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CASE REPORT

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Momentary giant T-waves hint the genesis of the electrocardiographic T-wave in human

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Abstract

T-wave morphology changes are linked to dispersion of ventricular repolarization. I encountered an 80-year-old man on hemodialysis manifesting momentary giant T-waves and QT prolongation on the 12-lead electrocardiogram, soon after initiating mechanical ventilation because of hypercapnic respiratory failure. A computed tomography of the brain showed no acute cerebrovascular accidents. An echocardiogram showed no left ventricular asynergy. Mechanisms that may be responsible for this phenomenon are discussed. Interpreting the giant T-waves with the concept of the three bipolar limb lead vectors, the Einthoven's triangle leads to recognize origin of the electrocardiographic T-wave.

KEYWORDS

giant T-waves, hydroxyzine, QT prolongation

1 | INTRODUCTION

Dispersion of ventricular repolarization has been recognized underlying the origin of the T-wave. There is, however, controversy, what type of dispersion, specifically whether transmural or apico-basal gradients in repolarization times contributes the most to the T-wave in the intact heart.[1] I report a case of giant T-waves with QT prolongation which hint the genesis of the electrocardiographic T-wave.

2 | CASE REPORT

A 80-year-old man, on hemodialysis for 24 years, underwent emergent surgery for diffuse peritonitis because of sigmoid colon perforation. Postoperative 8th morning, his hemodialysis day, he became comatose. Arterial blood gas showed pH 7.194, PCO_2 7.8 kPa, PO_2 10.5 kPa, bicarbonate 22.2 mEq/L under oxygen 2 L/minutes administration. He was manually ventilated with a bag-valve device, and his consciousness improved. A computed tomography of the brain showed small old infarcts. Midazolam 5 mg and hydroxyzine 25 mg were intravenously administered, and he was endotracheally intubated to get on mechanical ventilation. Electrocardiogram (ECG) 4 minutes after premedication (Figure 1A) revealed ventricular rate at 77 beats/minute. The mean QRS axis was 37 degrees. The QRS duration was 103 ms. Giant T-waves were present in all leads except III and QT interval was markedly prolonged (QT/QTc interval 660/748 ms; QT interval manually measured and QTc interval calculated by the Bazett's formula). An echocardiogram showed no left ventricular asynergy with an ejection fraction 58%. The ECG 22 minutes after initial ECG (Figure 1B) showed normal sinus rhythm at 84 beats/minute and the PR interval was 199 ms. The giant T-waves resolved but the QT prolongation (QT/QTc interval 640/757 ms) persisted. Laboratory studies showed leukocytes count 11.16×10^9/L, hematocrit 25.8%, aspartate aminotransferase 0.35 μkat/L, alanine aminotransferase 0.10 μkat/L, lactate dehydrogenase 3.00 μkat/L, creatine kinase 1.07 μkat/L, urea nitrogen 30.3 mmol/L, creatinine 585 μmol/L, sodium 134 mEq/L, potassium 6.0 mmol/L, chloride 101 mmol/L, calcium 1.9 mmol/L, magnesium 0.95 mmol/L, albumin 20 g/L. The QT/QTc interval decreased to 480/547 ms in the next morning and normalized to 360/431 ms 7 day after the initial presentation. He had no torsades de pointes (TdP).

