ADRIAMYCIN INDUCED PULSELESS ELECTRICAL ACTIVITY AND CARDIOVASCULAR COLLAPSE DURING GENERAL ANESTHESIA FOR VENTRICULO-PERITONEAL SHUNT INSERTION

- A Case Report -

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Abstract

We report a case of a 45-year-old female undergoing an emergency ventriculoperitoneal shunt surgery. The patient had brain metastatic lesions of breast carcinoma with associated hydrocephalus. She had received Adriamycin as a part of chemotherapy regimen for breast cancer. Her preoperative cardiovascular status was normal. Under general anesthesia, the patient had a sudden cardiovascular collapse. The patient had a pulseless electrical activity and required inotropic support for cardiovascular stability. The possible cause is discussed.

Keywords: Adriamycin; cardiac toxicity; neurosurgery; general anesthesia; pulseless electrical activity.

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Introduction

Anthracyclines, a class of broad spectrum antineoplastic drugs were introduced in 1960. Their side effect profile includes myelosuppresion, nausea and vomiting, and more notably cardiac toxicity. Cardiac toxicity expresses itself in both acute and chronic forms. The cardiotoxic manifestation of anthracyclines includes various forms of tachyarrhythmias, AV block, bundle branch block in acute form to chronic congestive failure as chronic manifestation[1,2]. A case is presented of a patient who having received Adriamycin for carcinoma breast, had cardiovascular collapse and pulseless electrical activity while undergoing ventriculoperitoneal shunt under general anesthesia.

Case Report

A 45-year-old female, 62 kg and height 164 cm was admitted in neurosurgical ward with complaints of nausea and vomiting since 25 days and altered sensorium for 3-4 days. She was a known case of carcinoma breast with multiple metastases.

All routine investigations were within normal limits and contrast enhanced computed tomography (CECT) of head showed periventricular ooze with extraventricular obstructive hydrocephalus.

In her past history, patient had received two cycles of chemotherapy with CAF regimen (cyclophosphamide, Adriamycin and 5-fluorouracil) in dose of cyclophosphamide and Adriamycin each 750 mg per cycle. Each cycle, separated by 3 weeks interval, and last cycle was given one month back. Echocardiography (ECHO) and multi-gated radionuclide (MUGA) scan 1 week after the second cycle showed normal left ventricular function with no regional wall motion abnormality and left ventricular ejection fraction of 62% at rest. Her medical history was remarkable for hypertension since four months for which she took irregular treatment.

An emergency ventriculoperitoneal shunt was planned. On arrival to operation theatre, her Glasgow Coma Scale was 11/15 with a motor

response of 5. Routine monitoring of pulse oximeter, electrocardiograph and non-invasive blood pressure were instituted.

General anesthesia was induced after 3 minutes of pre-oxygenation with fentanyl 120 mcg and sodium thiopentone 250 mg. Rocuronium 60 mg was given for tracheal intubation. Anesthesia was maintained with isoflurane in O_2 and N_2O (2:1). The monitor showed persistently high blood pressure, which did not respond to increasing concentration of isoflurane and bolus of fentanyl. Hence nitroglycerine (NTG) infusion was started at 1 mcg kg^{-1} min^{-1}. A 20 G cannula was placed in the right dorsalis pedis artery for continuous monitoring of arterial pressure. Within 2 minutes of starting NTG infusion, patient had hypotension and bradycardia with mean arterial pressure of 35 mmHg and heart rate of 58 beats per minute. The ECG at this point showed sinus rhythm with ST depression and T wave inversion. NTG infusion was immediately stopped. The peripheral pulses including carotid were not palpable. External cardiac compressions were started and a bolus of adrenaline 1 mg was given. With these measures the arterial pressure and heart rate increased. Peripheral pulses became palpable. As the blood pressure was not sustained, dopamine infusion was started at a rate of 7-10 mcg kg^{-1} min^{-1}. ECG changes reverted to normal gradually. The surgery was allowed to start. The patient had an uneventful anesthetic and surgical course of one hour. During the entire surgery patient received about 1.5 litres of crystalloid and produced 300 ml of urine.

After surgery, a double lumen central venous catheter was placed in the right internal jugular vein, for the purpose of monitoring and administering inotropic drugs. The central venous pressure measured 10 cm H_2O. Anesthesia was discontinued and neuromuscular blockade reversed. The patient did not respond to verbal commands or to painful stimuli and hence extubation was deferred. Patient was shifted to neurosurgical intensive care unit where she was weaned off dopamine over a period of 3 hours. Thereafter, she remained hemodynamically stable. Arterial blood gas analysis and serum electrolytes remained within normal limits in the ICU. Her neurological status, however, deteriorated in the days to follow. Repeat CT scan of head showed no new changes when

compared to preoperative scan. The patient finally succumbed to septicemia on 7th postoperative day.

Discussion

Although the precise mechanism of cardiotoxicity of anthracyclines is unknown, many theories have been implicated. The popular ones include free-radical formation by anthracyclines, impaired myocardial calcium homeostasis via alteration of the function of the cardiac sarcoplasmic reticulum and the formation of C-13 hydroxy anthracycline metabolites[3]. The risk factors associated with Adriamycin induced toxicity are increased age, previous heart disease of hypertension, concomitant radiation therapy, concomitant cyclophosphamide chemotherapy and female gender. Though co-administration of cyclophosphamide is found to increase the toxicity of Adriamycin[4], in many circumstances this becomes unavoidable especially in carcinoma breast patient where the efficacy of CAF regimen is well established[5]. The risk factors of hypertension, concomitant cyclophosphamide therapy and female gender were present in our patient. All of these could have aggravated the toxicity.

Matsuo and colleagues[4] reported a patient who had received doxorubicin for her carcinoma breast and developed bigeminy and trigeminy intraoperatively and post operatively. However, their patient remained hemodynamically stable in contrast to our patient who had cardiovascular collapse. In another case described by Takashi and colleagues[3], the patient had an intraoperative sino-atrial block. Their patient had received epirubicin for breast carcinoma.

The incidence of cardiomyopathy following doxorubicin is found to increase abruptly when the total cumulative dose exceeds 550 mg sqm^{-1} [6]. Our patient had received only two cycles of chemotherapy and the cumulative dose was far less than the toxic cumulative dose. Similarly, both, the patients in the cases described by Matsuo and colleagues and Takashi and colleagues. did not receive the toxic cumulative dose. This shows that though chronic form of cardiomyopathy can be correlated to

cumulative toxic dose, the acute cardiac toxicity may not be relevant to the total cumulative dose. ECHO and MUGA are most commonly employed to detect any early left ventricular dysfunction. Of these modalities ECHO is found to be less sensitive[7] whereas MUGA scan is found to be relatively more sensitive. Our patient had normal left ventricular ejection fraction (62%) at rest in MUGA scan. Similarly the patient described by Matsuo and colleagues also had normal TEE and ECG findings though they did not mention about the MUGA scan report. Hence cardiotoxic manifestations can occur especially under anesthesia even in the presence of normal scan findings in patients who have received Adriamycin.

In summary we present a case of cardiovascular collapse with pulseless electrical activity in patient who had received Adriamycin. The risk of cardiotoxicity may be expected in patients undergoing any procedure under general anesthesia even if the cumulative toxic dose is not reached. There are no reports of Adriamycin causing pulseless electrical activity and anesthetists must be aware of the possibility of this complication. Our case emphasizes the vigilant role played by the anesthestist and his knowledge of the cardiotoxic nature of Adriamycin required.

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