

# A Case Study of Severe QT Interval Prolongation Caused by Antidepressants

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**Abstract:** QT interval prolongation can be categorized into primary and secondary types according to its etiology. In this paper, we report a case of severe asymptomatic QT interval prolongation secondary to antidepressants. Regular follow-up and electrocardiogram monitoring is crucial when applying antidepressants, especially for patients without cardiac symptoms. This article presents case studies and examines existing literature on long QT syndrome to enhance the diagnosis and management of QT interval prolongation. This is especially relevant for non-psychiatric healthcare professionals who need to be attentive to the side effects of antidepressants to prevent potential adverse consequences resulting from oversight.

**Keywords:** Antidepressant; Asymptomatic QT interval extension; Follow-up; Electrocardiogram

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## 1. Case information

The patient, which was a 56-year-old woman, had a history of depression for half a year. She took oral quetiapine (0.1 g in the morning and 0.2 g in the evening) and escitalopram hydrobromide (20 mg, 1/day). She had no other medical history, and her previous electrocardiograms were normal. However, the patient had an abnormal electrocardiogram in a local hospital one day before admission, suggesting sinus rhythm and T wave inversion in leads III and V2–V6. The patient had no chest tightness, chest pain, palpitations, dizziness, black eyes, or other discomforts, so she came to the emergency department of our hospital. The results of three myocardial tests were as follows: creatine kinase-myocardial band (CK-MB), 1.62 ng/mL; cardiac troponin I (cTnI), 0.014 ng/mL; and myoglobin (Myo), 21.5 ng/mL. These values were all within the normal range. Her electrocardiogram is shown in (Figures 1a and 1b).