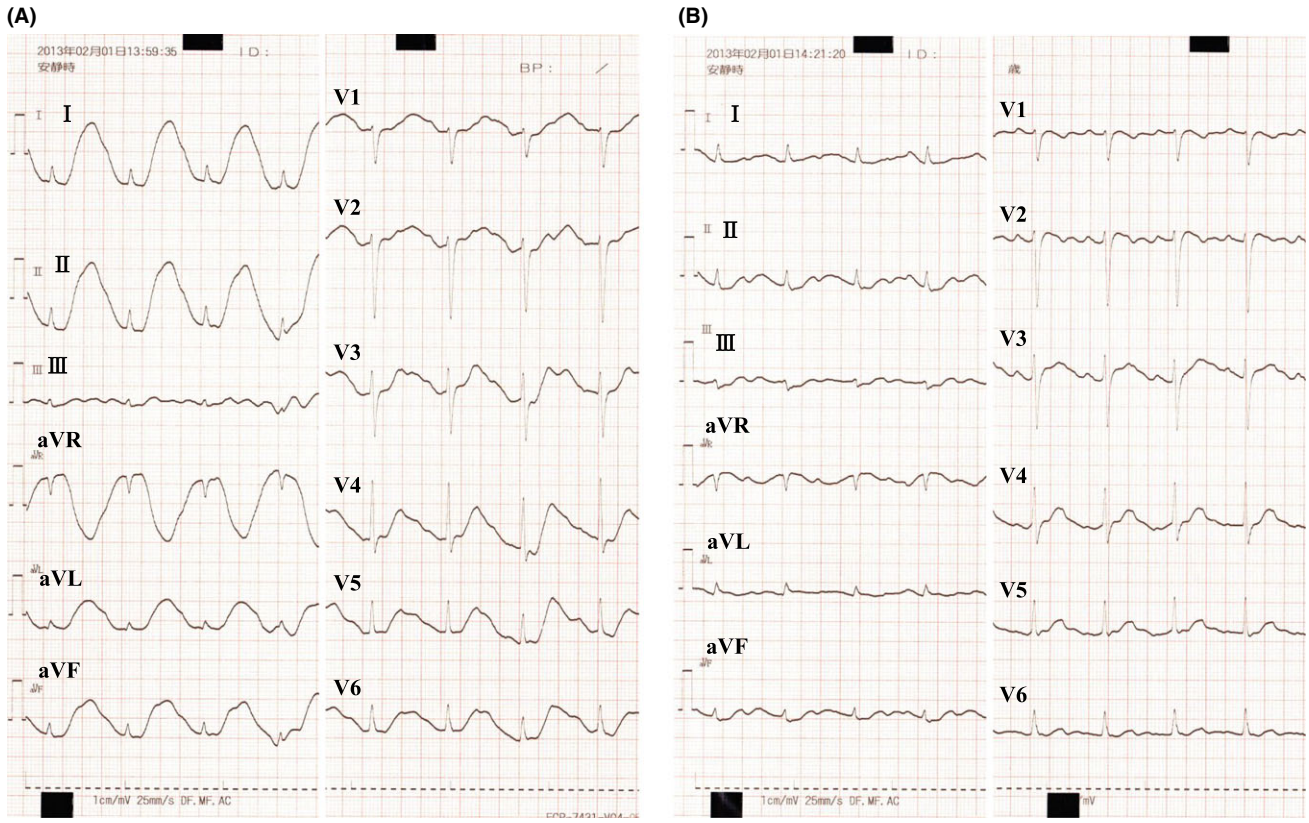

FIGURE 1 Serial electrocardiogram (ECG) of the patient 4 minutes after premedication (A) and 22 minutes after initial ECG (B)

