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CLINICAL INFORMATION

Allergic reaction to patent blue dye in breast surgery – case report[☆]



Marcus Vinícius M. Maranhão^{a,*}, Dyluzia Kelly Amaral da Nóbrega^b,
Carlos Eduardo Caiado Anunciação^a, Barbara de Alcântara Brito Maia^a,
Paulo Virgílio Dantas Mariano^a

^a Universidade de Pernambuco (UPE), Recife, PE, Brazil

^b Universidade Federal de Alagoas, Maceió, AL, Brazil

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Abstract We present a case of allergic reaction to patent blue in a patient who underwent excision of sentinel lymph node associated with segmental breast resection. About 20 min after the dye injection, the patient developed hypotension (BP = 70 × 30 mmHg) associated with increased heart frequency. The patient was treated successfully with decreased inspired fraction of inhaled anesthetic and fluid replacement. At the end of the procedure, she presented with bluish urticarial-like plaques on the head, neck, upper limbs, and trunk; hydrocortisone was then used. The patient recovered uneventfully and was discharged from the PACU 2 h after the end of surgery without skin changes, and was discharged from hospital on the morning after surgery. The incidence of allergic reactions with the use of patent blue is far superior to the hypersensitivity reactions seen with anesthetic and adjuvant drugs. Therefore, the anesthesiologist must be aware of cardiovascular instability associated with skin changes during the use of patent blue, for early diagnosis and appropriate treatment of this hypersensitivity reaction to this dye.

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PALAVRAS-CHAVE

Anestesia;
Anafilaxia;
Hipersensibilidade;
Azul patente

Reação alérgica ao corante azul patente em cirurgia de mama – relato de caso

Resumo Os autores apresentam um caso de reação alérgica ao azul patente em uma paciente submetida à exérese de linfonodo em sentinela associada a uma ressecção segmentar de mama. Paciente apresentou aproximadamente pós 20 minutos da injeção do corante hipotensão (PA = 70 × 30 mmHg) associada a aumento da frequência cardíaca. Foi tratada satisfatoriamente

[☆] Study performed at the Department of Anesthesiology, Hospital Universitário Oswaldo Cruz, Universidade de Pernambuco, Recife, PE, Brazil.

* Corresponding author.

E-mail: gabriel.n@uol.com.br (M.V.M. Maranhão).

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com diminuição da fração inspirada do anestésico inalatório e reposição volêmica. No fim do procedimento apresentava placas urticariformes azuladas em cabeça, pescoço, membros superiores e tronco e foi usada hidrocortisona. Evoluiu, sem intercorrências, na sala de recuperação pós-anestésica e teve alta duas horas após o término do procedimento cirúrgico sem a presença das alterações cutâneas. Alta hospitalar na manhã seguinte à cirurgia. A incidência de reações alérgicas com o emprego do azul patente é muito superior às reações de hipersensibilidade observadas com drogas anestésicas e adjuvantes. Portanto, o anestesiológico deve ficar atento à instabilidade cardiovascular associada a alterações cutâneas quando do uso do azul patente para o diagnóstico precoce e tratamento adequado dessa reação de hipersensibilidade com o emprego do corante.

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Introduction

Sentinel lymph node biopsy for early breast cancer surgical treatment has been widely used as part of routine protocol and, in most cases, it prevents total lymphadenectomy.^{1,2} Patent blue dye or the radioisotope technetium may be used alone or in combination to identify the lymph node.¹ However, there are reports of hypersensitivity reactions mediated by IgE to blue dye, with an average incidence of 1.8% (0.1% to 2.8%); in some cases these reactions can be severe and yield serious hemodynamic effects requiring vasoactive drugs.¹⁻⁴ This frequency is higher than the hypersensitivity reactions seen during anesthesia, which is around 0.01% to 0.02%.⁵

Another effect seen with the use of patent blue are pulse oximetry changes because it interferes with the wavelength reading used to measure the oxyhemoglobin.² The objective of this paper is to present a case of intraoperative allergic reaction after subdermal periareolar injection of patent blue dye.

