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Up-to Date Review And Case Report

Hereditary angioedema type II and dental extraction: case report and literature review

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Abstract – Introduction: The hereditary angioedema of type II (HAE type II) is a disease which, in the case of invasive acts such as dental extractions, can trigger potentially fatal laryngeal edema. **Observation:** A 64-year-old man presented to the hospital to perform dental extractions. The anamnesis revealed a history of hereditary angioedema of type II. The National Reference Center for Angioedema (CREAK) recommended a prophylactic protocol before performing this traumatic dental procedure in order to reduce the risk of post-operative edema. **Discussion:** The HAE type II is under- or misdiagnosed. The literature reports cases of death related to dental procedures in patients unaware of being a carrier of the disease. **Conclusion:** In case of certain evocative signs (recurrent edema, abdominal pain, family history, etc.), the odontologist must play an active role in the early detection of HAE type II.

Introduction

The hereditary angioedema (HAE) type II is a rare and life-threatening genetic disorder that is often under- or misdiagnosed [1]. It is caused by mutations in the SERPING 1 gene, which causes a qualitative defect in the C1 esterase inhibitor (C1-Inh), leading to an abrupt and localized release of bradykinin, a peptide with vasodilating properties. This leads to an increased vascular permeability which can lead to edema of the face, limbs, upper airways or digestive tract.

The edema is sudden, subcutaneous and/or submucosal, circumscribed, white, non-pruritic and disappears without sequelae in 2–5 days [1]. The appearance of HAE is spontaneous or caused by local trauma such as oral care, by taking certain medications or by emotional stress [2]. The first signs of HAE can occur at any age but most often begin in childhood [3].

Facial edema (*e.g.* following dental treatment) is at high risk for laryngeal damage, with a risk of death by asphyxiation in the absence of specific treatment. It is therefore essential, before treating any new patient, to collect a complete medical history and apply a specific protocol.

Observation

The reported case is that of a 64-year-old man referred by his dental surgeon to the dentistry department of his local university hospital for dental extractions. In this patient, a diagnosis of HAE type II had been made in 2009 by the CREAK. He also suffered from lumbar osteoarthritis and dyslipidemia. The patient was treated with icatibant (FIRAZYR®), 30 mg in case of an attack.

The first manifestations of the disease appeared within his childhood (5–6 years), as edemas with multiple localizations: abdomen, hand, foot, face. Despite a family history, the patient was diagnosed at 54 years of age. With age, the attacks seem to diminish in frequency and intensity. Spontaneous edema occurs, approximately every 3 weeks, touching a single finger and disappearing during the day. In 2020, endodontic treatment without a prophylactic protocol resulted in facial edema (without laryngeal involvement) that disappeared after 2–3 days. In 2017, dental extractions were performed and in 2018 implants were placed with a prophylactic protocol 6 hours before the intervention with a C1Inh concentrate (BERINERT®), 20 U/kg. In both cases, there were no post-operative complications.

At the intraoral clinical examination, the patient complained of discomfort in the maxillary teeth. The gum next to

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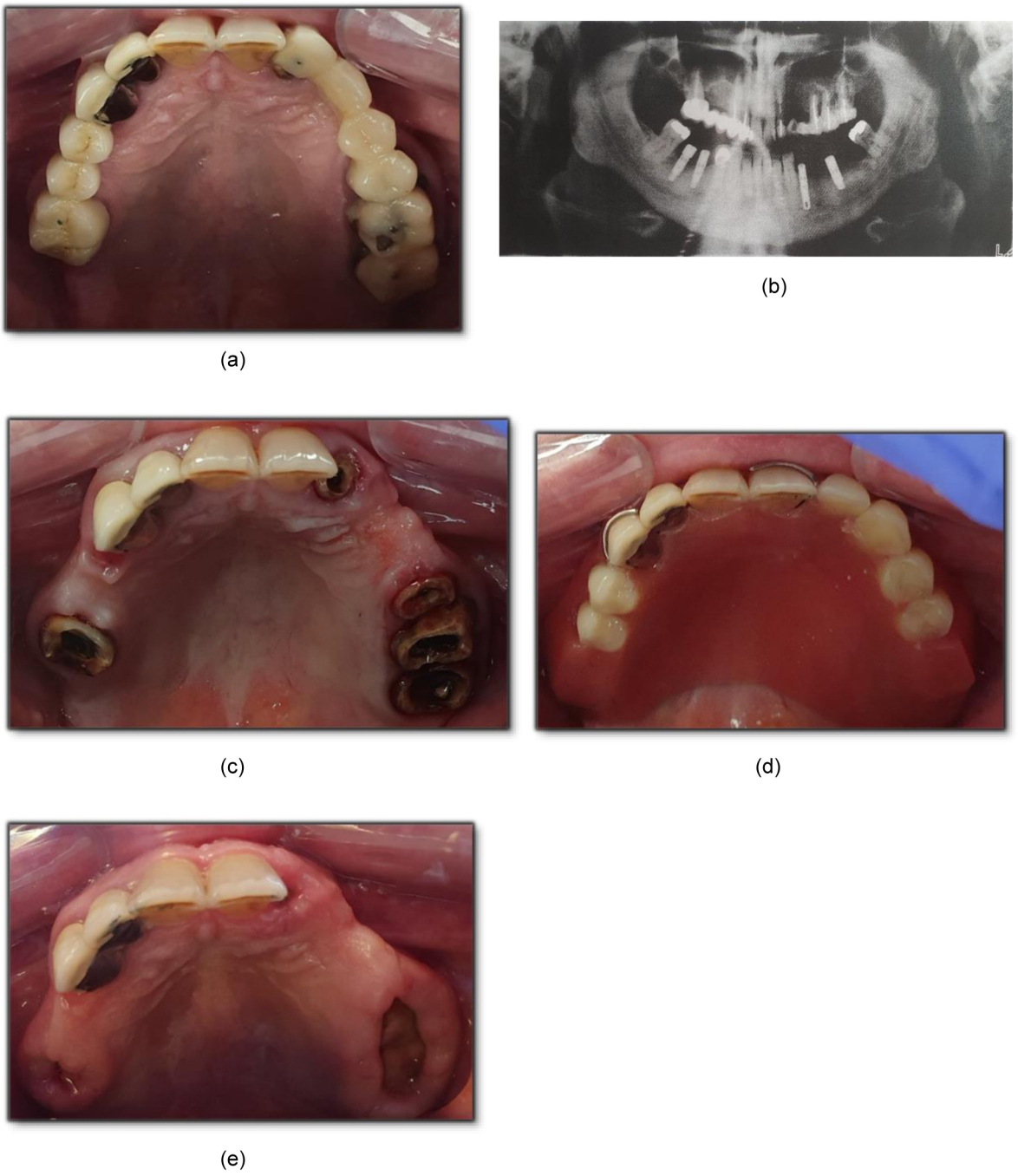

