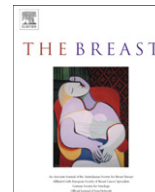


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Letter to the Editor

Isosulfan blue-induced anaphylactic reaction during sentinel lymph node biopsy in breast cancer

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To the Editor

In patients with breast cancer, the most important prognostic factor is whether there exists a metastatic involvement in axillary lymph nodes.¹ Histopathological examination of the sentinel lymph node (SLN) provides information about presence of metastasis in the remaining lymph nodes without application of axillary lymph node dissection. Radiolymphoscintigraphy and/or blue dye is/are used for detection of SLN in breast cancer. Isosulfan blue is the first dye approved by the United States Food and Drug Administration (FDA) in terms of sentinel lymph node biopsy (SLNB), and it is also one of the most commonly used blue dyes.^{2,3} Allergic and anaphylactic reactions to the Isosulfan blue used for SLNB in breast cancer may develop. In our article, we present a case of anaphylactic reaction induced by Isosulfan blue.

A 65-year-old female patient presented with a palpable lesion in her right breast. Clinical breast exam demonstrated a 1.5-cm mass in the upper outer quadrant. Mammography and breast ultrasonography revealed a 16 × 13-mm spiculated contoured mass in the upper outer quadrant of the right breast at 2 o'clock, and no suspicious lymph nodes were seen in the ipsilateral axillary region. Ultrasound-guided tru-cut biopsy of the lesion was performed, and the biopsy result was received as an infiltrating ductal carcinoma. Segmental mastectomy and SLNB were scheduled to be performed.

The patient, who was evaluated by the anaesthesia team during the preoperative visit the day before the surgery, was included in the American Society of Anesthesiologists Score group I (ASA-I), in consequence of her physical examination, radiology and laboratory results as well as evaluation tests of her intubation difficulty being found normal. Ten milligram of diazepam and 40 mg of famotidine premedication were ordered to be taken orally, at 10 o'clock in the evening and 30 min before the surgery.

When the patient was taken to the operating room, perioperatively basic monitoring with non-invasive blood pressure, continuous electrocardiogram (ECG), peripheral oxygen saturation by pulse oximetry (SpO₂) and end tidal carbon dioxide (ETCO₂) was carried out. The patient was preoxygenised and a remifentanyl infusion at a speed of 0.2 µg kg⁻¹ min⁻¹ was commenced. Anaesthesia

was induced with lidocaine 40 mg, propofol 180 mg and rocuronium 50 mg administered intravenously, followed by endotracheal intubation and automatic ventilator connection was provided subsequently. The patient was exposed to desflurane 5% Minimum Alveolar Concentration (MAC), O₂ 3 l min⁻¹ and remifentanyl 0.1 µg kg⁻¹ min⁻¹ for maintenance of anaesthesia.

For SLN mapping in breast cancer, 5 ml of Isosulfan blue was injected subcutaneously to the periareolar subcutaneous area 15 min later following anaesthesia induction. Sudden hypotension (50/30 mmHg) and bradycardia (40 beats min⁻¹) developed about 30 s after the Isosulfan blue injection. One milligram atropine was given immediately. The possibilities of toxic, allergic and anaphylactic reactions due to Isosulfan blue as well as the possibility that the patient might have suffered cardiovascular arrest were considered. Accordingly, anaesthetic gases and liquids were ceased and 100% O₂ ventilation was started, which failed to improve her blood pressure and bradycardia. Methylprednisolone 250 mg and phenyramine 4.5 mg were injected intravenously with a presumptive diagnosis of Isosulfan blue-induced anaphylactic shock, characterised with hypotension and bradycardia. One milligram of atropine was repeated owing to persistent hypotension and severe bradycardia. One milligram of epinephrine was administered intravenously as well. Cardiac arrest ensued afterwards and cardiopulmonary resuscitation (CPR) was immediately instituted. She was successfully resuscitated and after 2 min of CPR, her rhythm was restored to sinus rhythm. Heart rate and blood pressure went up to 100 beats min⁻¹ and 80/50 mmHg, respectively. Urgent arterial blood gas analysis and biochemical parameters were within normal limits. The heart rate and blood pressure began to rise. The blood pressure and heart rate went up to 160/90 mmHg and 120 beats min⁻¹, respectively. The heart rate was quickly normalised, with recovery of blood pressure to previous levels after esmolol administration. The anaesthesia was again resumed at a reduced dose. It was decided to resume the operation once vital signs seemed to be stable.

