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Life-threatening isosulfan blue induced anaphylaxis during laparoscopic hysterectomy

Laparoskopik histerektomi ameliyatı sırasında gelişen izosulfan mavisi ilişkili hayatı tehdit eden anafilaksi

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Abstract

The use of blue dye alone is the first described technique for sentinel lymph node (SLN) identification in patients with cervical carcinoma. In this procedure, Isosulfan Blue (IB), Methylene Blue or Patent Blue is injected into each quadrant of the cervix. We present an anaphylactic reaction to IB in a patient who underwent a laparoscopic hysterectomy. Approximately 15 min after the dye injection, the patient developed hypotension (55/35 mmHg) with an increase in heart rate (120 beats/minute) and a decrease of pulse oximetry to 85%. She was treated successfully with ephedrine, adrenaline, and fluid administration. When sterile drapes were removed, blue urticarial rashes all over the body were detected. The operation was halted, and the patient was transferred to the intensive care unit (ICU). Almost 4 hours after injection of IB, she experienced a second attack of bronchospasm under mechanical ventilation. She recovered uneventfully and was discharged from the ICU. The patient was referred to a skin prick test which was positive for IB. SLN biopsy for cervical cancers may have an increased risk of anaphylaxis probability due to administered blue dyes. It is crucial that the medical staff involved in these procedures be aware of anaphylactic reactions. This case report highlights the necessity of close monitoring of these patients in both the intraoperative and postoperative periods.

Keywords: Anaphylaxis, Sentinel lymph node, Hysterectomy, Isosulfan blue

Öz

Tek başına mavi boya kullanımı servikal karsinomlu hastalarda sentinel lenf nodu (SLN) tanımlaması için ilk tarif edilen tekniktir. Bu prosedürde, serviksin her çeyreğine İzosulfan Mavisi (İM), Metilen Mavisi veya Patent Mavisi enjekte edilir. Biz bu olguda laparoskopik histerektomi uygulanan bir hastada İM'ye karşı gelişen anafilaktik bir reaksiyonu sunduk. Boya enjeksiyonundan yaklaşık 15 dakika sonra hastada kalp atım hızında artış (120 atım / dakika) ve nabız oksimetresinde %85'e varan bir azalma ile hipotansiyon (55/35 mmHg) gelişti. Hasta, efedrin, adrenalin ve sıvı uygulaması ile başarılı bir şekilde tedavi edildi. Steril örtüler açıldığında, vücudun her yerinde mavi ürtiker döküntüleri tespit edildi. Operasyon durduruldu ve hasta yoğun bakım ünitesine (YBÜ) transfer edildi. Hasta İM'nin enjeksiyonundan yaklaşık 4 saat sonra, mekanik ventilasyon altında ikinci bir bronkospazm atağı yaşadı. Hasta sorunsuz bir şekilde iyileşti ve yoğun bakımdan taburcu edildi. Hasta, İM için pozitif olan bir deri testine yönlendirildi. Servikal kanserler için SLN biyopsisi, uygulanan mavi boyalara bağlı olarak artmış anafilaksi riski taşıyabilir. Bu prosedürlere dahil olan tıbbi personelin anafilaktik reaksiyonlara karşı dikkatli çok önemlidir. Bu olgu sunumu, bu hastaların hem intraoperatif hem de postoperatif dönemde yakından izlenmesinin gerekliliğini vurgulamaktadır.

Anahtar kelimeler: Anafilaksi, Sentinel lenf nodu, Histerektomi, İzosulfan mavisi

Introduction

Intraoperative identification of sentinel lymph node (SLN) status is both a major prognostic factor for patients with cervical carcinoma and a decision benchmark for adjuvant therapy. If the node is positive for tumor metastasis, a radical hysterectomy should be omitted, and adjuvant chemo-radiation is commonly administered [1,2]. The use of blue dye alone is the first described technique for SLN identification in patients with cervical carcinoma [3]. In this procedure, Isosulfan Blue (IB), Methylene Blue, or Patent Blue is injected into each quadrant of the cervix [4].

Anaphylaxis resulting from IB (CAS number: 68238-36-8) is well described in the literature. Multiple studies report rates of anaphylaxis to IB ranging from 0.1% to 1.1% [5]. A literature search for case reports available on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed>) from 2000 to 2017 using the search terms, anaphylaxis, isosulfan blue, sentinel lymph node and hysterectomy identified 35 results, of which the majority of cases were about breast or skin cancers, but none of them was about cervical cancer.

