Atypical anaphylactic reaction to Patent Blue during sentinel lymph node biopsy for breast cancer

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ABSTRACT

INTRODUCTION We present an unusual case of severe anaphylaxis to Patent Blue dye with atypical clinical features during sentinel lymph node biopsy (SLNB). The medical personnel involved with sentinel node biopsies should be alert, and familiar with this unusual entity. We also present current data from the literature.

CASE REPORT During a wide local excision for primary breast cancer and SLNB, and early during the operation, the patient became severely tachycardic and hypotensive without any signs of urticaria, rash, oedema, or bronchospasm. Resuscitation required the addition of noradrenaline infusion followed by an overnight admission to the intensive care unit. Raised serum tryptase levels supported the diagnosis of anaphylactic shock while skin tests showed a severe reaction to Patent Blue dye.

CONCLUSIONS: Severe, life-threatening anaphylaxis to Patent Blue dye may present without obvious previous exposure to the dye and without the cardinal signs of oedema, urticaria and bronchospasm making the diagnosis and management of such cases challenging. Correct diagnosis and identification of the causative factor is important and requires a specific set of laboratory tests that are not commonly requested in every-day medical practice. It is not clear from the literature whether the condition is common enough to justify pre-operative prophylactic or diagnostic measures.

KEYWORDS

Patent Blue – Isosulphan Blue – Anaphylaxis – Sentinel lymph node biopsy

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Intra-operative allergic reactions are caused mostly by muscle relaxants (70%), latex (10%) and antibiotics with a mortality rate of 3.5–4.7%. Blue dyes, used to identify the axillary lymphatics during sentinel lymph node biopsy (SLNB) are not among the common causes of anaphylaxis.^{1,2} The first life-threatening anaphylaxis to Isosulphan Blue was reported by Longnecker and colleagues in 1985. This paper aims to discuss atypical anaphylactic reactions to blue dyes used to facilitate SLNB and the appropriate diagnostic work-up.

Case report

A 51-year-old woman with a 22-mm high-grade invasive ductal breast carcinoma was scheduled to undergo wide local excision (WLE) of the primary tumour and SLNB under general anaesthesia. There was no other significant past medical, drug or family history.

Peritumoural injection with 15 MBq of radioactively labelled colloid Tc99m (1.25 ml; Nanocoll; Amersham

Healthcare Ltd, Buckinghamshire, UK) was administered 3 h before the procedure.

Anaesthesia was induced with Alfentanil 1 mg, morphine 3 mg and Propofol 200 mg and maintained with 70% nitrous oxide in oxygen and Sevoflurane. Immediately after induction, she was given Ondansetron 8 mg, Dexamethasone 8 mg, Augmentin 1.2 g and a further peritumoural injection with 4 ml of 1.25% Patent Blue V (Patent Blue V sodium Guerbet 2.5%) dye for the identification of the sentinel lymph node.

Ten minutes after the injection of the blue dye, the patient became tachycardic and hypotensive with peripheral vasoconstriction but no signs of urticaria, oedema, or bronchospasm. The initial measures (including adrenaline infusion at 0.05 mcg/kg/min) exacerbated the tachycardia with no improvement in blood pressure.

Noradrenaline infusion was commenced at 0.2 mcg/kg/min and 1 l of colloid solution was given together with 200 mg of hydrocortisone and 10 mg of chlorpheniramine. After a gradual improvement over the next 10 min,

the operation was recommenced and finished uneventfully. All postoperative work-up investigations were within normal limits apart from total serum tryptase levels, which were found to be elevated at 3 h (44.8 ng/ml). Twelve hours following the event, serum tryptase levels dropped (14.7 ng/ml) and eventually returned to normal, thus, excluding systemic mastocytosis and supporting the diagnosis of anaphylactic shock.

Skin tests (skin prick tests and intradermal tests) were performed for all involved agents demonstrating a severe reaction to Patent Blue dye injection and a mild reaction to Ondansetron.

Retrospective review of our database (years 1998–2006), including over 300 sentinel lymph node biopsies where a blue dye was used to identify the sentinel node, failed to show a similar case of anaphylaxis during surgery or any other form of allergic reaction to the specific blue dye.

Discussion

Our case is an example of severe, life-threatening anaphylactic reaction that presented without any evidence of bronchospasm, laryngospasm, and oedema or skin rash. The reaction was only characterised by severe and prolonged hypotension and tachycardia refractory to adrenaline injection. To our knowledge, there is no similar case in the literature combining this severity with these characteristics.

Radioisotopes and blue dyes are used for the identification of the sentinel lymph nodes and a combination of both increases the sensitivity of the technique.

First exposure and subsequent sensitisation results from the presence of Patent Blue and other dyes that have similar structure in objects from every-day life such as clothes, paints, inks, laxatives, suppositories, cosmetics, antifreeze, and carpets.^{1,5} Also, Patent Blue was used in food (E131) until 1974.² Moreover, it has been used in agriculture and medicine. An association between the dose of Patent Blue used and the incidence of anaphylaxis has been reported.⁴

Most allergic reactions to the blue dyes are mild, described as grade I (69–87%) and present with urticaria, pruritus, blue hives, and/or generalised rash.

More severe, grade 2 reactions comprise 3.2–8% of all reported reactions and present with transient hypotension (systolic blood pressure < 70) not requiring vasopressor support,^{1,4} while grade 3 reactions are very rare (1.1%) and present with severe cardiovascular collapse requiring vasopressor support.^{2,5} Anaphylactic reactions to Patent Blue

have been noted since 1966 and the incidence of such reactions is reported to be 0.6–2.8% with a mean of 1.8%.^{1,2}

There is a strong cross-reaction between Isosulphan Blue and Patent Blue but not with methylene blue which can be used in cases of documented hypersensitivity.² There is insufficient evidence to support any medical prophylactic regimen as yet.⁵

When an anaphylactic reaction is suspected, it should be confirmed using skin tests, and blood and urine investigations. The short half-life of histamine in blood (a few minutes) makes its application difficult in non-laboratory settings as opposed to plasma tryptase levels,^{3,4} which makes it a useful diagnostic test.^{5,5} Since the tryptase half-life is 1.5–2.5 h, the levels in plasma should be measured in the serum within 4 h of the onset of the suspected anaphylactic reaction.⁵ Measurement of an initial peak (> 11.5 ng/ml) and subsequent reduction to low levels within 24 h supports the diagnosis of anaphylaxis due to mast cell activation.⁵

To confirm hypersensitivity to the blue dye, either the skin prick test and/or the intradermal test can be used.⁴

Conclusions

Severe anaphylaxis requiring prolonged vasopressor support can occur with the use of Patent Blue dye for SLNB without obvious previous exposure to the dye. The reaction may not always present with all the hallmarks of anaphylaxis and can be difficult to recognise. Correct diagnosis and identification of the causative factor is important and requires a specific set of laboratory tests that are not commonly requested in every-day medical practice. It is not clear from the literature whether the condition is common enough to justify pre-operative prophylactic or diagnostic measures.

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