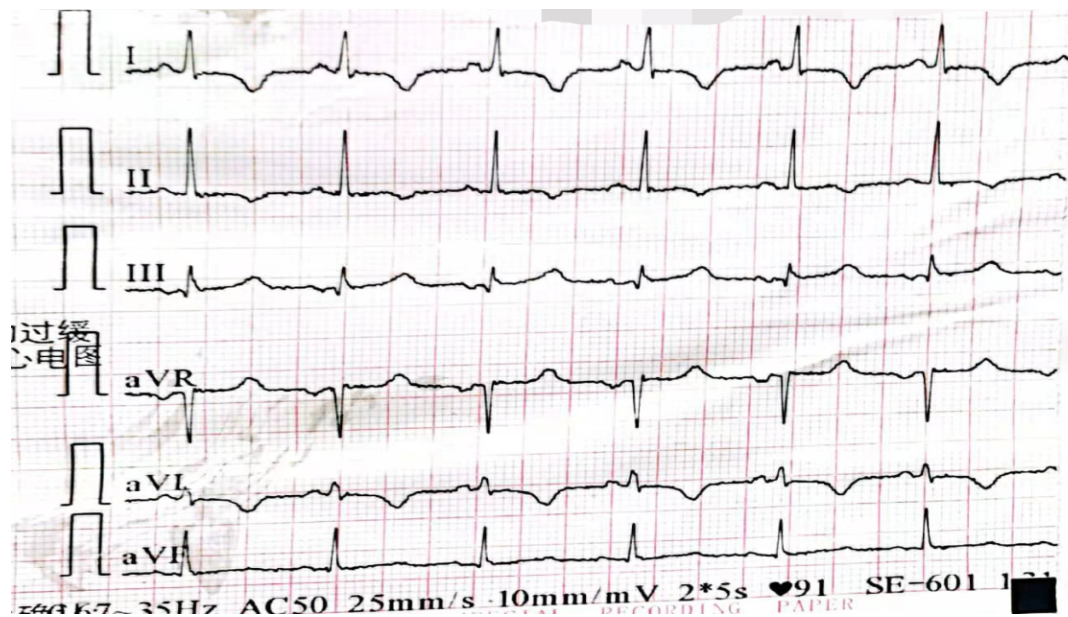


Figure 1a. ECG in emergency department March 10, 2021

