Perioperative management of a patient with hereditary angioedema with prophylactic administration of C1 esterase inhibitor

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ABSTRACT

Hereditary angioedema (HAE) is a rare autosomal dominant genetic disorder that causes a deficiency in or dysfunction of C1 esterase inhibitor (C1-INH). HAE attacks are caused by trauma, drugs, infection, or mental stress. Dental procedures in patients with HAE can trigger fatal laryngeal edema. We herein report a female patient with HAE who required tooth extraction.

A 58-year-old Japanese woman was referred to our hospital for dental caries. Maxillary teeth contained residual roots that could not be preserved, and mandibular teeth had poor plaque control and progressive periodontal disease. Therefore, consent was obtained from the patient to create dentures after extraction of all remaining teeth. The patient had recurrent edema since she was approximately 20years old. She was diagnosed with HAE due to C1-INH deficiency at our hospital. She had an HAE attack of the tongue and laryngeal edema and underwent emergency tracheotomy. Subsequently, she had repeated edema of the tongue and lips several times a month. She had edema following tooth extraction. She was referred to our hospital and her condition improved by intravenous administration of C1-INH. C1-INH and tranexamic acid were prophylactically administered 1 h preoperatively. Anesthesia was induced with intermittent infusion of midazolam and continuous infusion of dexmedetomidine. Local anesthesia was provided using 3% propitocaine with felypressin. The patient was transferred to the intensive care unit for further observation. There was no postoperative complication. She was discharged after 3days. No other HAE complications occurred during the perioperative period, and perioperative management went well. *Ryukyu Med. J., 39 (1~4) 45~48, 2020*

Key words: Hereditary angioedema(HAE), C1 esterase inhibitor (C1-INH), tooth extraction

Ⅰ. INTRODUCTION

Hereditary angioedema (HAE) is an autosomal dominant disorder that causes deficiency in or dysfunction of C1 esterase inhibitor (C1-INH). HAE is clinically characterized by sudden and recurrent attacks of angioedema. HAE is often caused by edema due to dental procedures and may cause fatal laryngeal edema; thus, sufficient consideration is necessary[1]. We herein report the case of successful management of tooth extraction with C1-INH in a

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patient with HAE who had a past history of tracheostomy due to pharyngeal edema.

Ⅱ. CASE REPORT

A 58-year-old Japanese woman was referred to our hospital for dental caries. Maxillary teeth contained residual roots that could not be preserved, and mandibular teeth had poor plaque control and progressive periodontal disease (Fig. 1). Therefore, consent was obtained from the patient to create dentures after extraction of all remaining teeth.

The patient had recurrent edema of the fingers, face, and lip since she was approximately 20years old. At 30years of age, she was diagnosed with HAE due to C1-INH deficiency at our hospital. Medical staffs explained that most HAE patients have a positive family history. HAE can be precipitated or exacerbated by minor trauma, emotional upset, infection, menstruation, pregnancy, cold exposure, certain foods or drugs. In addition, if edema was observed in the lips, tongue, and pharynx, they were instructed to see a doctor immediately. The patient's family history included HAE in her father and brother, who were diagnosed at our hospital. Her brother died of symptoms that were likely caused by laryngeal edema due to HAE. At 31years of age, she had an HAE attack of the tongue and laryngeal edema and underwent emergency tracheotomy. Subsequently, she had repeated edema of the tongue and lips several times a month, which we tried to treat by administering C1-INH (Berinert P®, CSL Behring, Marburg, Germany). At 36years of age, she had lip edema following tooth extraction at a dental office. She was referred to our hospital and her condition improved by intravenous

