CASE REPORT

A Critical Incident Report: Steroid-induced Anaphylactic Shock

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Abstract

Drugs used during the perioperative period by anesthesiologists are diverse often given rapidly and in large doses. Several drugs given intravenously are known to cause immunoglobulin E-mediated (IgE) (type I) hypersensitivity reactions, which may lead to severe anaphylactic shock. Amongst drugs commonly used to treat such events is hydrocortisone succinate. Although less frequently, hydrocortisone has also been reported to cause anaphylaxis in certain patients. Identification of the offending agent can be challenging in certain scenarios, such as preinduction phase of anesthesia when administered along with other drugs in a short span of time. Drug provocation tests and skin tests are known methods to check for allergenic potential, but protocols can be confusing and not widely accessible. We present a case report of an individual who developed anaphylactic shock two times before the responsible agent was identified.

Keywords: Anaphylaxis, Hydrocortisone succinate, Intradermal test, Skin prick.

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Introduction

Any drug can cause either an allergic or an idiosyncratic reaction in humans, and corticosteroids are often administered to treat these reactions in the perioperative setting.[1] However, unexpectedly at times, there have been cases when they were reported to trigger a severe allergic reaction, including life-threatening ones like anaphylactic. Very few cases of various steroid-induced anaphylaxis or shock have been reported worldwide.[2–4] Here is one such case report, where an individual developed anaphylactic shock twice due to the administration of hydrocortisone succinate. However, it was only confirmed when it was administered the second time since initially it was believed to have occurred due to one of the anesthetic drugs. This event has further highlighted the difficulty in the identification and testing of allergens in patients with allergies.

Case Description

A 32-year-old male, nonalcoholic, chronic smoker with no history of food allergy was accepted into the American Society of Anesthesiologists (ASA) class II, for laparoscopic interval appendectomy under general anesthesia with endotracheal intubation. On the day of surgery, the patient was taken to operation theatre (OT) and monitoring was established as per ASA standards. After following the surgical safety checklist, the patient was premedicated with an injection of glycopyrrolate 0.2 mg intravenous (IV), and an injection of fentanyl 100 µg IV. However, after fentanyl injection, the patient developed rashes over the injected arm. To prevent a severe allergic reaction, the patient was medicated with injection pheniramine 45.50 mg IV and injection hydrocortisone succinate 200 mg IV. At induction, propofol at 2 mg/kg IV and vecuronium at 0.1 mg/kg IV was given. Subsequently intubated with an 8.5 mm endotracheal tube and ventilated on volume-controlled mode. Maintenance of anesthesia was accomplished with sevoflurane (2%) along with O_2 and air (50:50).

Soon after induction, the patient developed tachycardia with a heart rate of 150–160/minute, and blood pressure (BP) of 80/60 mm Hg was recorded. Urticarial rashes were noticed all over the body, along with goose flash. No bronchospasm and wheeze were heard on auscultation. Suspecting an anaphylactoid reaction due to one of the anesthetic drugs, the patient was ventilated with 100% O_2. A second IV line was secured in the other arm with a rapid normal saline bolus. Passive leg raise was carried out to improve venous return. Despite the above measures, hemodynamic compromise persisted. Adrenalin infusion at 0.05 µg/kg/minute and noradrenalin infusion at 0.1 µg/kg/minute was then started, and the rate was increased until desired hemodynamic parameters were achieved. After 45 minutes the patient's parameters improved. Surgery was canceled for rescheduling. The patient was shifted to the intensive care unit for further monitoring, and stabilization was extubated.

Fentanyl was the most likely agent to have caused the anaphylaxis since the patient had developed a localized skin rash after administering the drug. Fentanyl, propofol vecuronium, and lignocaine in 1:10 dilution were tested for sensitivity by intradermal tests (IDT) 4 weeks after the first episode. The tests revealed sensitivity only to fentanyl. The anesthetic plan was modified accordingly, and open surgery was decided to be done under a combined spinal epidural.

After taking all precautionary measures, the patient was taken to OT 7 days after the test, IV line secured, and Ringer lactate

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started as per maintenance dose in the preoperative room. Prophylactically injection of hydrocortisone succinate 200 mg IV was given. Following the dose, the patient again recorded a heart rate of 150–160/minute, a BP of 70/40 mm Hg, and urticarial rashes all over the body with no bronchospasm or respiratory distress. The necessary drugs were, however, preloaded in anticipation of a recurrence of anaphylactic shock, and therefore, recovery was achieved much earlier. Since the anaphylactic shock had occurred prior to intubation this time around, the patient was successfully managed without mechanical ventilation. The subsequent IDT for hydrocortisone succinate was positive.