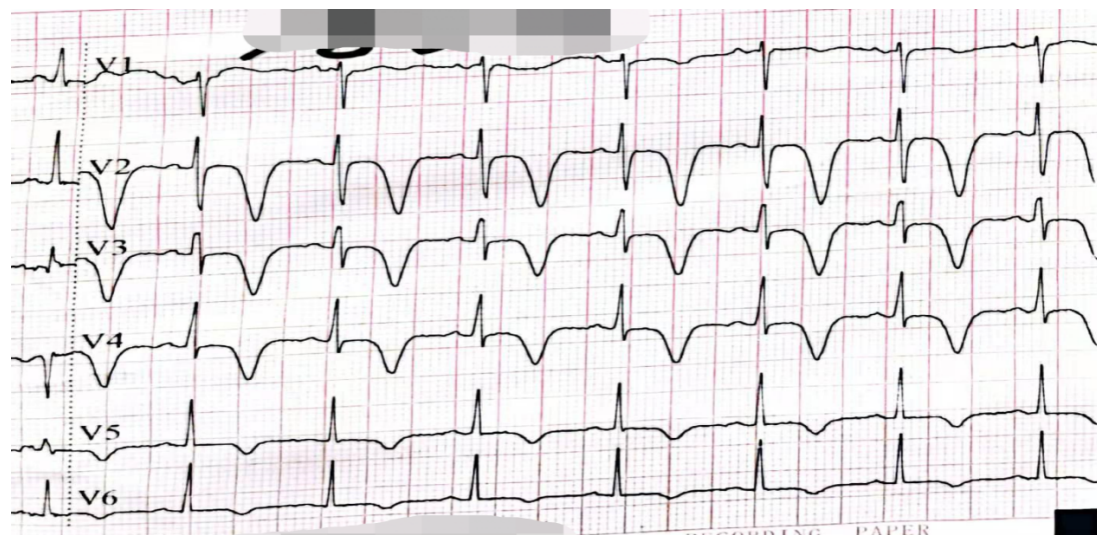
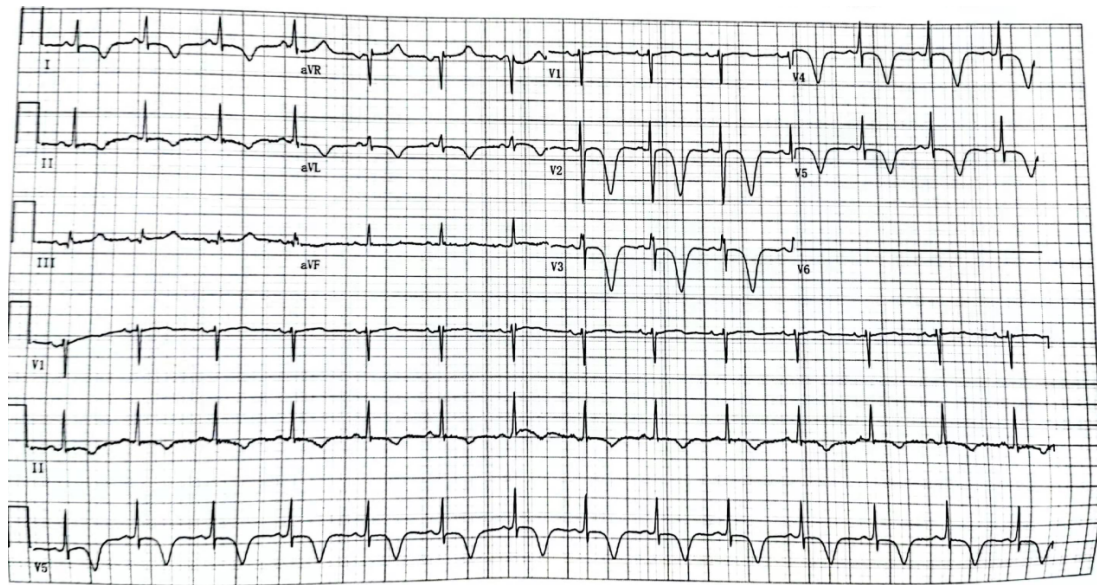
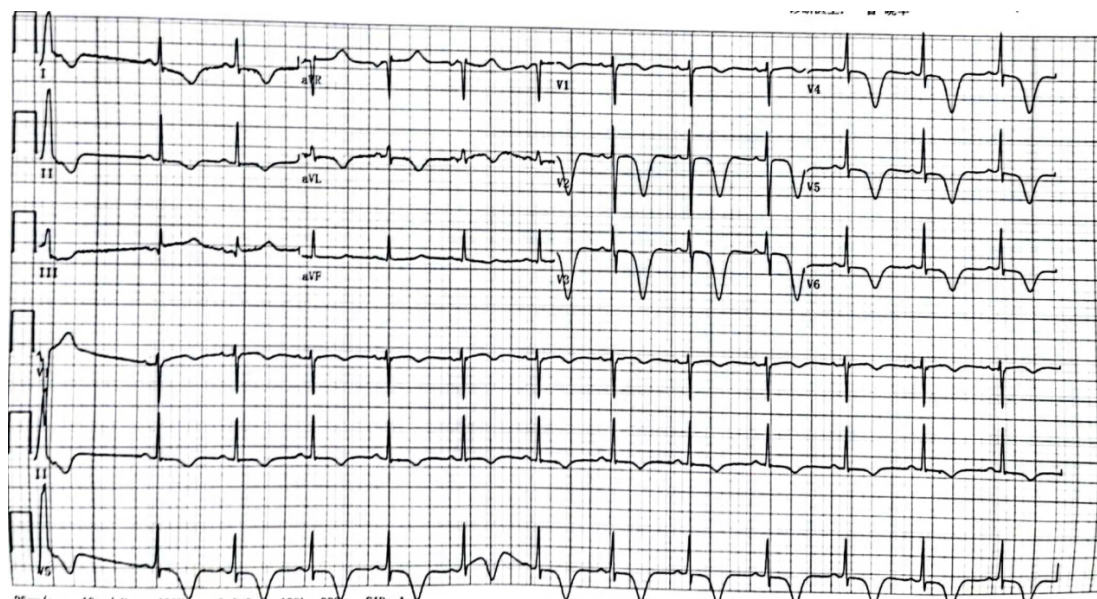


