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Case Report

Serious anaphylactic shock induced by hemocoagulase agkistrodon during anesthesia in a 5-year-old child

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Abstract: We report a case of serious anaphylactic shock in a 5-year-old child undergoing scheduled surgery blank space of a right femoral intramedullary nail removal. The boy had undergone right femoral elastic intramedullary nail fixation surgery 14 months prior, but had no history of allergies. Within 5 minutes of intravenous bonus injection of hemocoagulase agkistrodon (HCA) 1 unit, a widespread transient diffuse erythema was seen on the front of his chest. After 20 minutes, sudden, profound cardiovascular collapse occurred. The child was treated effectively and sent to a ward 5 hours later. In this period, he received intravenously infused 200 ml hydroxyethyl starch solution and epinephrine at a rate of 0.05-0.01 μg kg^{-1} min^{-1}. Total amount of dexamethasone sodium phosphate 14 mg was used. To the best of our knowledge, few case reports of HCA-induced anaphylactic shock in children exist. Our report will, therefore, increase awareness of the allergic potential of HCA among pediatric anesthesiologists.

Keywords: Hemocoagulase agkistrodon, complications, anaphylactic shock, children

Introduction

Hemocoagulase agkistrodon (HCA) is a single component thrombin-like enzyme extracted from Chinese moccasin snake (*Deinagkistrodon acutus*) venom. The chemical structure of HCA is a two-chain glycoprotein with a molecular mass of 29 kDa that contains 252 amino acid residues. HCA can shorten the coagulation and bleeding time of whole blood, as demonstrated using a mouse tail-cutting model [1]. A multicenter, prospective, randomized, controlled, double-blind stage III clinical trial that enrolled 432 sequential adult patients found that HCA has a high capacity for hemostasis and coagulation and can be safely used for resting capillary hemorrhage during abdominal surgery incisions [1].

Large multicenter trials have demonstrated that the anaphylactic responses of adults [2] and children [3] are different. Compared with adults, etiological factors for serious anaphylactoid responses seem to be particularly distinctive in children. HCA is an animal-derived protein, and hypersensitive responses have been reported after the use of analogous drugs [4].

While administering anesthesia to a 5-year-old child, we encountered a case of anaphylactic shock due to the use of HCA. To the best of our knowledge, few case reports of HCA-induced anaphylactic shock in children exist.

Case report

A 5-year-old child weighing 20 kg was admitted for scheduled surgery for right femoral intramedullary nail removal. The patient had been diagnosed with a right proximal femoral neck cyst and had undergone right femoral elastic intramedullary nail fixation surgery 14 months prior. During the first operation, HCA had been administered without incident. The patient had no previous history of atopy, asthma, or allergic responses to any drugs or food. The preoperative physical examination was unremarkable.

Before the induction of anesthesia, the patient's heart rate (HR) was 98 beats per minute (bpm), his arterial blood pressure (BP) was 95/55 mmHg, and his oximeter value (SpO_2) was 98%.

Inhaled 8% sevoflurane in 8 L/min O_2 was used for anesthesia induction. The anesthesia was

supplemented with 40 mg propofol, 6 μg sufentanil, and 4 mg cisatracurium after intravenous cannula placement. The child's trachea was intubated and mechanical ventilation was begun with sevoflurane 3% in 2 L/min 50% air/O_2 mixture. One unit of HCA (dissolved in 2 ml of normal saline) was intravenously infused prior to skin incision.

At that time, the hemodynamic parameters of the child were stable (BP 90/50 mmHg and HR 112 bpm). However, 5 minutes later, a widespread transient diffuse erythema was observed on his chest. An intravenous injection of 4 mg dexamethasone sodium phosphate was administered immediately to treat this allergic sign.

Then, 20 minutes later, just before the procedure was completed, the patient's BP dropped to 40/20 mmHg, his end expiratory CO_2 decreased from 34 mmHg to 22 mmHg, and his peak inspiratory pressure increased from 13 mmHg to 42 mmHg, though his HR remained stable, remaining between 110 bpm and 120 bpm. SpO_2 values could not be read because the waveform of the pulse was very weak. Heart sounds audible via the precordial stethoscope were also very weak. Sevoflurane anesthesia was discontinued and the child was ventilated with 100% O_2. Epinephrine (50 μg) was intravenously infused. Within 1 minute, his HR increased to 126 bpm, his BP increased to 100/55 mmHg, his peak inspiratory pressure dropped back to 18 mmHg, and his SpO_2 returned to 96%. His lung compliance returned to normal under manual ventilation. HCA anaphylactic shock was not suspected at this stage.

After several minutes, the child again presented with serious hypotension, bronchial spasms and a decrease in his pulse rate. Another dose of 50 μg epinephrine was given. An arterial catheter was placed on the right brachial artery and the arterial pressure was continuously monitored. Anaphylactic shock was now suspected because of a second exposure to HCA and repeated hypotension. Intravenous hydration was initiated with 200 ml of a hydroxyethyl starch solution accompanied by continuously-infused epinephrine at 0.05-0.01 μg kg^{-1} min^{-1} to break the serious refractory bronchial spasm and stabilize the patient's blood pressure. More dexamethasone sodium phosphate (10 mg) was also given.

