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Vonoprazan-associated long QT syndrome

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Being treated at a cardiology clinic for hypertension, hyperlipidemia, and pruritus dermatitis, a 67-year-old man had been taking lisinopril (10 mg), pravastatin (10 mg), and levocetirizine (5 mg) once daily. He was raced to a nearby hospital for abdominal pain, diagnosed with gastric ulcer, and started taking vonoprazan (20 mg) once daily. A follow-up electrocardiogram (ECG) performed 4 months later showed QT prolongation (Figure 1A), which had not been observed before initiation of the drug (Figure 1B). With no evidence of electrolyte abnormalities, he was switched from vonoprazan to famotidine because of suspected drug-induced long QT syndrome. ECG performed 1 week later showed improvement in QT interval (Figure 1C).

Vonoprazan is a potassium-competitive acid blocker (P-CAB) recently developed and approved for use in Japan, and inhibits the H^+/K^+-ATPase-mediated gastric acid secretion in a reversible and potassium-competitive manner.[1]

The human ether-a-go-go–related gene (hERG) potassium channel plays a key role in regulating cardiac excitability and maintaining normal cardiac rhythm. Inhibition of the potassium channels encoded by hERG is considered to be the main mechanism of acquired long QT syndrome.[2] Vonoprazan has been shown to have effects on the hERG channel current at the doses studied with an IC_{50} value of 4.8 μg/ml. In a phase I randomized trial of vonoprazan, its cardiac safety has been confirmed in healthy subjects without affecting QT/QTc interval.[3]

Since vonoprazan is metabolized mainly by CYP3A4, pharmacokinetic changes can occur with the combined use of CYP3A4

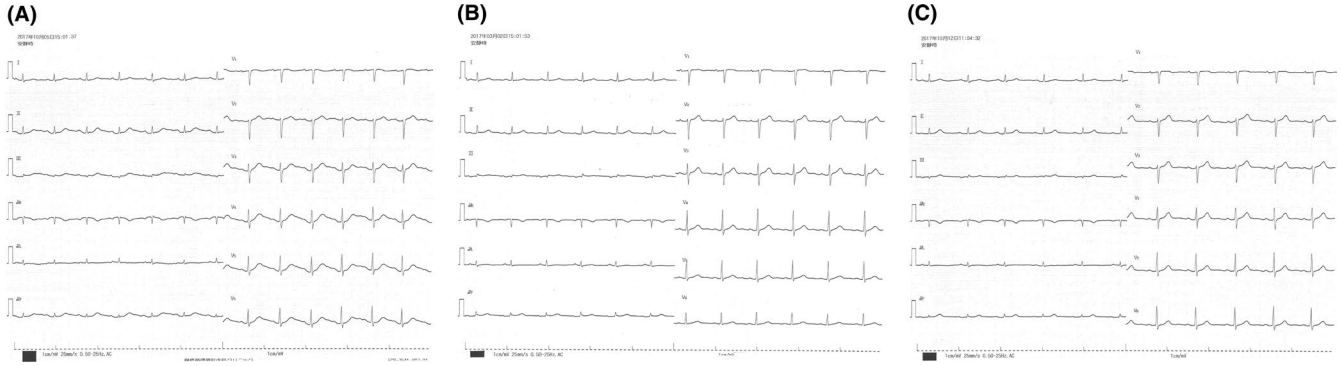

FIGURE 1 Electrocardiogram (ECG). ECG showed QT prolongation (A), which had not been observed at the initiation of vonoprazan 4 months before (B). ECG performed 1 week after switching from vonoprazan to famotidine showed improvement in QT interval (C)

inhibitors or drugs metabolized by CYP3A4.[4] Furthermore, of the medications this patient had been receiving, levocetirizine has been reported to be metabolized by CYP3A4.[5]

These led us to speculate that the increase in plasma concentration of vonoprazan associated with the concurrent use of levocetirizine suppressed the hERG channel resulting in QT prolongation.

To our knowledge, this is the first report describing a case of vonoprazan-associated QT prolongation newly occurring after initiation of the drug and improving after its discontinuation in a patient concurrently receiving a drug metabolized by CYP3A4.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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