Discussion

Identification of the responsible agent(s) for an allergic reaction during the perioperative period is not straightforward. Anesthesiologists use a large number of drugs perioperatively, rapidly, and in large doses, mostly causing IgE-mediated hypersensitivity reactions.[5,6] The most common offending agent causing anaphylaxis is the muscle relaxants, accounting for 60–70% of all anesthesia-related allergic reactions. Latex and antibiotics are the second and third most common causes of anaphylaxis in the perioperative setting. The difficulty is worsened when drugs used for its treatment also have the potential to cause these reactions. The first anaphylactic reaction to IV corticosteroids was described in the year 1974 after the treatment of acute severe asthmatic patients with methylprednisolone and hydrocortisone. Succinate esters of hydrocortisone and methylprednisolone are mostly responsible for type I allergic reactions.

Corticosteroids are categorized into four groups (groups A–D) based on their molecular configurations and stereochemistry. Hydrocortisone belongs to group A and can be responsible for causing hypersensitivity in any patient with or without prior exposure. This can be partially explained by the cross-reactivity that exists between different corticosteroid groups and also drugs within the same group. We have not been able to establish whether our patient has been previously exposed to any corticosteroid.[7]

The drug provocation test is considered the gold standard for confirming or excluding a diagnosis of drug allergy.[8] The test should be performed by trained personnel in a clinical setting with appropriate resuscitation facilities, after carrying out a risk-benefit analysis and when skin tests and/or *in vitro* tests have yielded negative results. Skin tests in the form of skin prick test (SPT), IDT, and patch test are relatively simpler to perform with procedures laid down. Recommended nonirritant-specific drug concentrations for β-lactam antibiotics, perioperative drugs, heparins, and radiocontrast media are available in the literature.

Apart from the skin testing, *in vitro* tests which include specific IgE antibodies and basophil activation tests, can be performed. However, reliable specific IgE antibody tests for most anesthetic drugs are lacking, and the basophil activation test is not yet mainstream.[9]

When suspecting systemic corticosteroids are responsible for an anaphylactic reaction, patch testing should be performed initially, and then IDT must be considered if the patch test is negative. The anti-inflammatory effect of corticosteroids may also mask its own patch test reaction leading to a false negative result. Since we did not have the facility to perform a patch test, we conducted IDT as per recommended dilutions. Ideally, a skin test should be performed 4–6 weeks after the initial insult.[10] Skin concentrations of a few drugs used in the perioperative setting are provided in Table 1.

Commonly, a contributory agent for the occurrence of adverse reactions is the excipient (carboxymethylcellulose and succinate salt) rather than the molecule. Some case reports have demonstrated positive SPT with sodium succinate, however, exhibited negative with hydrocortisone alone. It is therefore advisable to do allergological testing of every suspected substance administered along with all components. This will confirm the safety of the drug for future administration.

After the initial anaphylactic reaction, serological test for confirmation includes measurement of mast cell tryptase levels immediately, 1 and 24 hours after the event. The total IgE levels can also be measured; however, it will not be able to identify the offending agent.[10]

Early identification of a reaction during surgery may also pose a challenge. Since the patient is draped, the earliest cutaneous manifestations maybe are missed, and an anaphylactic reaction maybe is identified after hemodynamic compromise or bronchospasm has set in.

Conclusion

This case report explaining an anaphylactic shock due to hydrocortisone succinate highlights that perioperative physicians should be aware of the possibility of such severe

Table 1: Test concentrations for drugs commonly used perioperatively[9]

Drug		*SPT*		*IDT*	
Generic name	*Undiluted concentration (mg/mL)*	*Dilution*	*Maximum concentration (mg/mL)*	*Dilution*	*Maximum concentration (mg/mL)*
Thiopentone	25	Undiluted	25	1/10	2.5
Propofol	10	Undiluted	10	1/10	1
Ketamine	10	Undiluted	10	1/10	1
Etomidate	2	Undiluted	2	1/10	0.2
Midazolam	5	Undiluted	5	1/10	0.5
Fentanyl	0.05	Undiluted	0.05	1/10	0.005
Morphine	10	1/10	1	1/1000	0.01
Atracurium	10	1/10	1	1/1000	0.01
Rocuronium	10	Undiluted	10	1/200	0.05
Vecuronium	4	Undiluted	4	1/10	0.4
Succinylcholine	50	1/10	10	1/500	0.1
Local anesthetics	As per drug	Undiluted	As per drug	1/10	–

anaphylactic reactions due to systemic steroids. Deterioration of symptoms may not always suggest treatment failure but can also occur because of steroid administration owing to its capacity to cause allergic reactions. Corticosteroids should be used with caution in patients suffering from atopic diathesis. A thorough history of drug or food allergies must be sought from patients because they seem to have a higher risk of hypersensitivity. Preparation with prophylactic antiallergic measures, including alternative drugs, and injectable epinephrine is of paramount importance. Testing for allergens should be carried out in controlled environments while strictly adhering to proposed drug concentrations.

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