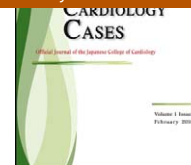




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## Case Report

# Torsades de pointes induced by garenoxacin in association with pacing failure in an elderly woman with VDD pacemaker

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### KEYWORDS

Garenoxacin;  
Pacemaker;  
QT interval;  
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**Summary** An 86-year-old woman was admitted to the hospital for syncope and convulsion 4 days after starting antibiotic therapy for pneumonia with oral garenoxacin 400 mg/day. She had a VDD pacemaker for complete atrioventricular (AV) block. Her electrocardiogram showed marked QT prolongation and during pacemaker interrogation pacing failure probably due to battery depletion induced torsades de pointes. After cessation of garenoxacin, QTc returned to normal range subsequently and a new pacemaker was implanted. In patients with risks of QT prolongation, garenoxacin should be used cautiously with QT interval monitoring.

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## Introduction

Garenoxacin is a novel quinolone that possesses antimicrobial activity against a wide range of bacteria. Like all fluoroquinolones, garenoxacin has the potential to induce torsades de pointes (TdP) but is thought to have the less QT prolonging effects [1]. This is the first case of torsades de pointes induced by garenoxacin in a patient without concomitant electrolyte imbalance and other QT prolonging medication.

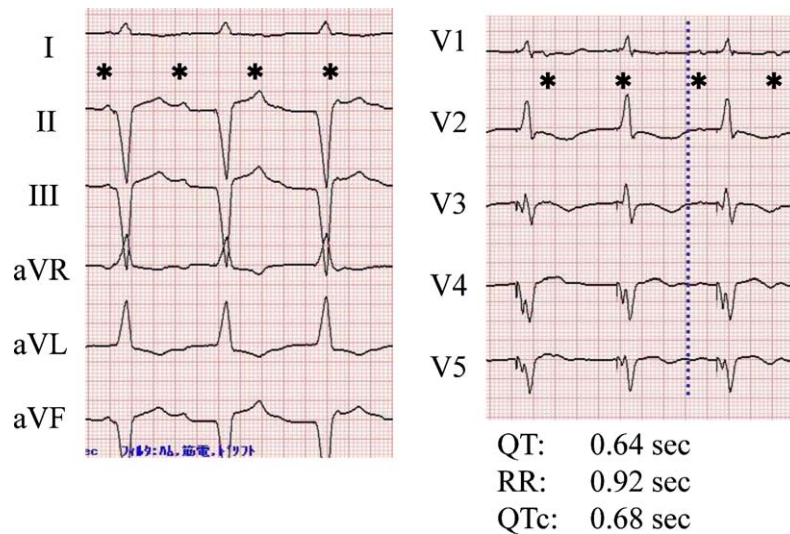
## Case report

An 86-year-old woman was admitted to the hospital for pneumonia and antibiotic therapy with garenoxacin 400 mg/day had been started for 4 days. The patient had syncope and convulsion one day after initiating oral administration of garenoxacin. She was referred to our hospital for closer examination of syncope and convulsion. VDD type pacemaker was implanted for complete atrioventricular (AV) block 10 years before. On admission, electrocardiography showed ventricular pacing at 65/min (VVI mode) probably due to pacemaker battery depletion. The QTc interval according to Bazett's formula was prolonged to 0.68 s (Fig. 1). To shorten the prolonged QT interval, reprogramming of the pacing rate up to 80/min was attempted,

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**Figure 1** Electrocardiogram (ECG) on admission. On admission VDD mode changed to VVI mode because of battery depletion. ECG shows inverted T wave in V2 and V3 with prolonged QT interval. Asterisk indicates P wave.

but pacing failure occurred suddenly during interrogation. Prolonged RR interval increased QT interval further and induced TdP (Fig. 2).

Her echocardiography showed diffuse hypokinesis of the left ventricle and decreased left ventricular ejection fraction of 25%. Laboratory data showed K of 3.9 mEq/L, Ca of 8.9 mg/dL, and Mg of 1.9 mg/dL. Serum level of creatine kinase was increased slightly at 226 IU/L, but creatine kinase MB fraction was not elevated (9 IU/L). Serum cardiac troponin I was negative. Serum concentration of garenoxacin on admission was 3.0  $\mu$ g/mL and it remained within the therapeutic range. No other QT prolonging drug was administered on admission. On the following day, garenoxacin was discontinued and a new VDD pacemaker was implanted. Pacing rate was changed from 40/min to 80/min gradually and QT/RR relation was evaluated (Fig. 3). The slope of linear regression line of QT/RR relation was increased to 0.25. QTc returned to normal level (0.46s) 14 days after cessation of garenoxacin with a basic pacing rate of 60/min.

