Letter to the Editor

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Suspected bradycardia due to interactions between HIV protease inhibitors and lidocaine: a case report

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Dear Editor,

We encountered a case of bradycardia that developed after the administration of lidocaine during general anesthesia in an HIV-positive patient on highly active antiretroviral therapy.

A 54-year-old, HIV-positive man (height 174 cm, weight 67 kg) was scheduled to undergo surgical resection indicated for tongue cancer. He tested positive for HIV at 41 years of age. Two years later, drug therapy with tenofovir and efavirenz was initiated. He complained of chest pain eight years after being diagnosed with HIV infection. Holter electrocardiography (ECG) revealed coupled, bigeminal and trigeminal ventricular premature contractions (PVCs). Echocardiography revealed a slight decrease in myocardial contraction (ejection fraction, 51%). Although some interventions were considered, no additional treatments were administered as the myocardial symptoms improved.

During preoperative examination, his habitual drugs were the nucleic acid reverse transcriptase inhibitor tenofovir and the protease inhibitors (PIs) darunavir and ritonavir. No abnormalities, including blood pressure, blood tests, urinalysis, chest X-ray, and spirometry were noted, except for the ECG findings. His heart rate was 83 bpm, and frequent PVCs were observed on a 12-lead electrocardiogram (ECG) (Fig. A).

General anesthesia was induced with propofol (130 mg), remifentanil (0.5 μg/kg/min), and desflurane (7%) in air and oxygen. At the beginning of the induction, ECG revealed ventricular quadrigeminy. A mixture of trigeminy was gradually observed, and the frequency of extraventricular beats increased further (Figure B). Thus, we administered 70 mg of lidocaine for the treatment of PVCs. After these drugs were administered, the PVCs ceased; however, the heart rate began to decrease (Figure C).

Rocuronium (50 mg) was administered to facilitate nasal tracheal intubation. No events occurred during intubation. After 3 min of intubation, the heart rate decreased to 39 bpm. We administered atropine (0.5 mg), and the heart rate increased to 52 bpm, a smaller increase than we expected. The total duration of anesthesia was

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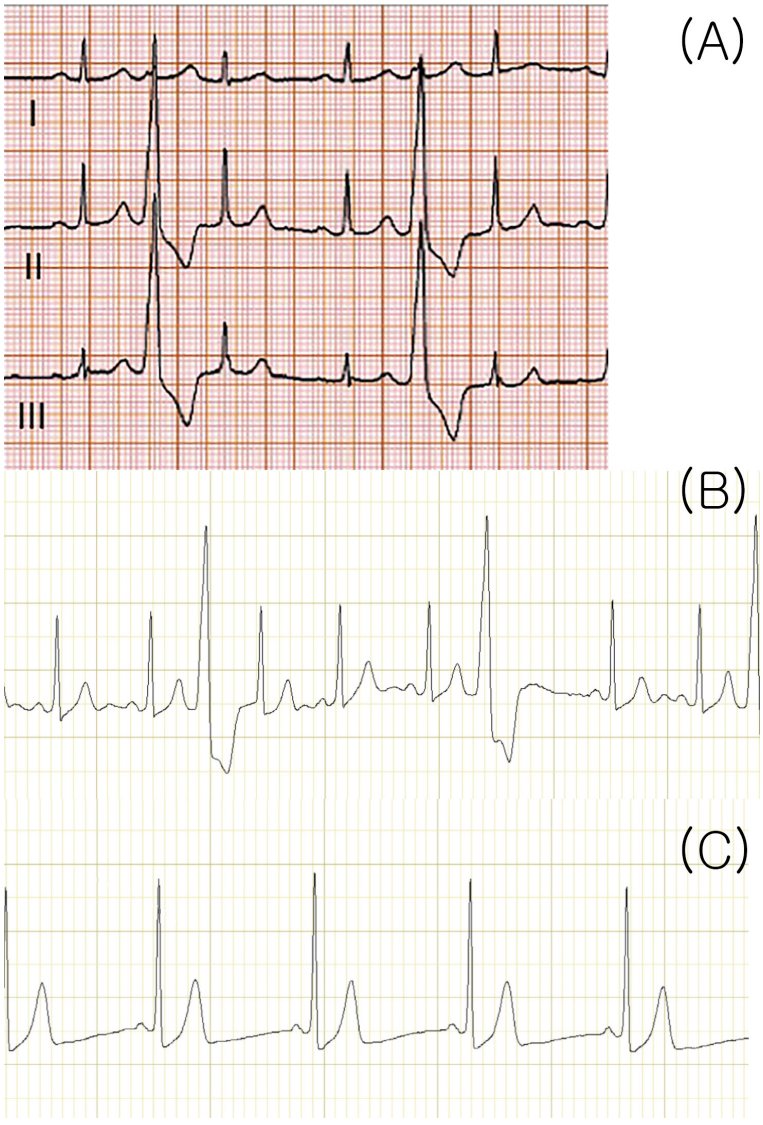

Fig. 1. (A) 12-lead electrocardiography (ECG) findings at the preoperative examination (heart rate [HR]: 83 bpm, 25 mm/sec). (B) ECG findings before the administration of lidocaine (HR: 78 bpm, 10 mm/sec). (C) ECG findings after the administration of lidocaine; the RR range increased, and the heart rate markedly decreased (HR: 43 bpm, 10 mm/sec).

126 min, and anesthesia was completed uneventfully, except for bradycardia during induction. The intraoperative heart rate fluctuated between 55 bpm and 60 bpm, and remarkable bradycardia did not recur.

In our patient, bradycardia occurred after the administration of lidocaine during the induction of general anesthesia. Lidocaine inhibits the activation of sodium channels and suppresses the generation of action potentials, which can lead to conduction disturbances such as bradycardia and sinus arrest [1]. PIs inhibit CYP3A4, an enzyme that participates in the metabolism of lidocaine. As a result, the action of lidocaine may have been enhanced in this case [2]. Another possible mechanism is that PIs may cause cardiac conduction inhibition [3]. However, our patient stopped taking PIs on the eve of the surgical intervention. Therefore, bradycardia in our patient was likely not caused by the direct effect of PIs.

The plasma concentration of lidocaine may increase in patients with liver dysfunction. Given that the liver function of our patient was normal, it is unlikely that the enhanced action of lidocaine occurred due to decreased

liver function.

Remifentanil, which can also cause bradycardia, was administered in the present case. When the heart rate decreased, intubation was performed. Therefore, intubation might have influenced the decrease in heart rate. The administration of lidocaine should be carefully performed in situations where bradycardia can easily occur as intractable bradycardia may develop.

HIV-positive patients are at a high risk of ventricular arrhythmias, and PIs also contribute to PVCs [4,5]. In HIV-positive patients using PIs, arrhythmia is not rare. When lidocaine is administered to treat PVCs under general anesthesia for HIV patients, attention should be paid to the interactions between PIs and lidocaine, as well as drugs and treatments that have vagotonic effects, to prevent the occurrence of severe bradycardia. Thus, in such patients, lidocaine may need to be administered in divided or reduced doses.

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