



Case Report

Anaphylactic shock due to intravesical administration of pirarubicin hydrochloride for the fifth time[☆]



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Abstract We report the first case of anaphylaxis induced by intravesical administration of pirarubicin hydrochloride during spinal anesthesia. The patient was a 64-year-old woman being followed up for transitional cell carcinoma of the bladder. Anaphylaxis occurred the fifth time pirarubicin hydrochloride was administered intravesically. Pirarubicin hydrochloride, an anthracycline antitumor antibiotic that is widely used for intravesical instillation chemotherapy, is administered at the end of surgery. Because this is about the time that the patient is leaving the operating room, attention to patient monitoring tends to be divided. Because anaphylaxis may occur at this time, staff should remain vigilant of the risk of anaphylaxis.

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1. Introduction

The incidence of anaphylaxis during anesthesia is estimated at 1 in 10,000 to 20,000 procedures, and it has been reported that neuromuscular blocking agents are the most common causes of anaphylaxis [1]. Cardiopulmonary collapse during regional anesthesia is thought to be an infrequent event with several reported causes, including high spinal anesthesia, hypovolemia,

acute myocardial infarction, pulmonary thromboembolism, and anaphylactic shock [2]. Therefore, anaphylaxis during regional anesthesia is considered an extremely rare event [3]. Pirarubicin hydrochloride is an anthracycline antitumor antibiotic that is widely used for intravesical instillation chemotherapy [4]. We report a case of anaphylaxis that may have been caused by pirarubicin hydrochloride. There have not been any previous reports of anaphylaxis induced by pirarubicin hydrochloride administered intravesically.

2. Case report

A 64-year-old woman being followed up for transitional cell carcinoma of the bladder was scheduled to undergo

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transurethral resection of a bladder tumor (TURBT). She had already experienced TURBT 4 times under spinal anesthesia, and intravesical administration of pirarubicin hydrochloride (30 mg) had been performed at the end of each TURBT. The patient's anesthetic records indicated no problems during the previous procedures. She had also been treated for sarcoidosis with prednisolone (5 mg/d) and was followed up for bronchial asthma without medication. She had no history of a drug allergy.

The patient was scheduled to undergo TURBT for the fifth time. Hyperbaric bupivacaine (2.2 mL; 5 mg/mL) was administered using a 25-gauge spinal needle. The highest level of hypesthesia was the Th4 dermatome. During TURBT, blood pressure was controlled around 130/60 mm Hg; and heart rate, around 65 beats/min. At the end of the surgery, pirarubicin hydrochloride (30 mg) was administered into the bladder. Five minutes after administration of pirarubicin hydrochloride, the patient complained of nausea and vomited. At the same time, her blood pressure decreased from 123/59 mm Hg to 60/37 mm Hg, and her heart rate increased from 67 beats/min to 104 beats/min. The patient's level of consciousness remained lucid. Resuscitation was begun immediately, including administration of oxygen (10 L/min) with a face mask, ephedrine hydrochloride (total 10 mg), phenylephrine hydrochloride (total 0.9 mg), and crystalloid infusion; however, the patient's blood pressure did not improve. Finally, noradrenaline (total 0.25 mg) was given intravenously, after which the blood pressure increased to 116/59 mm Hg. Although skin rash and wheeze were not noted, we suspected anaphylactic shock induced by pirarubicin hydrochloride. Therefore, we immediately discontinued pirarubicin hydrochloride and administered methylprednisolone (500 mg) and hydroxyzine hydrochloride (25 mg) intravenously. Arterial blood gas analysis showed pH 7.428, PaCO_2 36.7 mm Hg, PaO_2 232.0 mm Hg, HCO_3^- 23.9 mmol/L, actual base excess 0.30 mmol/L, and Sat O_2 99.3%.

After the patient's hemodynamics were stabilized, urticaria and erythema of the face and trunk appeared. Adrenaline (0.3 mg) was injected intramuscularly. Considering the risk of a biphasic anaphylactic reaction, we thought that the patient should be admitted to the intensive care unit for strict postoperative observation. Fortunately, the postoperative course was uneventful, and the patient was moved to the general ward on the first postoperative day.

3. Discussion

When cardiopulmonary collapse was noted in this case, ST-T elevation on the electrocardiogram, abnormal arterial blood gas values indicating pulmonary thromboembolism, and high spinal anesthesia were not observed. Therefore, judging from the clinical symptoms and progress, we

suspected anaphylaxis caused by pirarubicin hydrochloride. Generally, anaphylaxis induced by a drug administered intravenously occurs in a few minutes [5], but the exposure-reaction time for anaphylaxis induced by a drug administered intravesically is not known. There have been 2 reported cases of anaphylaxis induced by drugs administered intravesically. In 1 case, anaphylaxis happened 4 hours and 40 minutes after administration of hexaminolevulinate hydrochloride [6]. In the other case, the causative drug was epirubicin, but it was not specified when anaphylaxis occurred [2]. Because microvascular injury to the mucous membrane of the urinary bladder occurs during TURBT, we speculated that pirarubicin hydrochloride had been absorbed into the blood through the bladder's injured mucous membrane and that the patient had become sensitized to pirarubicin hydrochloride through repeated TURBT procedures. Pirarubicin hydrochloride is administered at the end of surgery, just before the patient leaves the operating room. Therefore, attention to patient monitoring tends to be divided. Operating room staff should consider the risk of anaphylaxis after intravesical administration of drugs and continue to monitor the patient carefully for at least a while.

There are several diagnostic tests for anaphylaxis, such as histamine and tryptase plasma concentrations, skin tests, and specific immunoglobulin E assays. A latex-specific immunoglobulin E assay for our patient was negative. Unfortunately, we did not measure concentrations of histamine and tryptase. Because anticancer agents strongly induce characteristics of tissue disorders, skin testing of anticancer agents is not generally carried out. In addition, the patient did not consent to further diagnostic testing because of the risk of anaphylaxis.

In conclusion, this is the first reported case of anaphylaxis due to intravesical administration of pirarubicin hydrochloride. We should always consider the possibility of anaphylaxis at the time of drug administration and must carefully monitor the patient's vital signs.

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