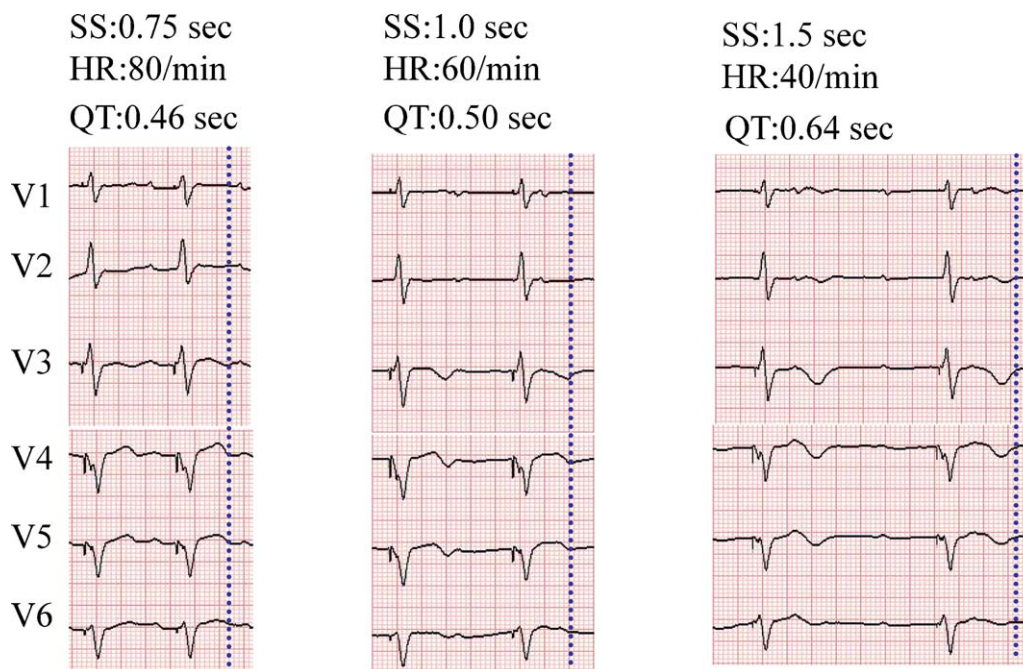
## Discussion

Inhibition of HERG channel currents by quinolones leads to prolongation of QT interval [2]. Milberg et al. demonstrated that several fluoroquinolones (ciprofloxacin, ofloxacin, moxifloxacin, and levofloxacin) increased QT interval and induced TdP associated with greater disparity of repolarization and triangulation of action potential in AV blocked rabbit hearts [3]. Sparfloxacin and grepafloxacin had been withdrawn from the market because of proarrhythmia due to TdP.

In our case, QT/RR relation was examined using implanted pacemaker the day after TdP episodes. The slope of QT/RR regression line (0.25) was steeper and was similar to the long QT syndrome type 2 patients because of excessive prolongation of QT interval at long RR intervals [4]. Steeper slope of QT/RR regression line is compatible with suppression of IKr induced by quinolones. TdP was triggered by the escape beat with a prolonged RR interval due to ventricular pacing failure. Not only the prolonged RR inter-



**Figure 2** Induction of torsades de pointes during pacemaker interrogation. A long-short RR sequence preceded torsades de pointes.



**Figure 3** Electrocardiogram during changes in pacing rate. Ventricular pacing rate was decreased gradually from 80/min to 40/min. QT interval was increased in association with RR interval prolongation.

val but also the different depolarization sequence prolonged both QT interval and T peak to end intervals further (Fig. 2).

Garenoxacin had no clinically relevant dose-dependent effects on the QT interval across a dose range from 50 to 1200 mg/day in the retrospective analysis of data from healthy volunteers [1]. Although QT-prolonging effects of garenoxacin seem to be lower than the other fluoroquinolones, there has been reported one case with garenoxacin-induced TdP [5]. An 82-year-old man had TdP after oral administration of garenoxacin for pneumonia. He had hypokalemia and also had disopyramide and the combination of electrolyte imbalance and class Ia antiarrhythmic drug in itself may induce prolonged QT interval and TdP. On the other hand, our case had no hypokalemia and had not had the other QT prolonging drug. As the pathogenesis of diffuse hypokinesia of the left ventricle, dilated cardiomyopathy seems to be the most probable because she had no history of coronary artery disease and no sign of secondary cardiomyopathy such as sarcoidosis. Hence, a direct effect of garenoxacin on QT prolongation and TdP induction was suspected. The prolonged RR interval induced by pacemaker malfunction due to battery depletion may also play an important role for the trigger of TdP episodes. It is recommended that like all other fluoroxacins [6], garenoxacin should be used cautiously in patients with risks of QT prolongation such as female sex, advanced age, and bradycardia.

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