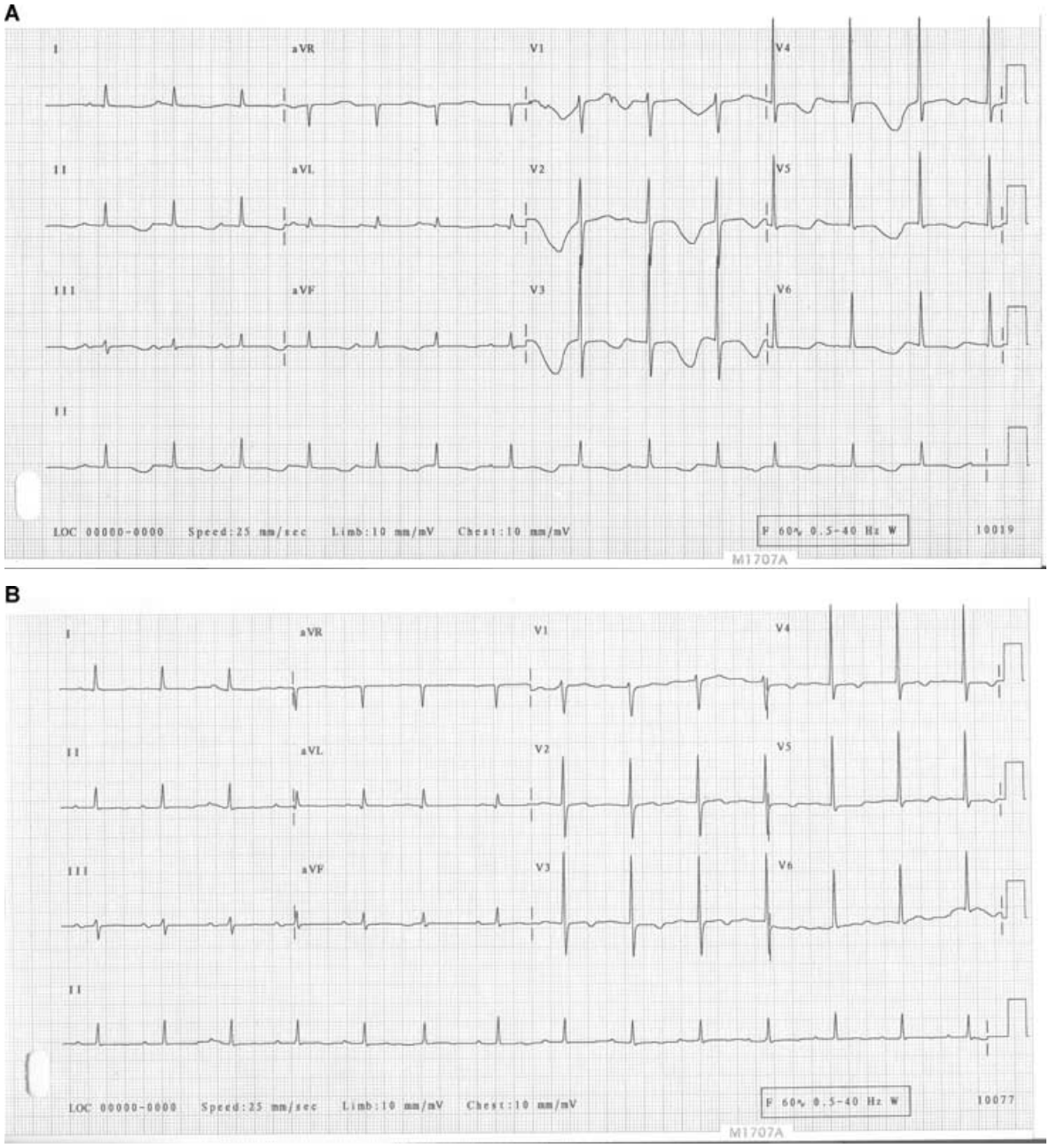

Figure 1. *(A) Prominent QT prolongation (QTc = 740 ms) was observed four hours after taking azithromycin. (B) A 12-lead EKG showing the normalization of the QT interval one day after the torsade de pointes. Some nonspecific changes in the repolarization were also noted in the EKG.*

Langendoff-perfused rabbit hearts. Erythromycin and clarithromycin led to early afterdepolarizations (EADs) and TdP after lowering the potassium concentration. However, no EADs or TdP occurred in the presence of azithromycin. The authors attributed the different patterns of the MAP caused by the azithromycin as being related to the lower incidence of TdP. (Azithromycin caused a rectangular pattern of the MAP prolongation.) Although this pattern protects the heart from TdP, the arrhythmia still can be possible because azithromycin can prolong the QT interval and MAP duration.

A post-market surveillance showed that only one case of an "arrhythmia" occurred in a patient with an old MI.[1] A search of Pubmed

Figure 2. *(A and B) An EKG showing torsade de pointes which was characterized by a short-long-short cycle initiating it and repetitive attacks of polymorphic ventricular tachycardia.*

using the keywords "Azithromycin," "Long QT syndrome," and "Torsade de pointes" revealed only a few case reports.[6–8] Most of those case reports described a long QT with the use of azithromycin, but no TdP resulted.[6,7] In one of the cases, PMVT was induced without a prolonged QT interval. The author suggested the careful use of that drug and careful monitoring of those cases.[8] In another case, TdP and a cardiovascular arrest were induced by azithromycin because it was used in a case with congenital long QT syndrome.[4] Therefore, it would be prudent to check the EKG and QT interval before using this medication.

In our case, there were no clues as to the cause of the TdP. In the case of multiple comorbidities and old age, azithromycin should be used very cautiously to avoid such a serious complication.

References

1. Zithromax ®(azithromycin for oral and injection) Package Inserts 4763, 5179.5191.
2. Samarendra P, Kumari S, Evan SJ, Sacchi TJ, Navarro V. QT prolongation associated with azithromycin/amiodarone combination. Pacing Clin Electrophysiol 2001; 24(10):1572–1574.
3. Granowitz EV, Tabor KJ, Kirchhoffer JB. Potentially fatal interaction between azithromycin and disopyramide. Pacing Clin Electrophysiol 2000; 23(9):1433–1435.
4. Arellano-Rodrigo E, Garcia A, Mont L, Roque M. Torsade de pointes and cardiorespiratory arrest induced by azithromycin in a patient with congenital long QT syndrome. Med Clin (Barc) 2001; 117(3):118–119.
5. Milberg P, Eckardt L, Bruns HJ, Biertz J, Ramtin S, Reinsch N, Fleischer D, et al. Divergent proarrhythmic potential of macrolide antibiotics despite similar QT prolongation: Fast phase 3 repolarization prevents early afterdepolarizations and torsade de pointes. J Pharmacol Exp Ther 2002; 303:218–225.
6. Russo V, Puzio G, Siniscalchi N. Azithromycin-induced QT prolongation in elder patient. Acta Biomed 2006; 77(1):30–32.
7. Matsunaga N, Oki Y, Prigollini A. A case of QT-interval prolongation precipitated by azithromycin. N Z Med J 2003; 116(1185):U666.
8. Kim MH, Berkowitz C, Trohman RG. Polymorphic ventricular tachycardia with a normal QT interval following azithromycin. Pacing Clin Electrophysiol 2005; 28(11):1221–1222.