

## Blue Dye, Blue Skin

A 59-year-old Chinese lady was scheduled for wide excision of an invasive ductal carcinoma of the left breast, with sentinel lymph node biopsy (SLNB). She had a history of mild depression treated with alprazolam and paroxetine. She was assessed to be ASA (American Society of Anaesthesiologists) Class 1. Her preoperative investigative workup was normal. There was no history of atopy or prior documented drug allergy.

Standard ASA monitoring was applied. General anaesthesia was induced with midazolam, fentanyl, lignocaine, and propofol, and maintained with isoflurane in nitrous oxide and oxygen. The airway was secured with a laryngeal mask airway. Patent Blue V dye was injected in the periareolar region by the surgeon, and the sentinel lymph node was dissected. Within 10 minutes, the patient had a marked drop in arterial blood pressure to a lowest level of 69/29 mmHg, associated with tachycardia but not hypoxaemia. This was refractory to fluid resuscitation, intravenous ephedrine and phenylephrine, but responded to bolus increments of adrenaline (1.5 mg in total). Forty minutes after the onset of hypotension, the patient's skin was noted to have a bluish discoloration (Figs. 1 & 2).

What do you see in these images?

- A. Peripheral cyanosis
- B. Blue urticaria
- C. Extravasation of blue dye
- D. Methemoglobinemia
- E. Blue naevus



Fig. 1. Blue discoloration seen on the patient's abdomen.



Fig. 2. Close-up view of the well-defined blue discoloration.

Figure 1 shows blue urticaria on a background of erythema which was found over the patient's face, abdomen and limbs. Figure 2 is a close-up view of the blue urticaria—note that the blue discoloration is well demarcated and confined to the urticarial plaques.

In view of likely anaphylactic shock secondary to Patent Blue V, the patient was intubated, given intravenous hydrocortisone and diphenhydramine, and started on an intravenous adrenaline infusion for persistent hypotension. Upon urinary catheterisation, her urine was found to be blue in colour (Fig. 3). The rest of the operation was discontinued and she was transferred to the surgical intensive care unit (SICU) for monitoring and continuation of resuscitation.

The patient's serum tryptase, measured within 1 hour of the onset of hypotension, was 15.825 µg/L. The results of all other laboratory investigations were normal. She had an uneventful recovery and was discharged from the SICU the day after. Outpatient skin prick testing to confirm the allergen was offered, but declined by the patient. Since our patient did not undergo the confirmatory test, the next best management as advised by the immunologist was to avoid all putative culpable blue dyes in the future—the anaesthetic drugs per se were deemed unlikely causative agents in view of the characteristic dermatological manifestation.

### Discussion

Patent Blue V is the dye of choice for intraoperative sentinel lymph node mapping for breast cancer. It belongs to the group of triphenylmethane dyes. Its ubiquitous use

Answer: B



Fig. 3. Blue urine collected upon urinary catheterisation.

as a synthetic food colouring by the general population causes sensitisation, which can lead to allergic reactions during its use in SLNB without obvious history of previous exposure. The incidence of Patent Blue V anaphylaxis is quoted to be 0.6% to 2.8%.<sup>1</sup>

Allergic reactions to Patent Blue V can be recognised most commonly by the characteristic blue urticaria, which presents as smooth, raised patches (wheals) on a background of erythema (flare). The blue discoloration is confined to the elevated patches as the interstitial edema contains serum proteins that are bound to Patent Blue V. In more severe cases, such as in this patient, the blue urticaria can be associated with one or more of the following—angioedema, cardiovascular collapse, and respiratory distress with bronchospasm and/or laryngeal edema. Blue discoloration of urine may also be present, as in the case of this patient, and may persist for days after administration of the dye. The temporal relationship (an average of 15 to 30 minutes) between the injection of Patent Blue V and the onset of symptoms of anaphylaxis is also a guide to diagnosis.

During an intraoperative anaphylactic reaction to Patent Blue V, adrenaline, antihistamines and corticosteroids have successfully been used to restore blood pressure and resolve symptoms. Postoperative monitoring in the intensive care unit (ICU) is recommended as a second event of anaphylaxis, despite no further exposure to the allergen (biphasic anaphylaxis), has been reported.<sup>2</sup>

As anaphylaxis to Patent Blue V is a Type I hypersensitivity reaction, serum tryptase levels can be used to support the diagnosis of anaphylaxis. A serum tryptase level of more than 11.4 µg/L indicates systemic mast cell activation. When compared to histamine, which has a blood half-life of minutes, tryptase has a blood half-life of about 2 hours. This patient had a serum tryptase level of 15.825 µg/L. The diagnosis can be confirmed by a skin prick test where positive results may be seen at dilutions of 1:10 and 1:100 of the challenge.

To prevent the occurrence of allergic reactions, Patent Blue V product information insert recommends testing for hypersensitivity by first injecting a small volume of solution and observing for an allergic reaction prior to injection of the full volume for identification of the SLN. Safer dye alternatives such as methylene blue, with comparable efficacy for SLN identification and cost-effectiveness to that of Patent Blue V, can be considered.<sup>3</sup>

## Conclusion

Collectively, the clinical symptoms (time of onset of the hypersensitivity reaction; the clinical signs and their severity) and the allergological investigations (elevated serum tryptase levels; positive skin prick test) help to determine the diagnosis of an anaphylaxis due to Patent Blue V dye.

Our case highlights the fact that blue dyes have the potential of causing life-threatening complications even after a non-systemic administration. We should remain alert for intraoperative changes that may be caused by blue dyes—hypersensitivity reactions and blue discoloration of skin and urine.

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