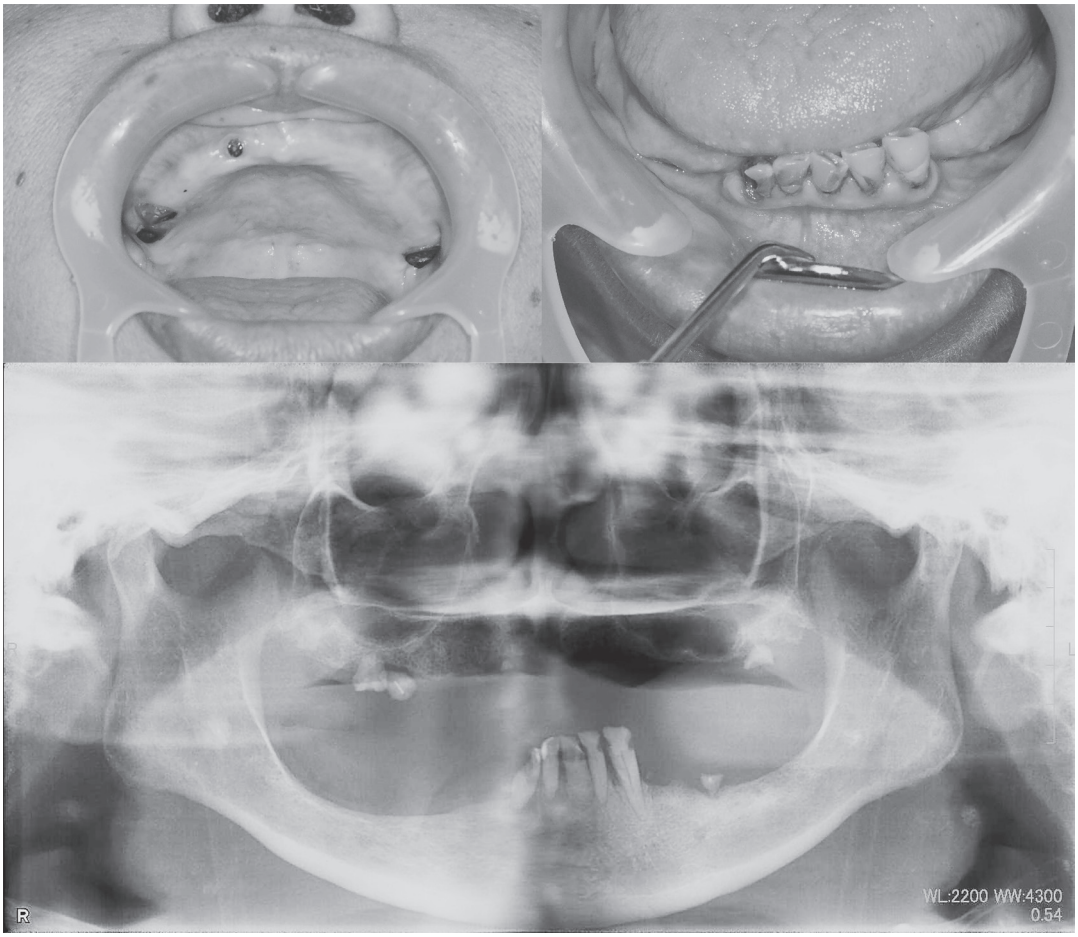

Fig. 1 **Clinical photograph and Panoramic radiographic image.**
a, b: Clinical photograph c: Panoramic radiographic image.
Maxillary teeth contained residual roots that could not be preserved, while mandibular teeth exhibited progressive periodontal disease.

administration of C1-INH. Furthermore, she developed edema of the soft palate following another tooth extraction at a dental office at 37years of age. She was referred to our hospital and intravenous administration of C1-INH was given. At 38years of age, she again developed lip edema following tooth extraction at our department, which was improved by intravenous administration of C1-INH.

She also had a medical history of diabetes mellitus, dialysis for chronic renal failure, abdominal incisional hernia, schizophrenia, and sleep apnea syndrome.

We elected to perform the procedure in the operation room because of the patient's history of frequent lip edema and abovementioned medical history, which would allow us to perform emergency tracheotomy or intubation if necessary.

In 2017, C1-INH was approved for treatment against HAE attacks in Japan. The patient's pre-anesthetic evaluation was unremarkable. C1-INH (1,000U) and tranexamic acid (1,500mg) were prophylactically administered 1 h preoperatively. Two additional doses of C1-INH and preparation for tracheotomy were on hold in case of need of midazolam.

