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CASE REPORT

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Prolonged ST segment and T-wave alternans with torsade de pointes secondary to hypocalcemia due to hypoparathyroidism: A case report

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Abstract

Hypoparathyroidism predisposes patients to hypocalcemia. Patients with hypoparathyroidism are thus at risk of electrocardiographic abnormalities, including T-wave alternans. T-wave alternans is poorly understood and lacks uniform diagnostic criteria. Its presence suggests myocardial electrical instability, and it has become an important sign for identifying patients at high risk of malignant arrhythmias and sudden cardiac death. We report a rare case of T-wave alternans with torsade de pointes due to hypocalcemia. The etiology of T-wave alternans may easily be overlooked. It should thus be thoroughly investigated to avoid misdiagnosis and poor outcomes.

KEYWORDS
hypocalcemia, hypoparathyroidism, torsade de pointes, T-wave alternans

1 | INTRODUCTION

Hypoparathyroidism (HP) is a rare syndrome caused by insufficient parathyroid hormone (PTH) secretion with or without impaired response. Clinical characteristics include hypocalcemia and hyperphosphatemia, with increased neuromuscular excitability and soft tissue calcification (Bilezikian et al., 2011). Unfortunately, epidemiological data on HP in China are not available (Powers et al., 2013).

T-wave alternans (TWA) refers to beat-to-beat variation in the shape, amplitude, or polarity of the T wave on an electrocardiogram (ECG) originating from the same pacemaker. It is not accompanied by changes in the QRS complex. It can be used to predict malignant arrhythmias and sudden cardiac death. In 1948, Kalter et al. (Kalter & Schwartz, 1948) reviewed 6059 ECGs and found a 0.08% incidence of TWA. They proposed a correlation between TWA and malignant arrhythmia and sudden cardiac death. Smith et al. (Smith et al., 1988) suggested that TWA has the same predictive value as invasive electrophysiology in assessing the risk of malignant arrhythmia and sudden cardiac death.

We report a case of prolonged ST segment and TWA with torsade de pointes secondary to hypocalcemia due to HP.

2 | CASE REPORT

A 56-year-old female was admitted to the ophthalmology department with a chief complaint of progressive blurred vision in both eyes for 3 years. There was no obvious cause for the blurred vision, and there was no eye pain, redness, photophobia, tearing, or difficulty opening the eyes. She reported no nausea, vomiting, dizziness, or headache, and she had no history of hypertension, diabetes, coronary heart disease, genetic diseases, or genetic predispositions to any diseases. She had undergone thyroidectomy for a thyroid neoplasm 11 years prior.

Jiang Liu and Hong Hou have contributed equally to this work.