Figure 1b. ECG in emergency department March 10, 2021

Upon reexamination in the emergency department, three aspects of myocardium appeared normal, and electrolyte levels were within the normal range. Cardiac ultrasound revealed minor aortic valve regurgitation, mitral valve regurgitation, and a decrease in left ventricular diastolic function. The ejection fraction (EF) value in the cardiac ultrasound was measured at 61%. After admission, three myocardial tests were performed: creatine kinase-myocardial band (CK-MB), 3.0 ng/mL; high sensitivity troponin I (hsTnI), 8.40 pg/mL; Myo, 14.3 ng/mL. Myocardial enzymes were also within the normal range. Electrolyte levels were normal, with K at 3.9 mmol/L. Cardiac CTA showed no apparent abnormalities. Her electrocardiogram showed no significant changes from the time of admission. The two electrocardiograms after admission are shown in **Figure 2** and **Figure 3** (Corrected QT Interval [QTc] was 505 ms and 506 ms, respectively). 24-hour dynamic electrocardiogram: sinus rhythm, 1549 premature ventricular contractions, one premature ventricular contraction, 15 premature atrial contractions, and ST-T changes were visible.

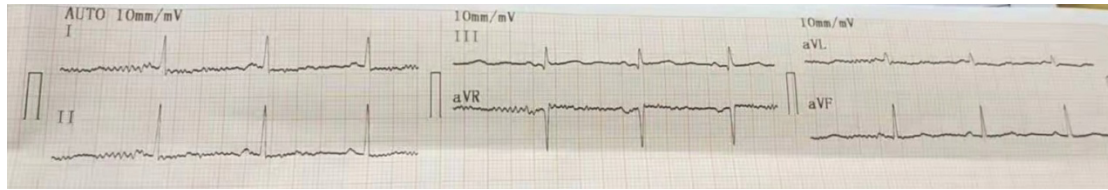


**Figure 2.** March 11, 2021, after admission

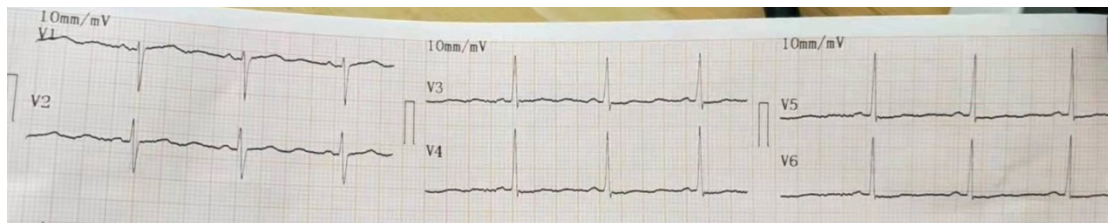


**Figure 3.** March 15, 2021, after admission

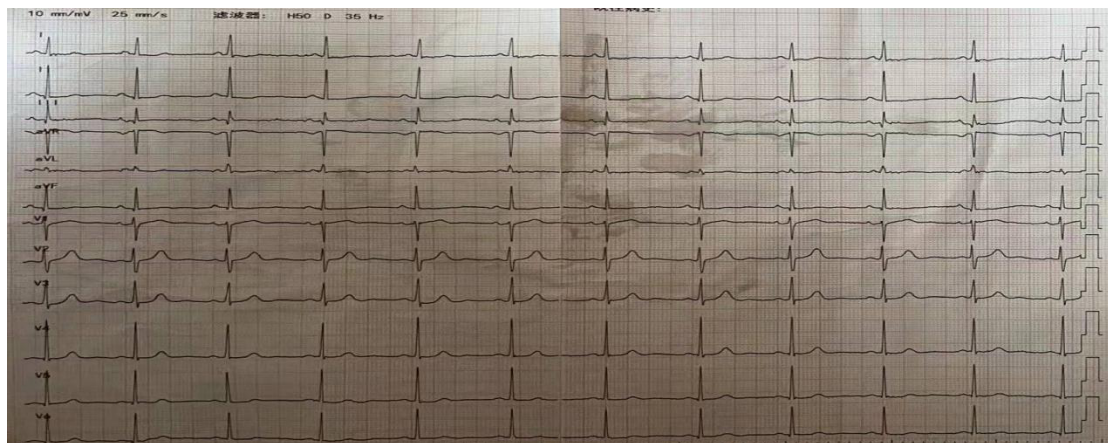
Based on the test results of this patient, and that she has no family history of QT interval prolongation, hereditary long QT syndrome was not considered. At the same time, electrolyte disorders, cardiomyopathy, and other cardiac organic diseases were also excluded. Research showed that selective serotonin reuptake inhibitors (SSRIs) cause QT interval prolongation in a dose-dependent manner. Therefore, considering the patient's recent history of antidepressant use, it is believed that the prolongation of the patient's QT interval is associated with the antidepressants. Therefore, the patient was recommended to consult a psychiatrist for medication adjustment. Subsequently, the antidepressant was switched to olanzapine. The follow-up electrocardiogram one month later (**Figures 4a and 4b**) displayed significant improvement. Subsequent electrocardiogram monitoring (**Figure 5**) indicated a return to normal QTc interval (375 ms).



**Figure 4a.** Follow-up in April 2021, 1 month after medication adjustment



**Figure 4b.** Follow-up in April 2021, 1 month after medication adjustment



**Figure 5.** Follow-up in December 2021 after half a year of medication dispensing

## 2. Discussion

Long QT syndrome (LQTS), also known as delayed repolarization syndrome, is characterized by prolongation of the QT interval on the electrocardiogram. It often manifests as palpitations and syncope and is prone to malignancy. It can lead to ventricular arrhythmias (torsades de pointes, ventricular fibrillation) or even sudden cardiac death <sup>[1]</sup>. LQTS can be divided into two types according to the cause: hereditary long QT syndrome (hLQTS) and acquired long QT syndrome (aLQTS).

hLQTS is mainly found in patients with family history or congenital predisposition. LQTS is primarily triggered by alterations in ion channels, typically resulting from loss-of-function mutations in potassium ion channels or gain-of-function mutations in sodium (calcium) ion channels. These changes lead to a reduction in the overall repolarization current <sup>[2]</sup>. Currently, the internationally accepted Schwartz scoring method is used for the diagnosis of hLQTS (**Table 1**), and a Schwartz score of  $\geq 3.5$  is diagnosed as LQTS <sup>[3]</sup>.

