CASE REPORT

Sino-Atrial Block During Anesthesia in a Patient with Breast Cancer Being Treated with the Anticancer Drug Epirubicin

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Epirubicin, a member of the anthracycline family, is a highly effective anticancer drug that is used to treat hematological malignancies and various solid tumors. Although epirubicin causes dose-dependent, irreversible cardiotoxicity leading to congestive heart failure, cardiac dilation, and structural evidence of myocardial cellular degeneration (1), these complications are rarer than with doxorubicin. Therefore, epirubicin is widely used. Here we present a case in which sino-atrial (S-A) block developed unexpectedly during general anesthesia in a patient who had been treated with epirubicin but had no cardiovascular symptoms before surgery.

Case Reports
A 55-yr-old woman was admitted for advanced breast cancer and was scheduled to undergo mastectomy under general anesthesia. She received 2 courses of chemotherapy (cyclophosphamide 750 mg · m$^{-2}$.d$^{-1}$, epirubicin 90 mg · m$^{-2}$.d$^{-1}$, and 5-fluorouracil 750 mg · m$^{-2}$.d$^{-1}$) for 52 and 29 days before the surgery. The total doses of the drugs were as follows: cyclophosphamide 1500 mg, epirubicin 180 mg, and 5-fluorouracil 1500 mg. She had not complained of any cardiovascular symptoms. Her preoperative electrocardiogram (ECG) and ultrasonic cardiograph were normal. In the operating room, her heart rate (HR) was regular (80 bpm), with sinus rhythm (Fig. 1A). The usual monitors were used. General anesthesia was then induced with propofol 80 mg, vecuronium bromide 7 mg, and fentanyl 100 μg. After tracheal intubation, her ECG revealed S-A block (Fig. 1B). The bradycardia did not improve with IV injection of atropine 1 mg (Fig. 1C). We suspected sick sinus syndrome and decided to postpone her operation.

After surgery, Holter ECG monitoring was performed for 24 h. Sinus arrests (>3 s) were detected 23 times, and ventricular escape was seen 10 times. The maximum interval of arrest was 4.3 s. The mean, minimum, and maximum HR were 59, 41, and 94 bpm, respectively. Cardiac catheterization was performed. The coronary arteriogram was normal. On the basis of these results, a permanent pacemaker was implanted. The mastectomy was performed subsequently, and the patient was discharged without any symptoms.

Discussion
Epirubicin has an antineoplastic efficacy comparable to that of doxorubicin, but it has smaller cardiotoxicity at identical cumulative doses. Although the precise mechanism of epirubicin-induced cardiotoxicity remains unclear, several hypotheses have been proposed. The most popular include free-radical formation by anthracyclines (2), impaired myocardial calcium homeostasis via alteration of the function of the cardiac sarcoplasmic reticulum (3), and the formation of C-13 hydroxy anthracycline metabolites (4).

Our patient had no history of heart disease, and her preoperative ECG and ultrasonic cardiograph were normal. Furthermore, after surgery, her cardiac catheterization showed no stenosis or spasm of the coronary arteries, suggesting that her S-A block resulted from epirubicin cardiotoxicity.

There are no reports that epirubicin causes S-A block. However, there are several reports of ECG abnormalities observed in doxorubicin-treated patients. Epirubicin is similar to doxorubicin both structurally and in its mode of action (5). There are reports of tachycardia, atrial and ventricular premature beats, ST-T changes (6), and transient prolongation of SaT and QaT in a rat model (7) with epirubicin. Therefore, epirubicin can induce S-A block during anesthesia, as in this case.

In summary, we report a case of S-A block during general anesthesia in a woman with breast cancer who had received epirubicin. Epirubicin is associated with increased cardiotoxicity. Anesthesiologists should be aware of the possible occurrence of S-A block with epirubicin, and, occasionally, planting a pacemaker might be considered even in asymptomatic patients.
References


Figure 1. Electrocardiography (ECG) recorded during anesthesia. A, ECG recorded before anesthesia. B, After tracheal intubation, her ECG revealed sino-atrial block. C, The bradycardia did not improve with the IV injection of atropine 1 mg.