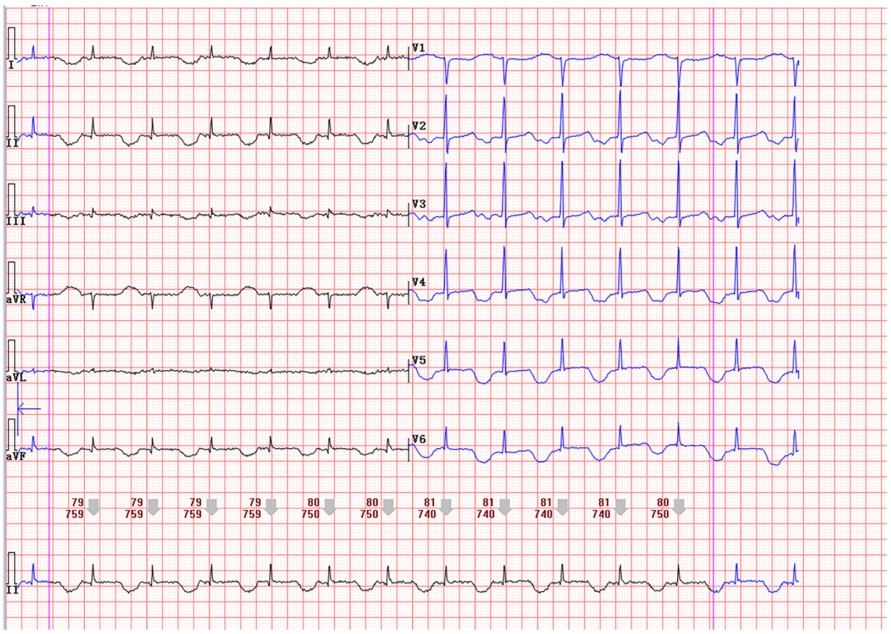

FIGURE 1 12-lead electrocardiogram showing prolonged ST segment and QT interval

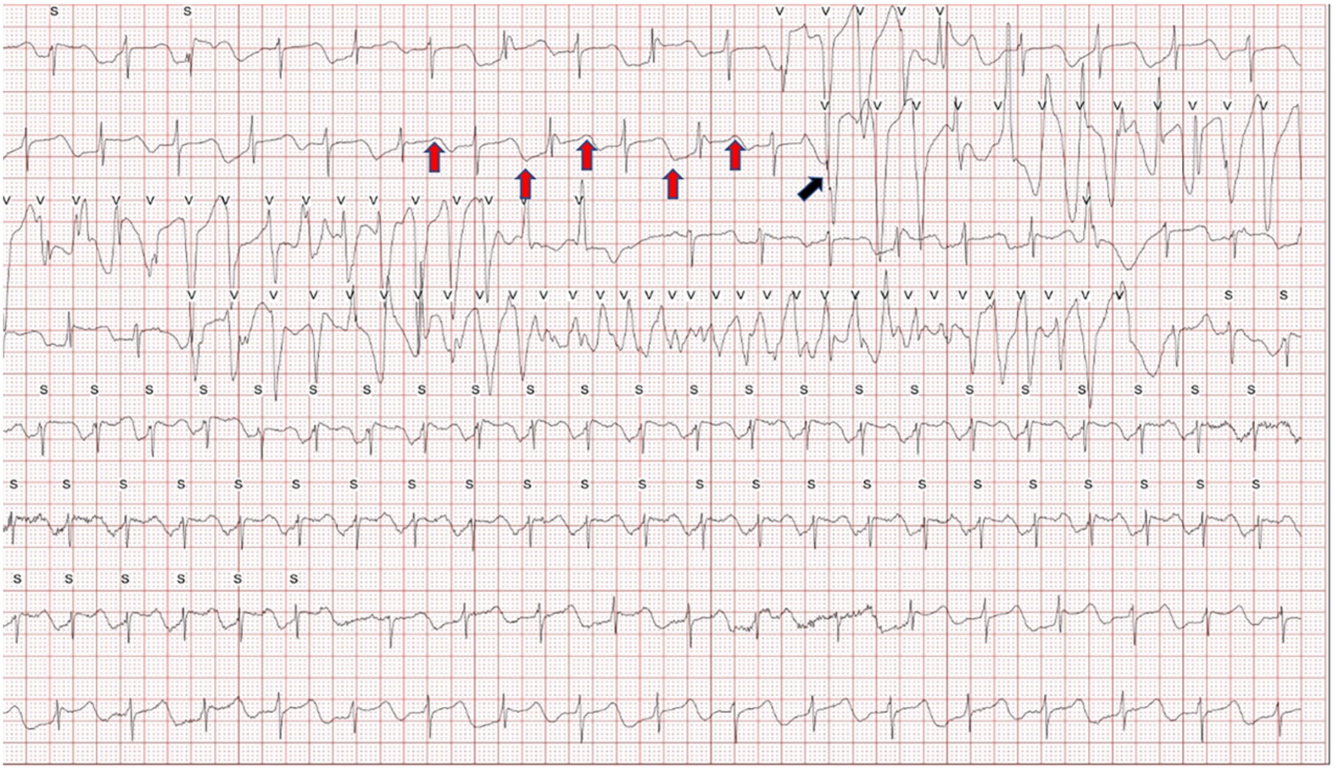

FIGURE 2 Continuous electrocardiographic monitoring at lead V2 indicates torsade de pointes with spontaneous conversion (black arrow) appearing after T-wave alternans (red arrows)

