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Blue Dye Leading to Blue Eyelids: Anaphylaxis after Sentinel Node Biopsy

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Abstract

Blue dye is used to facilitate Sentinel Node Biopsy (SNB) in breast cancer patients. Hypersensitivity reactions to this blue dye are reported in up to 2.7% of patients. A very rare presentation is the occurrence of anaphylactic shock with blue palpebral angioedema after injection of blue dye. Anaphylaxis is a known cause for the development of angioedema, but blue coloring of the skin appears extraordinary. The blue palpebral angioedema appears to be explained by a systemic effect of the blue dye.

Keywords: Sentinel node biopsy; Breast cancer; Patent blue V; Anaphylactic shock

Introduction

Anaphylactic reactions to Patent Blue V (PBV), a dye used to facilitate sentinel node biopsy (SNB) in breast cancer patients, are reported in 0.06-2.7% of the patients [1,2]. These reactions vary from cutaneous hypersensitivity manifestations (grade I hypersensitivity reactions) to anaphylaxis with hemodynamic instability (grade III hypersensitivity reactions) [2,3]. Rare presentations however do occur. We describe a case of blue palpebral angioedema after SNB with PBV.

Case Report

A 41-year-old woman presented at the surgical outpatient clinic with a right-sided nipple retraction. She did not report any other complaints of the breast and no palpable masses or clinically enlarged lymph nodes were detected at physical examination. Her medical history did not reveal any relevant comorbidities. Also, the patient had no known food or drug allergies. Mammography and ultrasound of the right breast showed multiple masses in the medial upper and lower quadrant, suspect for multifocal breast cancer. The 14G needle biopsy contained invasive ductal carcinoma. A Sentinel Node Biopsy (SNB) was performed, for definitive nodal staging prior to mastectomy and oncoplastic reconstruction. One day preoperative, 99^{m} technetium-nanocolloid (Tc-99) was injected peritumoral and a sentinel node was visualized in the ipsilateral axilla. The SNB was performed under general anesthesia. Propofol, sufentanil, granisetron and dexamethasone were administered at induction of anesthesia. Dexamethasone was administered as prophylaxis for postoperative nausea. No antibiotics or muscle relaxants were administered. 1 cc of PBV was injected intradermal peri-areolar in the quadrant of the tumor. Then, the blue and radioactive sentinel node was removed.

Ten minutes after the injection of PBV, the patient developed hypotension of 75/40 mmHg and a bradycardia of 30 beats per minute. She also developed blue palpebralangioedema and blue hives on the skin of the neck (Figure 1 and Figure 2). The anaphylactic shock was treated with intravenous fluid resuscitation, hydrocortisone, epinephrine and clemastine and the vital parameters were monitored. The blood pressure recuperated to 120/70 mmHg with a heartbeat of 90 beats per minute, within a couple of minutes. The patient recovered without further complications and the blue coloring of the palpebral region disappeared in several hours. No other ophthalmic symptoms such as blue coloring of the bulbar conjunctiva were observed. In this case, anaphylaxis was a clinical diagnosis. No specific laboratory tests were carried out to confirm anaphylaxis. The sentinel node was assessed pathologically and contained a macro metastasis.

Discussion

A wide variety of hypersensitivity symptoms are described after administration of PBV for SNB. Allergic reactions vary from cutaneous symptoms (erythema, urticaria, angioedema, blue hives) to systemic reactions with cardiovascular collapse and anaphylactic shock [4].

Rare presentations, such as blue palpebral angioedema as described in our patient, occur [5-7]. Anaphylaxis is a known

Figure 1: Blue palpebral angioedema.

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Figure 2: Blue hives on the skin.

cause for the development of angioedema, but the blue coloring of the skin appears extraordinary. Most likely, the blue angioedema is explained by a systemic effect of PBV. PBV is taken up in the bloodstream and excreted via the urine. Only a minimal amount of PBV, as used in the SNB, is necessary to develop blue lymph drainage and to color a patient's urine blue in the first postoperative day. In patients developing angioedema, severe vasodilatation occurs in the edematous tissue. In a dilated microvascular system, the systemic PBV could therefore be visible. Another explanation could be direct intravenous PBV uptake.

Knowledge of systemic reactions to PBV is important for surgeons as well as anesthesiologists. From an Australian and New Zealand surgeon panel, it is known that over 45% of breast surgeons have experienced the occurrence of hypersensitivity reactions in patients during SNB [3]. It appears that these hypersensitivity reactions to PBV are more frequently observed nowadays. This could be due to the increased use of PBV as a colorant in food and clothing [2,8]. Over the past decades, SNB has been used increasingly as a staging method for the axilla [9]. The extended necessity of SNB for further nodal staging in early detected clinically node negative breast cancer patients, also contributes to this hypothesis.

It appears that hypersensitivity reactions to PBV are not predictable. No cross-reactivity between blue dyes such as PBV and methylene blue and other substances is described so far; therefore it is hard to predict in which patients extra caution should be taken [1]. The onset time of anaphylactic symptoms however, does differ between mild and severe anaphylaxis. In patients developing a grade III reaction, symptoms tend to occur within 15-30 minutes after administration of PBV, while milder reactions can occur up to several hours after receiving PBV [4].

Since the incidence of a failed sentinel node identification is 3.6 times higher when no dual mapping with technetium as well as blue dye is used, omitting blue dye in this diagnostic modality is not desirable [1]. Watchful observation of the patient after PBV administration by surgeon as well as anesthesiologist is necessary. More research to finding alternative dyes for SNB could lead to changes in the risk of anaphylaxis in the future.

Currently, SNB is more often performed as a separate procedure, prior to neoadjuvant chemotherapy or direct oncoplastic breast reconstruction to avoid the risk of irradiation of the reconstructed breast. Since SNB seems to be a minor procedure, it is carried out under local anesthesia in selected patients. It is important for surgeons and anesthesiologists to remain aware of the fact that up to 2.7% of patients develop hypersensitivity reactions [1]. If the procedure is carried out under local anesthesia, intravenous access should be guaranteed by inserting at least one infusion needle preoperatively. This way, access for fluid resuscitation and inotropic substances is guaranteed in case of anaphylactic shock.

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