Case report

Quinolone Induced Torsades De Pointes: A Life Threatening Complication of Conventional Medication

Lanlalin Sojikul, Kunchanit Chongtanapipat, Kumpol Chintanavilas*

Abstract

The use of antibiotic drugs, particularly the quinolone group, can cause acquired QT prolongation and blockage of the potassium channel (Ik). We report a case of torsade de pointes (TdP) triggered by the use of ciprofloxacin to treat arteriovenous fistulas infection.

Keywords: Fluoroquinolone, Ciprofloxacin, Torsades De Pointes, Long QT interval, Polymorphic ventricular tachycardia

Chulabhorn International College of Medicine, Thammasat University, Pathum Thani, Thailand

* **Corresponding author:** Kumpol Chintanavilas, M.D., Chulabhorn International College of Medicine, Thammasat University, Pathum Thani, Thailand. Email : Kumpol07@staff.tu.ac.th, Tel. : +6662926599

Case information

A 59-year-old man with an end-stage renal disease requiring hemodialysis via arteriovenous fistula was admitted due to an infected left radiocephalic arteriovenous graft. His current medications at the time were atorvastatin, warfarin, losartan and doxazocin. Intravenous ciprofloxacin was administered for three days before radiocephalic vein ligation under general anesthesia was performed. At midnight after the operation, the patient experienced pulseless cardiac arrest, which was successfully treated with defibrillation and two cycles of CPR. A twelve-lead electrocardiogram taken just before cardiac arrest showed polymorphic ventricular tachycardia with waxing and waning patterns. After the restoration of spontaneous circulation, the electrocardiogram showed atrial fibrillation with QT prolongation (QTC increased from a baseline of 470 to 591 ms). Laboratory results revealed low magnesium levels and normal potassium levels (Mg 1.8 mg/dL and K 4.5 mmol/L). A coronary angiogram was performed, which showed a diffuse 20% lesion in the proximal left anterior descending artery with no significant obstruction. After intravenous administration of 1 gram of magnesium sulfate, correction of hypomagnesemia, and discontinuation of ciprofloxacin, the patient's atrial fibrillation returned to sinus rhythm the next day. The patient's QT interval returned to the baseline of 470 ms two weeks later, with no other cardiac arrhythmias reported.