Anesthesia was induced with intermittent infusion of midazolam at 1 mg/time (total 4mg) and continuous infusion of dexmedetomidine at 20 −32μg/h.

Local anesthesia was provided using 3% propitocaine with felypressin. The patient's respiratory status and hemodynamics and state of sedation remained stable throughout the procedure. The procedure time and sedation time were 28 and 70min, respectively.

The patient was transferred to the intensive care unit for further observation. There was no postoperative complication. She was discharged after 3days.

Ⅲ. DISCUSSION

HAE is a rare autosomal dominant disorder caused by C1-INH deficiency that affects an estimated 1 in 50,000individuals. There are various acquired types of angioedema such as angiotensin-converting-enzyme inhibitor-induced angioedema or edema due to mast cell mediators[1].

Most HAE patients have a positive family history. HAE can be precipitated or exacerbated by minor trauma (50% of cases), emotional upset (30 −40% of cases), infection, menstruation, pregnancy, cold exposure, certain foods or drugs (angiotensin-converting-enzyme inhibitors or estrogen oral contraceptives)[2]. HAE can also occur without any obvious trigger.

As a result of investigation of edema symptoms in 130,000cases of 221 HAE patients, the initial mean age of onset was considered to be 11.2years. The predominant seizure site (97.4%) of edema site was limbs, faces, reproductive organs, subcutaneous trunk, and abdomen. Other edema sites included laryngeal edema (0.9%), soft palate edema (0.6%), and tongue edema (0.3%)[3]. Severe and fatal symptoms include asphyxia due to airway obstruction from throat pharyngeal edema, and it has been reported that about 30% of airway obstructions by HAE result in death due to asphyxia[4].

More HAE patients with edema attacks due to tooth extraction have other surgical complications, as well as severe edema[5]. Deaths due to laryngeal edema after tooth extraction have also been reported, and severe edema may occur[6]. In the present case, the patient had an attack of tongue and laryngeal edema and an emergency tracheotomy was performed. Therefore, it is necessary to thoroughly examine interventions to prevent and ameliorate edema.

Furthermore, because HAE is triggered by dental treatment, which can cause life-threatening airway obstruction and laryngeal edema several hours to several days after the triggering treatment, dentists should be aware of HAE.

Bork et al. reported edema in 124 (21.5%) of 577 extraction cases that did not receive any preventive methods. Among 128 of 705 tooth extraction cases who had short-term prevention by Cl-INH replacement therapy, edema was found in only 16 cases (12.5%)[7].

According to the World Allergy Organization in collaboration with the European Academy of Allergy and Clinical Immunology guideline[1], C1-INH concentrate should be used for preprocedural prophylaxis as close as possible to the start of the procedure. However, the standard dosage has not yet been established and product-approved indication may vary by country. Most experts use either 1,000units or a dose of 20units/kg of pdC1-INH. In

Japan, it became possible to administer C1-INH for the purpose of suppressing HAE attacks in 2017. C1-INH is administered as 1,000—1,500IU within 6h before invasive treatment. In this case, 1,000IU C1-INH were given 30 min before the start of the procedure. The patient had three HAE attacks following tooth extraction before C1-INH prophylaxis was approved in Japan. However, the patient has not developed edema since we administered preoperative C1-INH.

Tranexamic acid has been used for preprocedural prophylaxis in the past but is not recommended by most experts in attendance at the guideline meeting[1]. Therefore, irrespective of dental treatment invasiveness, preparation of C1-INH seemed to be necessary regardless of whether C1-INH was prophylactically administered.

Precipitating triggers mentioned above should be avoided. Local or general anesthesia can be safely performed in such patients. Local anesthesia with sedation is preferred wherever possible because of superior suppression of the stress response and avoidance of airway manipulation can be achieved.

We experienced successful management of tooth extraction in a patient with HAE who had a past history of tracheostomy due to pharyngeal edema. Successful perioperative management requires prophylactic C1-INH, diligent monitoring, and measures to avoid airway edema triggers.

Ⅳ. CONCLUSION

While it is rare to encounter HAE, this condition can have fatal consequences. Therefore, dentists should pay careful attention to HAE, including perioperative management of HAE in dental treatment.

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