Case report

Female patient, 45 years old, 72 kg, ASA P2, referred from the Oncology Center (CEON) of the Oswaldo Cruz University Hospital, University of Pernambuco (UPE), Recife, scheduled for segmental resection of the left breast with sentinel lymph node resection. During preanesthetic evaluation, the patient reported history of hypertension and use of enalapril, without other comorbidities; she denied smoking and allergies to medicines, foods, and latex, and reported being a social drinker, using tranquilizers (bromazepam), and having undergone previous anesthesia without complications. Preoperative tests, such as cardiac examination, blood count, coagulation, biochemistry (urea, glucose, creatinine, AST, ALT), and urinalysis were normal. The patient was not premedicated. At the operating room, venoclysis was performed at the left upper limb with 20G Teflon catheter. Basic monitoring with cardioplex, pulse oximeter, and noninvasive blood pressure showed normal sinus rhythm, heart rate (HR) of 90 bpm, oxygen saturation (SpO₂) of 98%, and blood pressure of 130 × 70 mmHg. After preoxygenation with 100% O₂ via face mask and administration of cefazolin

(2 g), induction of anesthesia was achieved with fentanyl (250 μg), propofol (150 mg) and rocuronium (50 mg). Tracheal intubation was performed with a 7.5 mm cuffed tube and basic monitoring complemented with capnography; controlled mechanical ventilation with 570 mL tidal volume and 12 ipm respiratory rate. At that point, cardiorespiratory parameters evidenced normal sinus rhythm, HR 85 bpm, SpO₂ 100%, ETCO₂ 30, and PA 110 × 65 mmHg. Maintenance of anesthesia was achieved with sevoflurane (2–2.5%) and O₂/N₂O (50/50%). Immediately before the incision, a subdermal periareolar injection of 2.5% patent blue (2 mL) was performed. About 20 min after the blue dye injection, hypotension (70 × 30 mmHg) and increased HR (100 bpm) occurred without changes in heart rhythm, SpO₂, and capnography. Ringer's lactate (400 mL) was administered and end-tidal sevoflurane concentration decreased to 1.5%. About 10 min after volume replacement and a decrease in the fraction of inspired halogenated, blood pressure was 100 × 60 mmHg and HR 90 bpm, without changes in the remaining parameters. The anesthetic-surgical procedure went through without complications. Dipyrone (2 g) was used for postoperative analgesia. The duration of surgery was 50 min. At the end of the procedure, atropine (1 mg) and neostigmine (2 mg) were used for neuromuscular blockade reversal. After surgical field removal, the presence of numerous urticaria-like plates (bluish) was observed mainly in the face, neck, upper limbs, and thorax (Figs. 1 and 2). Hydrocortisone (500 mg) was administered. The patient quickly awakened from anesthesia and was extubated in the operating room. She was conscious, complained of mild pruritus, free of pain, and with cardiovascular and respiratory stability (blood pressure: 150 × 90 mmHg, HR: 95 bpm, and SpO₂: 98%). The patient presented with nausea, received ondansetron (8 mg), and was taken to the post-anesthesia care unit (PACU). After 60 min, the patient had no skin changes and was discharged from PACU 120 min after surgery. The patient was discharged from hospital the morning after surgery without complications.

Discussion

The most commonly used dyes for sentinel lymph node identification are isosulfan blue (commonly used in Europe)



Figure 1 Presence of numerous urticaria-like plaques on the face, neck, upper limbs and chest.



Figure 2 Presence of numerous urticaria-like plaques.

and patent blue (commonly used in Brazil and the United States) and less frequently methylene blue.^{1,6} Both the isosulfan blue and patent blue belong to the group of triarylmethane dyes. Patent blue has an additional hydroxyl group.¹ Numerous immediate hypersensitivity reactions have been attributed to dyes and there may be a cross-sensitivity between the two drugs.^{1,6} In contrast, methylene blue has been considered safer than patent blue and is an effective option to it to identify the sentinel lymph node, a fact, however, contested by some authors.¹ There is evidence that about 2.7% of the population would be allergic to blue dye, which may be due to sensitization caused by repeated exposure to some products, such as textiles, cosmetics, paper, leather, and drugs containing these dyes.¹ After the intradermal or intraparenchymal injection, patent blue is taken up by the lymphatic vessels from draining area, binds to albumin, and two thirds are absorbed in the first hour while the totality in 24 h. It is excreted in the urine and bile, and the patient urine may turn blue for up to 24 h.^{1,3}

