An Uncommon Cause of Intraoperative Hypotension: Delayed Red Man Syndrome

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J Neuroanaesthesiol Crit Care 2019;6:40–42

Abstract

Intraoperative hypotension is commonly encountered under anesthesia. Varied causation of intraoperative hypotension can often delay the recognition of its cause. Vancomycin, a bactericidal antibiotic and often used in neurosurgical setting, is known to cause "red man syndrome." Prompt recognition of the etiology for intraoperative hypotension could be challenging in intraoperative setting. We present a case of intraoperative hypotension in a patient undergoing endoscopic skull base surgery, which was caused by a delayed red man syndrome. Delayed red man syndrome is a rare clinical entity and must be borne in mind while evaluating a case of intraoperative hypotension in patients who are on vancomycin therapy.

Keywords
- vancomycin
- hypotension
- neurosurgery

Introduction

Intraoperative hypotension has multifactorial causation, and its adverse effects on postoperative outcome are well established.[1] Prompt recognition of the etiology for intraoperative hypotension could be challenging in a scenario where there is simultaneous administration of multiple anesthetic drugs, antibiotics, blood and blood products, and other surgically triggered events such as blood loss and air embolism. We present a case of life-threatening intraoperative hypotension in a patient who underwent endoscopic skull base surgery, which turned out to be a delayed "red man syndrome" due to vancomycin. Our search of literature showed that delayed red man syndrome is a rare clinical entity, and its presentation as an intraoperative hypotension has never been reported. A written informed consent regarding publication of this report was obtained from the patient.

Case Report

A 31-year-old woman weighing 60 kg with no co-morbid conditions, diagnosed with third ventricular colloid cyst, underwent surgical excision of the same. Two months later, she complained of continuous clear nasal discharge. She was diagnosed of having postoperative cerebrospinal fluid (CSF) leak for which she was taken up for elective transnasal endoscopic CSF leak repair with intravenous (IV) vancomycin and ceftriaxone as empiric antibiotic regimen for suspected meningitis. The patient had no known drug allergies or a history of past adverse anesthetic reactions. The patient had received vancomycin therapy for 3 days, and on the day of surgery, she received IV injection of vancomycin 1 g as an infusion over 90 minutes prior to shifting to the operating room. She also received injection of ondansetron 8 mg and injection of pantoprazole 40 mg as premedications.

The patient underwent standard anesthesia induction with preinduction monitors consisting of electrocardiogram (ECG), pulse oximetry (SpO_2), and noninvasive blood pressure (NIBP). Anesthesia was induced with injections of fentanyl 2 μg/kg and propofol 2 mg/kg. Injection vecuronium 0.1mg/kg was used to achieve muscle relaxation to facilitate tracheal intubation with 7.5 mm ID endotracheal tube. Post induction, left radial artery was cannulated for invasive blood pressure (BP) monitoring. A lumbar drain was inserted at L4–5, and infusion of 10 mg fluorescein in 50 mL saline dye was started to aid in detection of the leak site. Anesthesia was maintained with sevoflurane (minimum alveolar concentration [MAC]: 0.7–0.9) and an infusion of injection of fentanyl 1 μg/kg/h and injection of atracurium 0.5 mg/kg/h. Normal saline was used as irrigating fluid for the endoscope by the neurosurgeon. After 30 minutes into the surgery, an episode of rapidly progressive hypotension with tachycardia

received
August 10, 2018
accepted after revision
August 25, 2018
published online
January 25, 2019

DOI https://doi.org/10.1055/s-0038-1674266
ISSN 2348-0548.