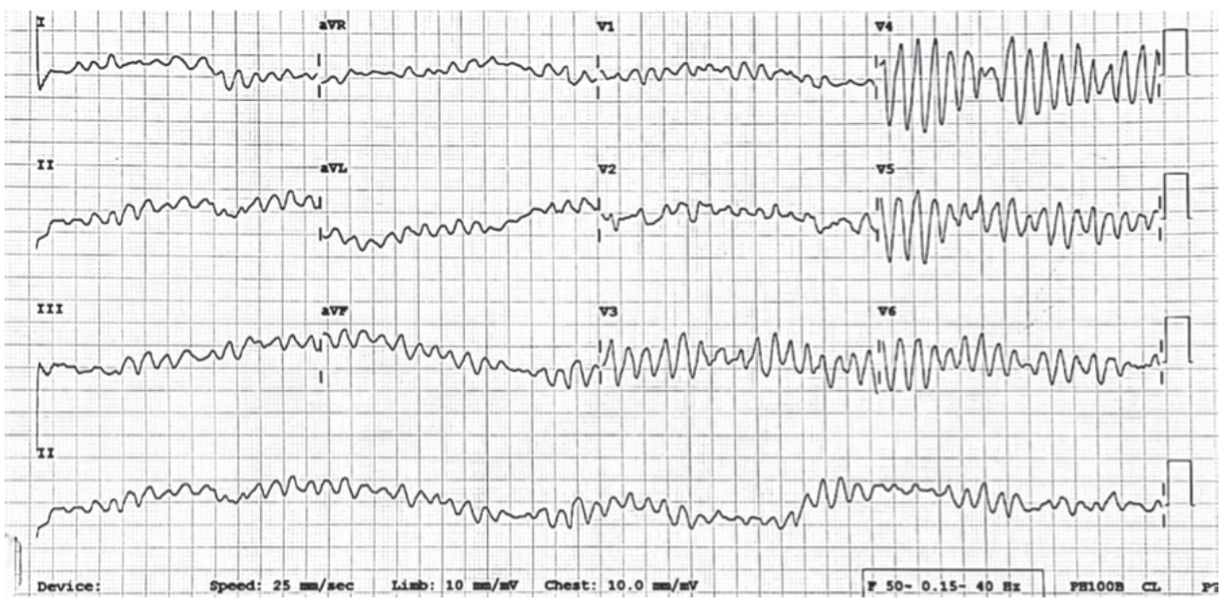

Figure 1 The patient's ECG of the polymorphic ventricular tachycardia with waxing and waning patterns coincides with Torsade de Pointes.

Discussion

Ciprofloxacin, a broad-spectrum fluoroquinolone antibacterial drug, is commonly prescribed for the treatment of bacterial infections in various organ systems. The main mechanism of fluoroquinolone is inhibiting bacterial DNA gyrase, which can lead to an acquired QT prolongation and blockage of the potassium channel (IK), resulting in early afterdepolarization and ventricular arrhythmias such as Torsade de Pointes [1]. Although ciprofloxacin appeared to be the lowest risk for QT prolongation and TdP rate[2], our case demonstrated an example of a ventricular arrhythmia from ciprofloxacin usage in a borderline QT prolonged patient.