The patient was sent to the postanesthesia care unit after cardiovascular stability was achieved, and his need for epinephrine decreased over the next few hours. After 5 hours, the infusion of epinephrine was discontinued without any resulting fluctuation in the patient's blood pressure, and the patient was sent back to the ward. The child remained without sequelae after being discharged home with instructions for allergy monitoring.

Discussion

The short time delay between the injection of HCA and the described events as well as the erythema several minutes after the HCA injection are clear clinical evidence supporting the presence of anaphylactic shock, although we did not perform a related investigation to support the diagnosis of anaphylaxis.

An anaphylactic response under anesthesia is a rare event that is estimated to occur in between 1 in 5,000 and 1 in 25,000 cases of anesthetic use; mortality due to it is estimated to be 3.4% [5]. Anaphylaxis in response to intravenous agents occurs in 1 in 5,000 to 1 in 15,000 cases in which general anesthetic is used; mortality due to it is reported to be 4-6% [6].

When anaphylactic response occurs, the clinical presentation of a surgical patient is similar to that of a conscious patient. However, under anesthesia, the most common presentation is an increase in peak airway pressure followed by arterial desaturation, wheezing, hypotension and tachycardia. Skin changes such as urticaria and angioedema may be obscured by surgical drapes [7]. Therefore, because certain features may not be noted immediately, the observed manifestations may be attributed to other causes such as hypotension secondary to blood loss or myocardial depression and wheezing due to hyperreactive airways. Therefore, it is important to consider the possibility of anaphylaxis when allergic reactions occur under anesthesia.

Allergic reactions to medications are divided into two classifications: immune system-mediated and direct drug reactions not related to the immune system. Four types of immune system-mediated reactions have been described. Type I reactions are anaphylactic or immediate hype-

rsensitivity reactions, which require past exposure to the antigen for sensitization to occur. The type I reaction is IgE-mediated and may be life-threatening. According to its manifestation, HCA-induced anaphylactic shock may belong to this type. Following a previous exposure, IgE antibodies are created that attach to surface receptors of basophils and mast cells. The level of mast cell degranulation is affected by the dose of the stimulus, the affinity of the antigen to IgE antibodies and the quantity of bound IgE antibodies. Mast cell degranulation results in the liberation of leukotrienes, histamine, prostaglandins, tryptase and eicosanoids. It also induces the biosynthesis of cytokines. Five separate stages exist, ranging from mild cutaneous responses linked with systemic reactions to serious cardiovascular responses and bronchospasms to apnea and cardiac arrest.

The recognition of clinical factors that predispose patients to drug hypersensitivity is of great importance. Patients who have a history of atopy (specifically those with asthma, hay fever, dermatitis or food allergies), hypersensitivity of undetermined etiologies, or who have undergone several surgical procedures appear to be at high risk of experiencing an allergic reaction [8].

In this case, the child had no history of allergies or atopy; however, he was at risk of HCA sensitization because of its use in the previous operation. The first instance of serious hypotension in the child was managed by discontinuing sevoflurane anesthesia and administering an intravenous infusion of epinephrine. However, the diagnosis of anaphylactic shock had not been made at this point. When serious hypotension resumed, high amounts of continuous epinephrine and crystalloids and colloids were needed to maintain blood pressure. More steroids were given after the diagnosis of serious anaphylactic shock due to an HCA allergy was made. The majority of serious anaphy. lactic responses are successfully managed within 40 minutes [2], which is consistent with this case.

Clinical treatment of acute anaphylactic shock consists of acknowledging the issue, halting the administration of the antigen and beginning therapeutic treatment with epinephrine, antihistamines and corticosteroids, as well as intravascular fluid expansion. Stabilization is essential, followed by a search for the underlying cause of the anaphylactic response.

Mild systemic reactions may be managed with antihistamines or subcutaneous epinephrine if they are not life-threatening and progress slowly. Severe reactions require prompt treatment. Following the administration of oxygen, and ventilatory and cardiovascular support if required, the treatment of choice is epinephrine. However, consensus concerning the emergency medical management of anaphylaxis is lacking in key international guidelines [9]. No histamine antagonists were used in the reported case. The use of steroids and antihistamines is still often recommended for acute reactions [10].

In summary, anaphylactic responses are uncommon during anesthesia, but their high rates of morbidity and mortality are concerning. Immediate identification of the allergy, withdrawal of the antigen and commencement of therapy are all critical to improving outcomes. To the best of our knowledge, HCA-induced anaphylactic shock in children has not been reported previously, possibly because of the short time to market and small-scale clinical usage of HCA. Our report will, therefore, increase awareness of the allergic potential of HCA among pediatric anesthesiologists.

Disclosure of conflict of interest

None.

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