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CLINICAL REPORT

Anesthesia management for emergency laparotomy in a pediatric patient with suspected hereditary angioedema

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Abstract Hereditary angioedema (HAE) is caused by complement factor 1 inhibitor (C1-INH) deficiency, and its mode of inheritance is autosomal dominant. We present a case of an 8-year-old patient who required emergency laparotomy after a traffic accident. General anesthesia with tracheal intubation was necessary. The patient's mother and maternal grandmother had been diagnosed with HAE. HAE is associated with high mortality when airway edema is caused by tracheal intubation. It was impossible to rule out HAE preoperatively in the patient. Therefore, we presumed that he had HAE and treated him with pasteurized C1-INH concentrate. The patient underwent laparotomy uneventfully. Several days after the operation, the laboratory data revealed that the perioperative plasma complement 1 q subunit (C1q) protein level and C1-INH function were not lowered. The diagnosis of HAE was not confirmed, but it was not possible to rule out the diagnosis either. The prophylactic use of a C1-INH in this case may be justified, because the procedure was an emergency and because of the high mortality associated with tracheal intubation in patients with HAE.

Keywords Emergency operation · Hereditary angioedema · Pediatric

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Abbreviation

HAE	Hereditary angioedema
C1	Complement factor 1
C1-INH	Complement factor 1 inhibitor
C1 q	Complement 1 q subunit

Introduction

Hereditary angioedema (HAE) is the result of complement factor 1 inhibitor (C1-INH) deficiency, and its mode of inheritance is autosomal dominant. HAE may present with recurrent swelling without urticaria and usually without itch [1]. The swelling may affect any part of the body, including the extremities, face, trunk, gastrointestinal tract, genitourinary regions, and airway tract [2]. It has been reported that tracheal intubation triggers laryngeal edema in HAE, leading to mortality in 30%–40% of cases [3]. We report a case of a pediatric patient, suspected of having HAE, who required emergency surgery under general anesthesia with tracheal intubation.

Case report

An 8-year-old boy was admitted to the emergency room for acute abdominal pain after he had fallen off his bicycle. Abdominal computed tomography showed free air in his abdominal cavity. The free air suggested a perforated intestine, and emergency laparotomy was indicated. His past history included pyloromyotomy for pyloric stenosis when he was 1 month old. He had shown signs of bronchial asthma 1 month before the accident, but he was not on regular pharmaceutical treatment for asthma.

At a preoperative interview, the patient's mother informed an anesthesiologist that she and her mother had been diagnosed as having HAE. The patient's C1-INH protein level or function had not been quantified previously and he had not been diagnosed as having HAE. Our laboratory could not analyze his C1-INH protein level or C1-INH function immediately. We decided to treat the patient as an HAE suspect, because of the family history and the autosomal dominant form of inheritance. Therefore, we searched for C1-INH concentrates within the Kyoto–Osaka–Kobe metropolitan area (approximate population of 18 million) and could find only two bottles available within an hour. The search requests were made by the hospital pharmacy to CSL Behring, which is the sole supplier of C1-INH concentrate. The two bottles (Berinert P; CSL Behring, King of Prussia, Philadelphia, USA) were stored at Kyoto University Hospital in a neighboring city and they were delivered immediately. We administered one bottle (500 U) of C1-INH prophylactically before the surgery.

On arrival at the operation room, we attached standard monitors to the patient. General anesthesia was induced with 3 mg midazolam, 0.1 mg fentanyl, and 150 mg thiopental. The trachea was intubated with a 5.5-mm internal diameter (ID) tracheal tube and the cuff was inflated with 1 ml of air. Muscle relaxation was obtained with 3 mg vecuronium. We maintained anesthesia with sevoflurane and air in oxygen. We added vecuronium and fentanyl as needed. Perforation in the small intestine was confirmed and sutured. No swelling of the intestine was observed. After the operation, we reversed the muscle relaxant and extubated the tracheal tube when the patient was awake to follow easy commands.

Postoperatively, the patient was transferred to a pediatric ward, where he received a second dose of 500 U of C1-INH concentrate. The results of the serological study for HAE were reported several days after the operation. The complement 1 q subunit (C1q) protein level was 9.1 mg/dl preoperatively and 9.5 mg/dl 3 days after the operation (normal range, 8.8–15.3 mg/dl). The C1-INH function was 94% preoperatively and 218% 3 days after the operation (normal range, 80%–120%). Accordingly, the patient could not be diagnosed serologically as having HAE. He was discharged uneventfully 7 days after the operation.