Physical examination indicated no abnormalities in the heart, lungs, or abdomen. Specialist examination revealed opacity of the lens and vitreous. ECG showed a prolonged ST segment (0.28 s) and QT interval (586 ms) (Figure 1), and electrolyte examination was recommended. The results were as follows: Ca^{2+}, 1.25 mmol/L (2.11–2.52 mmol/L); Mg^{2+}, 0.68 mmol/L (0.75–1.02 mmol/L); P^{3+}, 1.66 mmol/L (0.85–1.51 mmol/L); K^{+}, 3.8 mmol/L (3.5–5.5 mmol/L); no other electrolyte abnormalities were reported. Calcium supplementation was administered immediately, and the patient was transferred to the cardiology department. Coronary angiography showed no abnormalities, but Holter monitoring showed TWA with torsade de pointes (Figure 2). Considering the patient's history, thyroid function tests were ordered. The results showed a PTH level of 4.7 pg/ml, and after consultation with an endocrinologist, HP with associated hypocalcemia was diagnosed. Oral calcium (0.25 μg calcitriol capsules t.i.d., 600 μg calcium carbonate D3

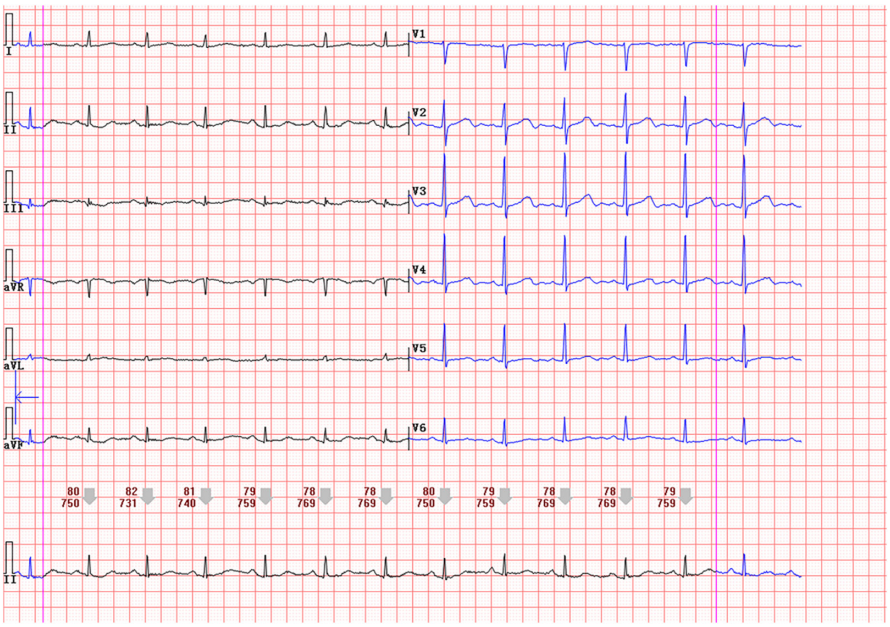

FIGURE 3 After 1 week of treatment, a 12-lead electrocardiogram shows that the ST segment has returned to normal, and the T-wave alternans has disappeared

tablets b.i.d.) was prescribed. Electrolyte examination after 1 week showed a Ca^{2+} level of 1.94 mmol/L. The ST segment returned to normal, and the TWA disappeared (Figure 3). The patient was instructed to take calcium supplements regularly and undergo regular electrolyte and ECG re-examination. Electrolyte examination after 1 month showed a Ca^{2+} level of 2.32 mmol/L and a PTH level of 56 pg/ml, and the prolonged ST segment and the TWA were not found on ECG.