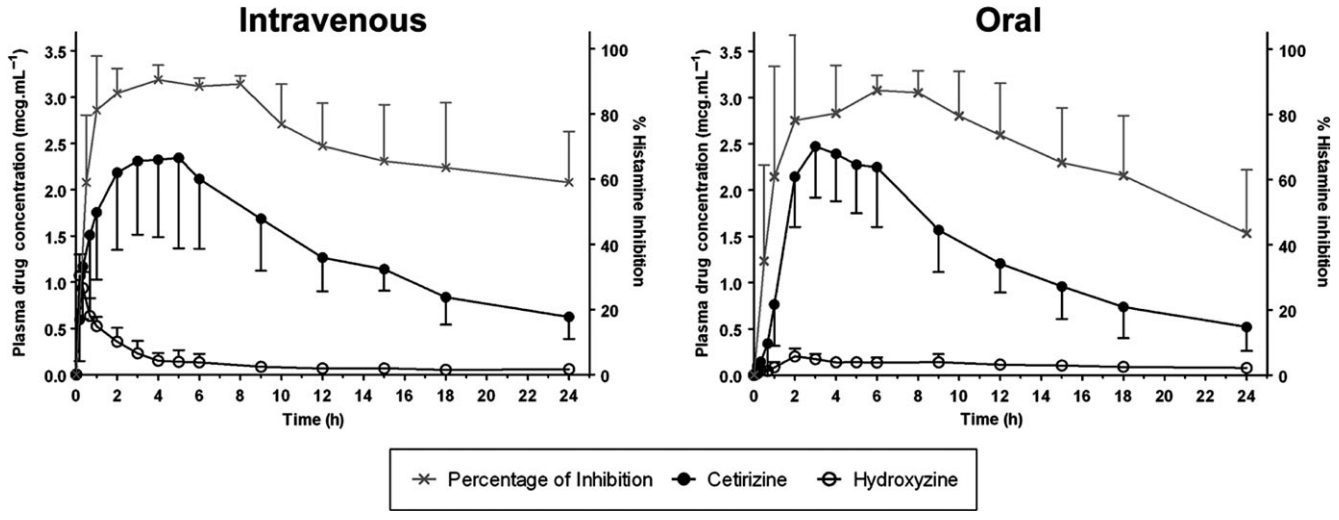

FIGURE 2 Plasma hydroxyzine and cetirizine concentrations after intravenous and oral administration of 2 mg/kg hydroxyzine to six healthy dogs. Partly modified from Bizikova P, et al[4] with permission

3 | DISCUSSION

Large upright peaked T-waves and QT prolongation have been described in association with intracranial diseases or Takotsubo syndrome.[2] He had no evidence of acute cerebrovascular accidents nor Takotsubo syndrome. Hyperkalemia was notable, but corrected calcium for hypoalbuminemia 2.3 mmol/L and magnesium level were within normal limits. In suspecting drugs induced-ventricular repolarization changes, hydroxyzine was identified as the only drug able to induce QT prolongation. Hydroxyzine is a first-generation antihistamine, antagonist of central and peripheral H_1 receptors with anticholinergic properties. Marketed in Japan as the hydroxyzine

hydrochloride 25 mg/mL and 50 mg/mL, it has been approved in the management of anxiety, tension and depression in neurosis, in premedication prior to anesthesia, and in preventing perioperative nausea and vomiting. A 34-year-old female was reported to experience syncope after taking oral hydroxyzine 75 mg/day with a marked QT prolongation.[3] She was found to harbor the A614V-human ether-a-go-go-related gene (HERG) mutant and hydroxyzine concentration-dependently inhibited both wild-type (WT) (a concentration producing one-half the maximal response, IC_{50} 0.62 μmol/L) and WT/A614V (IC_{50} 0.52 μmol/L)-HERG K^+ currents.[3] As there was no ECG showing QT prolongation before this event, hydroxyzine may create abnormal repolarization properties from scratch.

Pharmacokinetics of hydroxyzine 2 mg/kg dose in healthy dogs[4] showed that the plasma concentration of hydroxyzine after intravenous administration peaked at 1.09 μg/mL and declined promptly (Figure 2), whereas the corresponding after oral administration did not rise as large as the intravenous administration and peaked at 0.16 μg/mL. Hydroxyzine was rapidly converted to its active metabolite cetirizine with the maximum concentration of approximately 2.2 μg/mL regardless of the route administration. The intravenous concentration curve was obtained after hydroxyzine 2 mg/kg dose infused over a period of 5 minutes to the six dogs weighted between 9.9 and 29.9 kg[4] namely infusion rate was from 4.0 to 12.0 mg/minute. By drug information, hydroxyzine should not be infused intravenously over 25 mg/minute, but I suspect that the hydroxyzine 25 mg was bolus injected as premedication.

Among the bipolar limb leads, the lead III did not record the giant T-wave (Figure 1A). The lead III, whose axis is 120 degrees on the Einthoven's triangle would record approximately perpendicular gradient of apico-basal repolarization potential of his heart because his mean QRS axis was 37 degrees. Amplitudes of T-wave in the precordial leads, whose vectors point from the Wilson's central terminal to the precordial electrode sites on the horizontal plane were not more remarkable than those in the bipolar limb leads. In rabbit left ventricle, the rapidly activating component of the delayed rectifier K^+ current (I_{Kr}) is greater in the apex than the basal regions and I_{Kr} blockers cause more significant action potential duration prolongation in the apex than in the base.[5] Rapidly peaked concentration of the hydroxyzine, which inhibits the HERG K^+ current resembling I_{Kr}[3] could contribute to generation of the giant T-waves by amplifying the apico-basal dispersion of ventricular repolarization. Too high an infusion rate of a QT-prolonging drug may be an additional risk factor for occurrence of TdP in susceptible patients.

CONFLICT OF INTERESTS

Author declares no conflict of interests for this article.

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