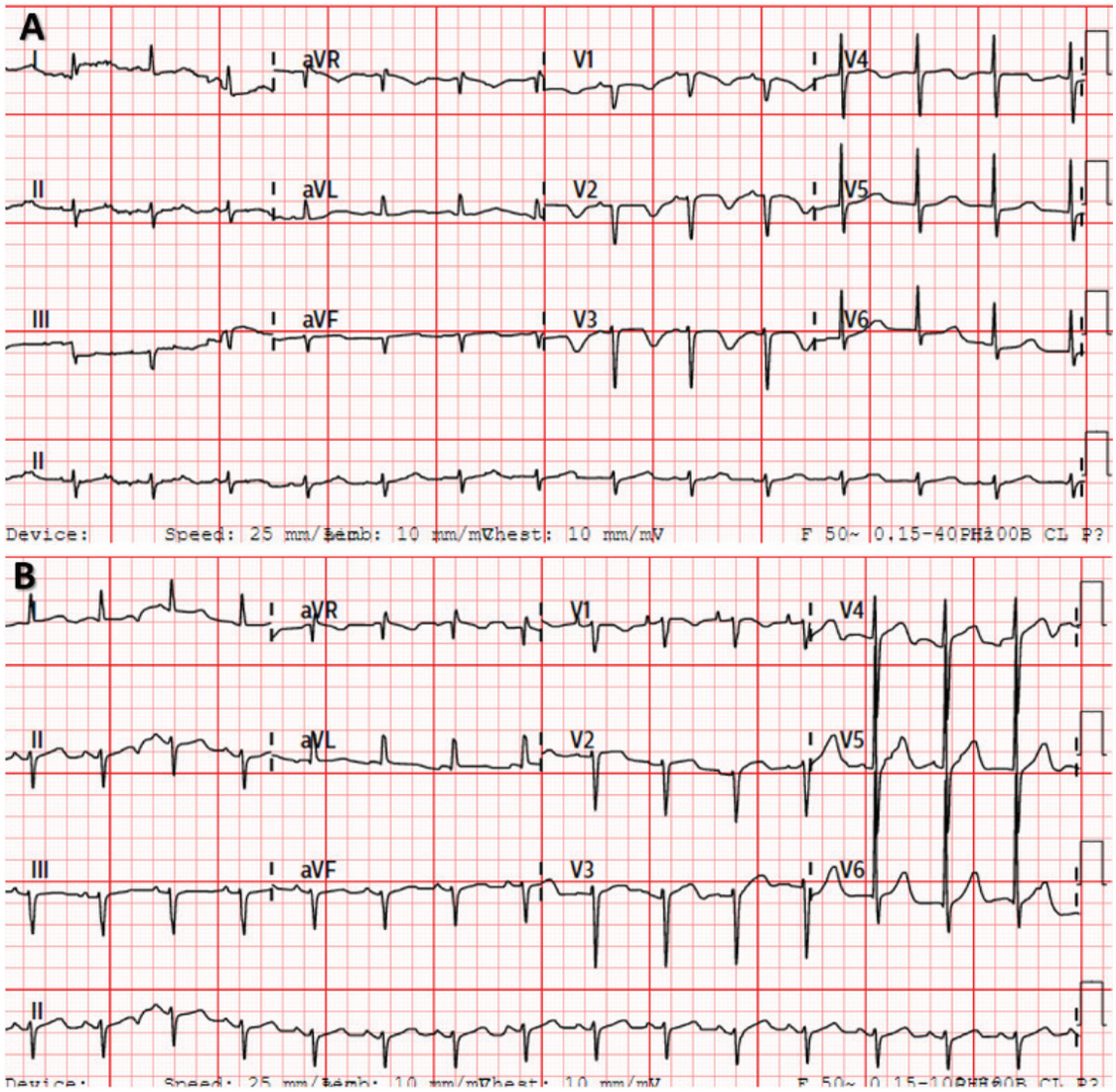

Figure 2 The patient's electrocardiogram, with (A) indicating the prolonged QT interval of 591 ms observed after the polymorphic ventricular tachycardia event, (B) indicating the baseline QT interval of 470 ms observed two weeks later

This patient suffers from Torsades de Pointes (TdP), a type of polymorphic ventricular tachycardia. The key characteristic findings on an electrocardiogram (ECG) include a waxing and waning pattern due to the twisting of QRS complexes around an isoelectric line. The onset of ventricular arrhythmias begins with premature ventricular contractions (PVCs) showing R waves superimposed on T waves as the 'R-on-T' phenomenon. Additionally, a "long-short" initiating sequence on the ECG may also be present[3]. The impact of this arrhythmia can lead to an in-hospital mortality of 10.7% and 1-year mortality of 25.0%[4].

One of the main mechanisms underlying TdP is the abnormal prolongation of the repolarization phase. This is caused by blockage of the delayed rectifier potassium current (Ikr), which results in decreased potassium efflux and an excess of positive ions inside the cellular membrane, ultimately leading to a prolonged repolarization phase. This prolonged repolarization is manifested as a prolonged QT interval on the surface electrocardiogram (ECG). In addition, conditions that cause small inward currents, such as Na window current and Na/Ca exchange current, create suitable conditions for a large prolonged membrane

depolarization, which is prone to late calcium channel reactivation and results in ectopic beats. This phenomenon creates the pathognomonic R-on-T phenomenon in TdP[5].

Drug-induced QT prolongation is defined as a QTc of 500 ms or greater or an increase of 60 ms or greater in QT interval. Our patient has end-stage renal disease as the main risk factor, other patient factors that can increase the risk of developing drug-induced long QT syndrome, include female sex, age over 65 years, structural heart disease, hepatic insufficiency, and electrolyte abnormalities such as hypokalemia, hypomagnesemia, or hypocalcemia. Certain medications, such as diuretics and multiple QT-prolonging drugs, can also increase the risk[6]. To assess the risk of drug-induced QT prolongation, there are various risk assessment tools available such as the Tisdale risk score, the MedSafety Scan (MSS) QT prolongation risk score and the Risk of QT drug-drug interactions assessment tool. A baseline prolonged QT interval without a diagnosis of long QT syndrome (2 points from modified long QT diagnosis score) in this patient was also included in these risk scores. High-risk patients should undergo regular ECG monitoring until the steady state of the torsadogenic agent is reached[7].