3 | DISCUSSION

TWA refers to beat-to-beat variation in the shape, voltage, or polarity of the T wave on an ECG. Currently, no recognized diagnostic standard for TWA exists. A positive result is generally considered as a TWA amplitude of over 1.9 μV lasting at least 1 min when the heart rate in an exercise stress test is under 110 beats/min, and the alternans ratio is approximately 3%. In 2007, TWA physician guidelines indicated that the magnitude of TWA reflects continuous ECG instability and that larger TWA magnitudes are associated with higher risk; when TWA is ≥46 μV, the risk of sudden cardiac death in patients is significantly increased (Molon et al., 2007). TWA is associated with changes in the functions of calcium, potassium, and slow sodium channels, leading to increased dispersion of repolarization and increased susceptibility to tachycardia. Tachycardia, increased sympathetic tone, myocardial ischemia, heart failure, and electrolyte disturbances can lead to TWA, which can progress to torsade de pointes. This requires immediate treatment.

The two most recognized theories on the cellular electrophysiological mechanism of TWA are the action potential duration (APD) restitution theory and the calcium cycling theory. According to the APD restitution theory, the dynamic, unstable changes in TWA can cause changes in myocardial cell membrane voltage, which is associated with the diastolic interval between APD and the previous heartbeat. Under constant heart rate conditions, if a single heartbeat manifests as prolonged APD, it must be followed with a shorter diastolic interval. According to restitution theory calculations, the APD is also shortened afterward, extending the diastolic interval; this presents as a long-short-long APD cycle. When the APD restitution slope is greater than 1, cardiomyocyte repolarization occurs alternately, and the uncoordinated repolarization appears as TWA on ECG.

According to the calcium cycling theory, intracellular Ca^{2+} cycling is an important basis for the alternation of repolarization in cardiomyocytes. Shimizu et al. (Shimizu & Antzelevitch, 1999) showed that the maintenance of TWA depends on the intracellular Ca^{2+} concentration, which can inhibit TWA at lower concentrations. A dynamic equilibrium exists between Ca^{2+} released by ryanodine receptors on the endoplasmic reticulum and Ca^{2+} reuptake by SERCA2a under normal conditions. When this equilibrium in the myocardium is disrupted, such as when heart rate increases, the diastolic period is relatively shortened, Ca^{2+} cycling is affected, and this auto circulation cannot be completed fully and effectively. This affects the electrical activity of the myocardium and prevents coordination of the repolarization process, leading to possible TWA (Slawnych et al., 2009). Similarly, Navarro-Lopez et al. (Navarro-Lopez et al., 1978) proposed that TWA results from decreased Ca^{2+} levels, which may be related to the interference with calcium transport mechanisms in cardiomyocytes.

In this case, hypocalcemia was caused by HP. TWA disappeared after the hypocalcemia was corrected. Corrective changes in calcium transients can lead to action potential time course alternation, which is the basis for the development of TWA. In addition, increased Ca^{2+} in cardiomyocytes leads to increased late sodium current by activating calmodulin kinase-II pathways, which reduces the repolarization reserve of cardiomyocytes and increases the dispersion of repolarization, leading to the development of malignant arrhythmia. Therefore, the treatment of this patient included etiological

treatment, regular calcium supplementation, and regular electrolyte examination, ECG, and endocrinological follow-up.

T-wave alternans is relatively low, and it is difficult to identify with the naked eye in clinical practice. This makes it prone to misdiagnosis and missed diagnosis, presenting a major challenge for ECG technicians and clinicians. TWA is an important predictor of torsade de pointes; therefore, ECG technicians and clinicians must be able to identify its associated changes on ECG. The treatment of TWA includes immediate electrolyte supplementation (calcium, potassium, and magnesium), identification, and treatment of the root cause and correction of reversible underlying causes, regular electrolyte and ECG re-examinations, and the avoidance of drugs that prolong the QT interval.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Jiang Liu and Hong Hou: Conceptualization, Investigation, Writing – Original Draft Preparation, Writing – Review & Editing. Hui Xu and Yazhuo Chen: Conceptualization, Investigation. Xiaoling Su: Writing – Review & Editing.

ETHICAL APPROVAL

Written informed consent was obtained from the featured patient in this case report.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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