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We believe that this is the first case of intraoperative anaphylaxis after injection of IB during cervical cancer staging. This case report describes an episode of severe anaphylaxis, characterized by bronchospasm, which occurred after intracervical injection of IB. The literature on management of severe reactions is subsequently reviewed. Using this case report of intraoperative anaphylaxis to IB and an overview of the literature, we attempt to draw attention to this important group of dyes and their potential to cause intraoperative anaphylaxis.

Case presentation

TA 38-year-old woman (weight: 68 kg; height: 170cm) was scheduled for a laparoscopic abdominal hysterectomy because of atypical endometrial cells on biopsy. Her only comorbidity was asthma, and she reported using salbutamol (Vent-O-Sal[®]) as a rescue inhaler during an asthma attack. She did not have drug, food, or other allergies. Past surgical and anesthetic history included endometrial biopsy under moderate sedation (with propofol, midazolam, and fentanyl citrate), which was uneventful. Her preoperative laboratory workup and chest radiogram, as well as her electrocardiogram (ECG), were normal.

Before the operation, she was premedicated with 80 mg prednisolone for asthma. In the operating room, standard American Society of Anesthesiologists monitors were applied. Her arms were positioned at her sides, and soft gel pads were applied around her hips, elbows, and shoulders. General anaesthesia was induced by propofol, fentanyl, and rocuronium. After endotracheal intubation, anesthesia was maintained with a 50%/50% oxygen/air mixture and sevoflurane with an end-tidal concentration of 2%. Mechanical ventilation was delivered by volume-controlled ventilation with a tidal volume of 500 mL, respiratory rate of 12 breaths/min, and positive end-expiratory pressure of 5 cm H₂O. The surgical procedure began with SLN mapping, and 3 ml of IB was injected into the cervix while the patient was in the lithotomy position. Approximately 15 minutes later, the patient experienced acute hypotension and desaturation during the incisions for laparoscopy trocars. Her blood pressure suddenly dropped to 55/35 mmHg and pulse oximetry decreased to 85%, while her heart rate increased to 120 beats/minute. In the meantime, peak inspiratory pressure increased to 42 mmHg, suggesting severe bronchospasm. The operation was halted, the inspired O₂ concentration was increased to 100%, and sevoflurane was discontinued. A total of 30 mg ephedrine and 0.2 mg adrenaline (1:10000) were applied intravenously in a few minutes. As her mean arterial pressure (MAP) continued to decrease to 30 mmHg, 1000 ml of colloid and 500 ml of crystalloid solutions were administered. Additionally, a 0.01 mcgr.kg⁻¹.min⁻¹noradrenaline infusion was started in peripheral veins. A few minutes later, MAP increased to 55-60 mmHg and the pulse oximetry reading reached 100%. After observing periorbital edema and blue urticarial rashes all over the face, sterile drapes were removed, and similar blue urticarial rashes were detected all over the body. An arterial line was placed in the right radial artery, and a central venous catheter was inserted into the right jugular vein. The patient was then transferred to the intensive care unit (ICU) for close hemodynamic monitoring and mechanical ventilation support. A thorax computed tomography

was performed to rule out pulmonary embolism, but no pulmonary pathology was detected. During ICU follow-up, antineurotic edema on the eyelids (Figure 1), persistent blue urticarial rashes on the auricle (Figure 2), and blue urine discoloration (Figure 3) were considered to be an anaphylactic reaction to IB dye.



Figure 1: Presence of blue urticarial rashes all over the face and periorbital edema



Figure 2: Blue urticarial rashes on the auricle Figure 3: Blue urine discoloration

Almost 4 hours after injection of IB, she experienced a second attack of bronchospasm under mechanical ventilation. She received intravenous 4 mg prednisolone every 6 hours for the next 48 hours and 40 mg intravenous pheniramine maleate every 12 hours for the next 24 hours. Her blue urticarial rashes resolved, and she was extubated uneventfully on the second day of ICU admission. She was discharged from the hospital after several days without a residual effect. She was referred to a skin prick test (SPT), and a positive SPT was obtained for IB dye. SPT for propofol and egg was negative. She underwent laparoscopic hysterectomy without SLN mapping six weeks later. The second procedure was completed uneventfully. The authors obtained written permission from the patient to publish this report.