Emergency treatment of torsade de pointes consists of removing any torsadogenic stimulus and suppressing early afterdepolarizations (EADs), which may include accelerating the heart rate to reduce the QT interval. In this patient, discontinuation of ciprofloxacin was implemented. Initial treatment should include correcting hypokalemia and hypomagnesemia and administering intravenous magnesium sulfate. Magnesium sulfate suppresses torsade de pointes by decreasing the influx of calcium ions, inhibiting calcium influx via L-type calcium channels and reducing the amplitude of EADs. However, care should be taken due to the high risk of magnesium toxicity especially in renal insufficiency patients[8]. Apart from the treatment plan approached in our case, there is a wide range of treatments available for these circumstances. The administration of isoproterenol can increase the heart rate due to its properties as a non-selective b1/b2-adrenoceptor, which shortens the QT interval. Moreover, transvenous pacing has been proven to increase the heart rate and suppress or abolish episodes of TdP. In the case that the patient has a hemodynamic compromise, it can be treated with unsynchronized cardioversion, beginning with 100 joules. Nevertheless, for patients who failed to respond to the regimen described above, IV lidocaine, a class 1B antiarrhythmic drug, can be selected as an alternative. It has been shown to shorten the QT interval due to its property of blocking voltage-gated Na^+ channels (VGSC/NaVs)[9]. Automatic implantable cardioverter defibrillator (AICD) consideration in reversible TdP, such as drug induced TdP, should be avoided[10].

In conclusion, quinolone antibiotics have been associated with QT prolongation, which can increase the risk of life-threatening ventricular arrhythmias. It is important to monitor and manage any underlying abnormalities that may predispose patients to QT prolongation, such as electrolyte imbalances, heart disease and genetic factors. Prompt and appropriate acute management is essential for improving clinical outcomes in these cases.

Financial support: The authors received no financial support for the publication.

Compliance with Ethics requirements: All case information and the procedures performed in this case report involving human patients were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflict of interest: The authors declare that they have no conflict of interest.

Author contributions: The author's indicated in parentheses made substantial contributions to the following task of the case report : Initial conception (K.Chi.); Management of case in the report (K.Chi.); Supervised the project (K.Chi.); Analyzed the data (K.Cho., L.S.); Contribute to the interpretation of the case (K.Chi., K.Cho., L.S.). All authors discussed the result and contributed to the final manuscript.

References

1. Roden DM. Drug-induced prolongation of the QT interval. *New England Journal of Medicine.* 2004;350(10):1013-1022. doi:10.1056/nejmra032426.

2. Briasoulis A, Agarwal V, Pierce WJ. QT prolongation and torsade de pointes induced by fluoroquinolones: infrequent side effects from commonly used medications. *Cardiology.* 2011;120(2):103-110. doi:10.1159/000334441.
3. Viskin S. Long QT syndromes and torsade de pointes. *Lancet.* 1999;354(9190):1625-1633. doi:10.1016/S0140-6736(99)02107-8.
4. Mantri N, Lu M, Zaroff JG, et al. Torsade de Pointes: A nested case-control study in an integrated healthcare delivery system. *Annals of Noninvasive Electrocardiology.* 2021;27(1). doi:10.1111/anec.12888.
5. Luo CH, Rudy Y. A dynamic model of the cardiac ventricular action potential. II. Afterdepolarizations, triggered activity, and potentiation. *Circulation Research.* 1994;74(6):1097-1113. doi:10.1161/01.res.74.6.1097.
6. Roden DM. Predicting drug-induced qt prolongation and torsades de pointes. *The Journal of Physiology.* 2016;594(9):2459-2468. doi:10.1113/jp270526.
7. Peter J. Schwartz and Raymond L. Woosley. Predicting the unpredictable: Drug-induced qt ... - JACC journals. Journal of the American College of Cardiology. 2016. Accessed May 13, 2023. https://www.jacc.org/doi/abs/10.1016/j.jacc.2015.12.063.
8. Ismail Y, Ismail AA, Ismail AAA. The underestimated problem of using serum magnesium measurements to exclude magnesium deficiency in adults; a health warning is needed for "normal" results. *cclm.* 2010;48(3):323-327. doi:10.1515/cclm.2010.077.
9. Inoue H, Matsuo H, Mashima S, Murao S. Effects of atrial pacing, isoprenaline and lignocaine on experimental polymorphic ventricular tachycardia. *Cardiovasc Res.* 1984;18(9):538-547. doi:10.1093/cvr/18.9.538.
10. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J.* 2022;43(40):3997-4126. doi:10.1093/eurheartj/ehac262.