**Table 1.** Schwartz score for the diagnosis of long QT syndrome

Parameter	Score
Electrocardiogram <sup>a</sup>	
QTc <sup>b</sup>	
≥ 480ms	3
460–479 ms	2
450–459 ms (male)	1
QTc recovery ≥ 480 ms 4 min after exercise test	1
Torsade de pointes <sup>c</sup>	2
T wave alternation	1
T wave notch	1
Bradycardia <sup>d</sup>	0.5
Clinical manifestations	
Fainting <sup>e</sup>	2
With stress	1
Without stress	0.5
Congenital deafness	
Family history	
Family members with confirmed LQTS <sup>e</sup>	1
Family members with unexplained sudden cardiac death under the age of 30	0.5

Patients are diagnosed with LQTS if they score  $\geq 3.5$  points; LQTS is suspected with scores ranging from 1.5 to 3 points, and it's excluded if the patient scores  $\leq 1$  point. The scoring criteria include: a) excluding drugs or other diseases affecting electrocardiogram changes, b) calculating QTc using Bazett's formula ( $QTc = QT/\sqrt{RR}$ ), c) if torsade de pointes and syncope co-occur, only one score is selected, d) a resting heart rate lower than the 2nd percentile of the age group, and e) if the same family member exhibits two items simultaneously, only one is used for scoring.

Common causes of aLQTS include electrolyte disturbance (hypokalemia, hypomagnesemia), taking drugs that prolong the QT interval, and cardiomyopathy [4]. The patient, in this case, was a middle-aged female. Although her QTc was  $\geq 480$ ms, there was no abnormality in her previous ECG. She was previously healthy and had no family history of heart disease. Therefore, she was diagnosed with aLQTS. Common causes of acquired Long QT Syndrome (aLQTS), such as electrolyte imbalances and cardiomyopathy, were ruled out in this case. The patient had a history of taking antidepressants, and after adjusting the antidepressant medication, the QTc interval returned to normal. This indicates that the patient had asymptomatic acquired Long QT Syndrome triggered by the use of antidepressants.

QT interval prolongation is often related to antipsychotics, antidepressants, or anti-infectious drugs [5]. Prolonged QT interval can easily cause fatal torsade de pointes, and patients often have clinical manifestations such as palpitations, convulsions, and syncope [6], and severe cases are life-threatening. The QT interval and heart rate are closely related. The faster the heart rate, the shorter the QT interval, and the slower the heart rate, the longer the QT interval [7]. After correcting for the heart rate factor, it is expressed as QTc. It is usual for QTc

to be lower than 450 ms in women and lower than 430 ms in men. The longer the QT interval, the greater the possibility of torsade de pointes, and 500ms is usually used as the critical value. QTc prolongation requires vigilance for the occurrence of torsade de pointes<sup>[8]</sup>, but not all QTc prolongation leads to torsade de pointes and sudden death.

In cases of severe arrhythmia, such as torsade de pointes, it is essential to discontinue any medications that may prolong the QT interval. If potassium supplementation is not contraindicated, intravenous potassium chloride can be administered to shorten the QTc interval. Magnesium sulfate, diluted to 1 g of 25%, can be given via intravenous infusion at a rate of 2–8 mg/min. Additionally, intravenous lidocaine at a dosage of 1–3 mg/kg may be attempted. For patients with bradycardia, a small dose of isoproterenol (0.5-1mg) can be added to 500ml of 5% glucose for intravenous infusion. It is important to note that drugs like amiodarone, propafenone, verapamil, and quinidine should be avoided in the treatment of torsade de pointes. If drug therapy fails to terminate torsade de pointes, temporary cardiac pacing and low-energy (< 50 J) direct current shock cardioversion may be considered as options.<sup>[9]</sup>

In short, to reduce the incidence of QT interval prolongation in patients with antidepressants, it is necessary to fully understand the indications of the medication, and regular electrocardiogram reviews and follow-up are required to ensure patient safety. If there is a significant unexplained QT interval prolongation or sudden fainting, the medication should be promptly discontinued, and appropriate measures should be taken. Furthermore, electrolyte imbalances like hypokalemia and hypomagnesemia should be corrected without delay. Additionally, when prescribing antidepressants, antipsychotics, or other medications that may prolong the QT interval, caution should be exercised.

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## Disclosure statement

The authors declare no conflict of interest.

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