There are three degrees of severity associated with the hypersensitivity reactions to patent blue:^{3,4} grade I (69–87%), characterized by bluish color urticaria, pruritus, and general rash; grade II (3.2–8%), characterized by hypotension (systolic blood pressure <70 mmHg) without the need for vasopressor, and absence of bronchospasm and laryngospasm; grade III (1.1%), characterized by severe cardiovascular collapse that require vasopressor, suspension of the surgical procedure, and patient's transfer to the intensive care unit. The early signs of allergic reaction are hypotension and skin rash without bronchospasm or airway edema. Although an initial manifestation, the skin changes are not always immediately seen because of the drapes.⁵ The late onset of hypersensitivity occurs between 10 and 45 min after the dye injection (mean = 17 min), unlike the usual hypersensitivity reactions seen during anesthesia that occurs earlier, which often slows down the differential diagnosis of allergic reaction.^{3,5} Skin reactions disappear from 1 to 20 h.³ Treatment varies according to the severity of the allergic symptoms. In patients with grade I or II, drug treatment is based on corticosteroids (hydrocortisone, dexamethasone), antihistamines (diphenhydramine, promethazine), and volume replacement with crystalloid. In patients classified as grade III, there is a need for vasopressor (epinephrine, metaraminol, etilefrine, ephedrine, noradrenaline). Vasopressor response may be obtained with a starting dose of the drug or may require prolonged drug infusion.^{1–4} Cardiovascular system depression may be prolonged and require cardiovascular support and admission to the intensive care unit. Cardiac arrest is infrequent, with satisfactory resuscitation.⁶ We found no case of death in the literature due to allergic reaction to patent blue. Noteworthy to anesthesiologists is that the allergic reactions to patent blue may be biphasic with the occurrence of a subsequent episode of hypotension between six and 8 h after the initial event. Patients should be monitored in the PACU or ICU during this period, even if hemodynamically stable.⁵ Positive skin test for allergies to patent blue and increased serum histamine levels (normal value $\leq 10 \text{ nmol L}^{-1}$), IgE, and tryptase (due to mast cell degranulation; normal value = $13.5 \mu\text{g L}^{-1}$) are usually present in these patients.^{5–8} Because of histamine short elimination half-life (15–20 min), collecting blood 30 min after the hypersensitivity reaction

is recommended. Serum tryptase has a peak plasma level within an hour and remains high for 6 h.⁵ Two samples of tryptase with 60 and 120 min are recommended. Normal tryptase levels do not exclude a hypersensitivity reaction, as some allergic reactions are mediated by basophils and complement activation, which does not increase the serum levels of tryptase.⁶ The hypersensitivity test by injecting a small amount of the drug and waiting a few minutes to check for these allergic reactions has been recommended. However, the use of test dose is controversial and there is no evidence of reduced anaphylaxis.⁹ The skin test (skin prick or, mainly, intradermal) in which a much smaller volume than the test dose is used seems to be the ideal test with high sensitivity and specificity to identify patients with hypersensitivity to patent blue.⁹ Allergic patients and those using angiotensin converting enzyme inhibitors or angiotensin II receptor inhibitor are at risk to develop allergic reactions with the use of patent blue.⁵

Another effect seen with the use of patent blue is interference in pulse oximeter readings, which causes an apparent decrease in oxygen saturation. This interference is due to the absorption peak of the patent blue light (638 nm) be very close to that of deoxyhemoglobin (660 nm).⁵ The increased light absorption in this region may be interpreted by the pulse oximeter as the presence of deoxyhemoglobin and falsely decrease oxygen saturation.⁵ Latency and duration of oxygen saturation fall depend on the site of injection of patent blue. Intravascular injection causes an immediate and severe drop in oxygen saturation that persists for a few minutes.⁵ When administered into the mammary parenchyma, a reduction of 11% (5% on average) occurs 15–30 min after injection.⁵

Hypersensitivity reactions to patent blue are much more frequent than those usually seen during anesthesia and may range from skin changes to severe and prolonged cardiovascular depression and require admission to the intensive care unit and cardiovascular support. Our patient

had a hypersensitivity reaction grade II due to subcutaneous injection of patent blue, which evolved satisfactorily without sequelae. Therefore, anesthesiologists should be aware of allergy to patent blue in case of cardiovascular instability and look for the presence of skin changes that confirm the clinical diagnosis of hypersensitivity reaction, which may be supplemented by measurement of serum tryptase, histamine and IgE, as well as skin tests.

Conflicts of interest

The authors declare no conflicts of interest.

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