was witnessed. Surgeons were notified immediately, and any vascular injury or acute blood loss was immediately ruled out. Possibility of venous air embolism was ruled out as there was no fall in end tidal carbon dioxide ($EtCO_2$), which was > 3 mm Hg during the hypotensive episode. Over the next few minutes, the heart rate increased to over 150 beats/min, and BP decreased precipitously from 128/70 to 60/30 mm Hg. A bolus of 500 mL 0.9% normal saline and multiple boluses of injection of phenylephrine 100 μg failed to raise the BP. Peak airway pressure reached 40 cm H_2O from 20 cm H_2O, and SpO_2 dropped from 100% to 90%. Meanwhile as we exposed her left hand to insert an additional IV cannula, there was generalized redness of the skin. Further examination revealed similar rashes on the opposite hand, neck, and upper torso and bilateral wheeze on chest auscultation. An anaphylactic or anaphylactoid reaction was suspected, and injection of epinephrine 100 μg intravenous bolus, followed by injection of epinephrine infusion 0.01 μg/kg/h was administered along with injection of hydrocortisone 200 mg and injection of diphenhydramine 50 mg. The patient responded immediately to the therapy with a BP of 130/80 mm Hg, SpO_2 of 98%, and reduction in peak airway pressure to 28 cm H_2O. After achieving stable hemodynamic and respiratory status, surgery was recommenced and completed in an hour. The patient was shifted to the intensive care unit (ICU) post-surgery for postoperative monitoring. Epinephrine infusion was tapered off over 2 hours, and trachea was extubated. Cardiovascular work-up did not reveal any abnormalities, and plasma tryptase levels were sent. The patient was monitored in the ICU for the next 48 hours. Immunology consultation and allergy testing to all the anesthetic drugs, vancomycin, and fluorescein dye done on day 5 revealed hypersensitivity to vancomycin.

Discussion

Intraoperative hypotension is commonly encountered in neurosurgery patients and is known to be associated with adverse perioperative outcomes, myocardial injury after noncardiac surgery, and high long-term (1 year) mortality.[2,3] Lower pre-induction BP, emergency surgery, elderly age, male sex, and autonomic dysfunction are independently associated with intraoperative hypotension.[4] Deep plane of anesthesia, intraoperative blood loss, anaphylaxis, etc. are the common identified causes of intraoperative hypotension under general anesthesia. Endoscopic skull base surgeries present the risk of intraoperative hemodynamic compromise due to vascular or dural sinus injury and air embolism.[5] The incidence of perioperative anaphylaxis/anaphylactoid reaction is 1 in 10,000 to 20,000 and is one of the common causes of intraoperative hypotension.[6]

In our case, major vascular injury and sudden blood loss were immediately ruled out. There were no exposed venous sinuses, and the fall in $EtCO_2$ was secondary to fall in BP, thus ruling out the incidence of venous air embolism. The appearance of rash with flushing of skin, wheeze on auscultation (suggestive of bronchospasm), increased airway pressures, and cardiovascular collapse helped us to diagnose hypersensitivity reaction as the cause of hypotension. Diagnosing anaphylactic/anaphylactoid reactions can be difficult in the intraoperative period.[6] Patients under general anesthesia receive multiple drugs in close succession, are unconscious, and presence of surgical drapes delay recognition of cutaneous signs.[6]

Vancomycin is commonly used in neurosurgery patients and is known to cause "red man syndrome," an anaphylactoid reaction, with an incidence between 3.7 and 47%.[7] Red man syndrome presents with generalized flushing of skin, bronchospasm, laryngeal edema, hypotension, arrhythmia, and myocardial depression resulting in cardiovascular collapse.[7] Red man syndrome is encountered when the drug is given at a rapid rate of infusion (> 10 mg/min) with signs of reaction appearing approximately 4 to 10 minutes after the initiation of infusion or soon after its completion. Delayed red man syndrome is a rare entity and has been reported to occur in patients who had received vancomycin for longer than 7 days, with no prior incident.[7] In our patient, the reaction occurred after 2 hours of drug administration during the intraoperative period, thus making it difficult to suspect a hypersensitivity reaction to vancomycin. Also, our patient had received vancomycin only during the past 3 days. Anaphylactoid reactions such as red man syndrome are known to occur in cases when the causative drug is co-administered with opiate, muscle relaxants, or contrast agents causing enhanced mast cell degranulation due to bidirectional synergism.[8,9] We infused injections of fentanyl and atracurium intraoperatively, which could have potentiated the delayed hypersensitivity reaction to vancomycin in our case. Postcrisis, intensive care admission should be considered for monitoring, as the condition may last up to 32 hours, and biphasic reactions are reported in up to 20% of cases.[10] Patients should be monitored in ICU for at least 12 to 24 hours. Immunological consultation and identification of allergen should be done to prevent similar adverse events in the future.[10]

Conclusion

Delayed red man syndrome is a rare clinical entity and must be borne in mind while evaluating a case of intraoperative hypotension in patients who are on vancomycin therapy.

Funding
None.

Conflict of Interest
None declared.

Note
The manuscript has been read and approved by all the authors; the requirements for authorship as stated earlier in this document have been met, and each author believes that the manuscript represents honest work.

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