Discussion

The combination of laparoscopic intraoperative SLN mapping and radical laparoscopic surgery is a feasible modality for the management of patients with early cervical carcinoma [6]. IB, otherwise known as lymphazurin blue, binds to albumin and other local proteins and is absorbed by the lymphatic system, which makes it suitable for SLN biopsies [7]. Anaphylactic reactions induced with IB have been previously reported with an incidence ranging from 0.1% to 1.1 [5,8]. Its incidence has presumably increased because of the growing use of the dye to delineate lymphatic spread of cancerous tissues [9]. Smurfish blue urticaria, biphasic cardiovascular collapse, hypoxia, and

bronchospasm have been interpreted as related to anaphylactic reactions [10,12].

IB dye-induced anaphylaxis is an IgE-mediated type I hypersensitivity reaction involving basophils and mast cells [13]. During the IgE-mediated anaphylaxis, released mediators produce a symptom complex of bronchospasm and upper airway edema in the respiratory system, and vasodilation and increased capillary permeability in the cardiovascular system [14]. Treatment should be directed to blood pressure and airway management. Primarily, our patient had experienced a sudden drop in blood pressure and pulse oximetry mimicking a massive pulmonary embolism. Ephedrine is suggested as the first-line treatment of intraoperative hypotension during general anesthesia and a better choice to maintain cardiac output, so we administered intravenous ephedrine to our patient [15]. As her blood pressure continued to fall, we applied intravenous adrenaline to provide a more prominent α -1 effect. Although we did not consider anaphylaxis as a differential diagnosis in the first step, intravenous adrenalin administration probably prevented the exacerbation of bronchospasm.

In the current case, accompanying asthma disease might have exacerbated bronchospasm. The Association of Anesthetists of Great Britain and Ireland has warned that individuals with a history of asthma appear to be at increased risk of anaphylaxis [16]. Also, the IB product inserts states that reactions are more likely to occur in people with a family story of bronchial asthma, significant allergies, and previous reactions to triphenylmethanes. Biphasic bronchospasm in the ICU follow-up might be related to pre-existing asthma [12].

Raut et al. [17] studied whether prophylactic intravenous glucocorticoid, diphenhydramine, and famotidine administration just before or at induction of anaesthesia could prevent anaphylaxis. They reported that no episodes of hypotension were observed and none of the patients required vasopressors, ventilator support, or intensive care. Although our patient had received prednisolone prophylaxis, an anaphylactic reaction developed with severe hypotension contrary to the previous report. We believe that, although anaphylaxis could not be avoided, the severity of reactions had been reduced by the pre-treatment with a glucocorticoid regimen.

The sudden drop of the pulse oximetry might not be associated with bronchospasm and airway obstruction. Vokach-Brodsky et al. [18] demonstrated that IB alters the absorbency properties of blood and interferes with pulse oximetry that may be interpreted as arterial desaturation. Thus, the decreased pulse oximetry reading of 85% in our case can be explained by not only the hypoperfusion state of the patient's hypotension but also the interference of measuring the absorption of IB and oxyhemoglobin.

Liang et al. [11] suggested that patients who exhibit any hemodynamic instability should not have further surgery in the same setting. Due to their recommendation, we decided to postpone the operation to investigate the certain cause of anaphylaxis.

In the previous reports, preoperative testing, using minimum dye volume, using an alternative dye or no dye have been proposed to reduce the risk of life-threatening IB-induced anaphylaxis [19]. In the current case, we decided not to

administer IB during the second operation in consensus with the surgeons.

Positive skin test for allergies to patent blue and increased serum histamine levels, IgE, and tryptase (due to mast cell degranulation) are usually present in these patients. Serum tryptase has a peak plasma level within an hour and remains high for 6 h [20]. 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 [21]. Unfortunately, in our institution and in our city tryptase levels cannot be measured in laboratories. Hence, we could not report any tryptase level for this patient.

SLN biopsies for cervical cancer operations have an increased risk of anaphylaxis due to administered blue dyes. It is crucial that the medical staff involved in these procedures be aware of the signs and symptoms of anaphylactic reactions. This case report highlights the necessity of close monitoring of these patients in both the intraoperative and postoperative periods.

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