Discussion

HAE is characterized by rapidly progressing edema in the skin, genitalia, intestine, and airway [2]. The attacks are triggered by trauma, stress, or direct laryngeal stimulation by a tracheal tube. These edemas do not respond to conventional edema treatments, such as corticosteroids, epinephrine, or antihistamines, because HAE is linked to lowered C1-INH protein level or function rather than to histamine [4]. Airway edema caused by HAE can be fatal, with a mortality rate of 30%–40% [3].

The incidence of HAE is estimated to be 1: 50000 and no ethnic group differences have been reported [1]. However, the number of diagnosed HAE patients in Japan is around 40 (personal communication disclosed at the HAE meeting in Tokyo, Japan 11 July 2009 by CSL Behring). Therefore, more patients are presumed to be undiagnosed.

HAE is classified into three types. Type I is characterized by lowered C1-INH protein level and type II is characterized by a normal C1-INH protein level with lowered C1-INH function [2]. Both types show an autosomal dominant form of inheritance. Type III, which has been described recently, shows different characteristics of the disease [1].

A diagnosis of HAE is made by clinical symptoms and by measuring complement factors, such as C1-INH protein level, C1-INH function, C1q, or C4 [1]. A diagnosis of HAE in our patient could not be confirmed before the emergency operation. HAE was suspected because of the family history and the abdominal pain [2]. It takes several days to obtain the serological results of C1-INH function or the C1q protein level. After considering the autosomal dominant inheritance and high mortality rate resulting from laryngeal edema triggered by intubation, we decided to treat the patient as an HAE suspect. Two days after the operation, we were informed that the preoperative C1q and C1-INH function had been normal. The diagnosis could not be confirmed as HAE, but normal C1-INH alone does not exclude HAE [2]. It has been reported that about half of HAE patients experience their first HAE attack after the age of 12 years [5]. As the patient was 8 years old, it was possible that he could have experienced the first attack during the perioperative period.

The treatment of HAE is classified into three types: long-term prophylaxis, short-term prophylaxis, and the treatment of acute HAE attacks [1, 2]. Long-term prophylaxis is indicated for patients with frequent or severe episodes of edema and consists of anabolic steroids and antifibrinolytics. Short-term prophylaxis is indicated for patients with HAE who are not on long-term prophylaxis but who are scheduled for surgical procedures that require tracheal intubation. Short-term prophylaxis consists of either a 5-day course of anabolic steroids or treatment with a C1-INH concentrate just before surgery. However, virilization and premature epiphyseal closure prevent the chronic use of anabolic steroids for prophylaxis in children. The treatment of acute attacks is by an intravenous supply of C1-INH in the form of either a concentrate or fresh-frozen plasma.

The present treatment of choice for the short-term prophylaxis of HAE is C1-INH concentrate [1]. The clinical use of C1-INH concentrate is approved in the European

Union and Japan. However, in countries such as the United States, where C1-INH concentrate is not yet approved, fresh-frozen plasma must be substituted for it,and this exposes the patients to the risks of infection associated with blood transfusions. The recommended dose of fresh-frozen plasma is 10 ml/kg, but scientific evidence for its use in HAE is not well studied [1].

HAE and its implications in anesthesia management have been reviewed, but standard treatment for an emergency case in a child has not been established [2]. This is the first study to report the prophylactic administration of C1-INH in an emergency operation to a patient who was suspected of having HAE because of the family history. It has been reported that adult HAE patients have had successful elective surgery under general anesthesia after receiving prophylactic pretreatment [6]. However, to the contrary, it was reported that a 15 year-old patient had an HAE attack after tonsillectomy under general anesthesia with tracheal intubation, although the patient had received prophylaxis with a C1-INH concentrate [7].

In the United Kingdom and Hungary, HAE patients are systematically diagnosed and alerted about their condition [4]. Some patients are advised to keep a bottle of C1-INH concentrate in the refrigerator in their house. C1-INH concentrates are stored regionally [4]. However, such a system does not exist in Japan; because of the cost (108,191 yen/500 U bottle) and the rarity of the disease, only a few hospitals store the C1-INH concentrate. We were very fortunate that we could locate concentrated C1-INH in a neighboring city. It is desirable to establish a systematic network for the storage of C1-INH concentrate in Japan, if the cost of its purchase and storage is deemed allowable.

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