In the axillary region, Isosulfan blue-positive two SLNs were excised and they underwent frozen sectioning. Segmental mastectomy was performed to remove the mass marked with the wire before documentation of status of the frozen sections. Microscopic

examination of frozen sections revealed carcinoma infiltration of SLNs so that we proceeded to carry out level 1–2 axillary dissection.

The patient was observed in the postoperative care room for 2 h after the surgery due to serious adverse reactions she had suffered perioperatively. Postoperatively, the patient was awake, conscious and the vital signs were stable. Visual ability, verbal responsiveness and motor skills were evaluated and they were also within normal limits. Her blood pressure was 120/75 mmHg, heart rate 90 beats min⁻¹ and oxygen saturation while breathing ambient air was 99%. The patient was discharged from our unit 1 week later and was referred to the Oncology outpatient department for adjuvant chemoradiotherapy.

Isosulfan blue is in the triphenylmethane-based rosaniline type dye group. It is the 2,5-disulfone isomer of patent blue, and it is an inert dye physiologically.² The incidence of the allergic reactions induced by Isosulfan blue used for determination of SLN ranges from 0.7% to 1.9%.⁴ The reported allergic reactions are: localised swelling in the application area of the dye, pruritus on the hands, neck and abdomen, decrease in the oxygen saturation, oedema on the face and glottis and anaphylactic reactions.⁵ In Axillary Lymphatic Mapping Against Nodal Axillary Clearance trial (ALMANAC) study, in 5853 SLN biopsy studies carried out by using Isosulfan blue, light reactions developed in 51 procedures, 0.9% of all, after injection of blue dye. Reactions severe enough to require vasopressor or to terminate the process were very rarely observed. These were seen in only four, that is, 0.07% of the 5853 patients.⁶ In the SLNB study of Kaufman et al. carried out in 2008 by applying Isosulfan blue to 3339 patients, mild reactions at a rate of around 0.06% were observed and no serious reactions were encountered.⁷

Anaphylactic reactions arise secondary to bounding of drug-specific immunoglobulin E (IgE) antibodies to mast cells and basophils; and they lead to an intensive histamine release due to intracellular degranulation.^{5,8} One or more of cardiovascular collapse, erythema, angioedema, bronchospasm, classical urticaria or other rash types as well as gastrointestinal and pulmonary symptoms may occur as the symptoms of the anaphylactic shock, which may develop during anaesthesia. Treatment of anaphylaxis that develops during anaesthesia is made by ceasing the anaesthesia, applying 100% oxygen, intravenous fluid, antihistamines, epinephrine and steroid.¹ The anaphylactic shock arising during SLNB against blue dye is potentially fatal and should be considered as a medical emergency. Montgomery et al. have classified anaphylactic shocks as follows: Those with only allergic skin reactions are grade 1, the temporary hypotensions that do not require vasopressor support are grade 2 and the temporary hypotensions

requiring vasopressor support are grade 3.⁹ If there is a cardiac involvement during anaphylaxis, it is called grade 4. Since 1966, only a few cases of grade 4 Isosulfan blue-induced anaphylaxis with cardiac involvement, as in our case, have been reported in the English literature.²

The surgical team should always keep in mind the possibility of serious Isosulfan blue-induced reactions and should be capable of ensuring immediate intervention as quickly as possible.

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