Fig. 1. Iconographies of the clinical case. (a) Intraoral photography in preoperative. (b) Orthopantomogram. (c) Maxillary occlusal view in peroperative. (d) Removal partial denture. (e) Postoperative view.

the teeth n°25-26-27 was inflammatory. Two temporary bridges, from tooth n°13 to tooth n°16 and from tooth n°22 to tooth n°27 were present and mobile (Fig. 1a). The survey revealed periodontal pockets in teeth n°16-22-25-26-27. A recurrence of decay lesions was observed in these same teeth. In the mandible, the teeth were healthy and asymptomatic. The orthopantomogram showed periradicular radiolucency in teeth n°16-22-25-26-27 and horizontal alveolisis reaching 1/3 of the root height (Fig. 1b).

After multidisciplinary consultation, an appointment was scheduled to perform avulsions of teeth n°16-22-25-26-27 (Fig. 1c). In the context of an hospitalisation, the following protocol was set up following the recommendations of the CREAK: a C1Inh concentrate injection (BERINERT®), 20 U/kg, in the 6 hours preceding the procedure to be completed in the event of an attack with icatibant (FIRAZYR®), 30 mg. During the procedure, additional precautions were taken in order to limit the risk of post-operative edema: the choice of a para-

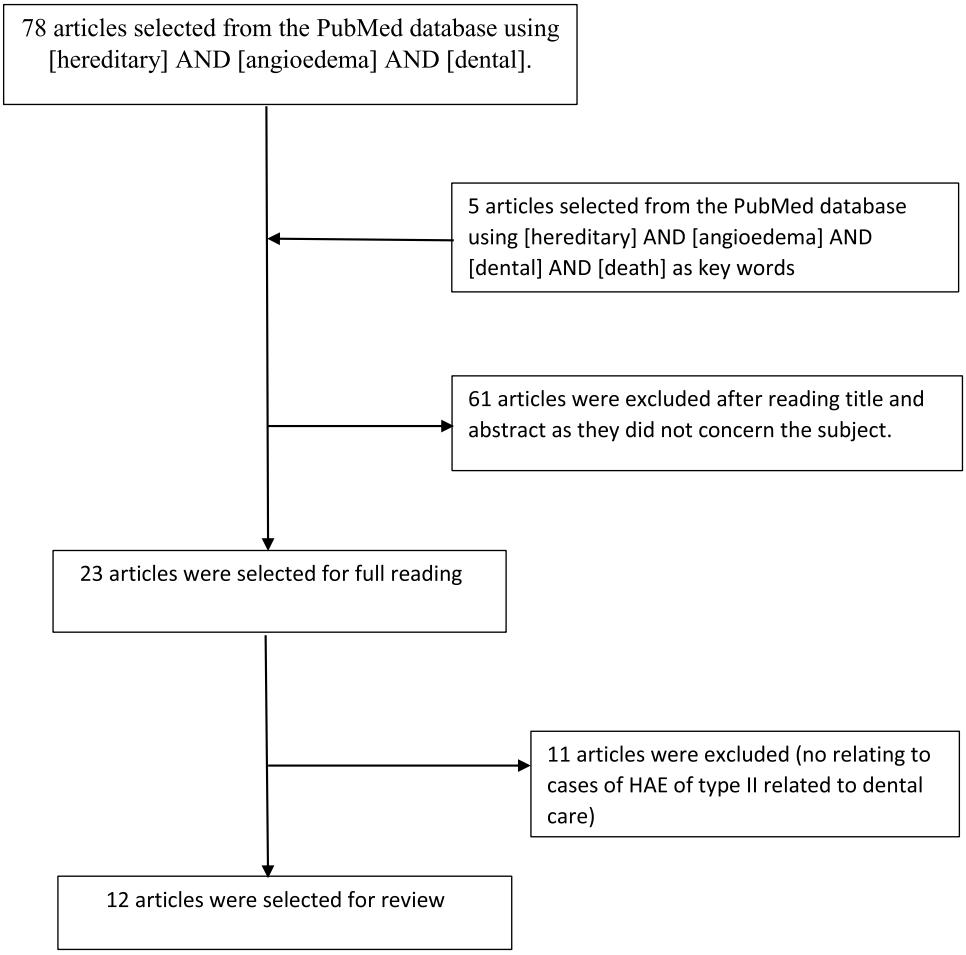

Fig. 2. Flow chart.

apical local anesthetic (articaine with epinephrine 1/200000) was made and injected slowly to prevent any risk of trauma.

Likewise, multiple-rooted teeth extractions were performed with root separation, and flapless. (Fig. 1c).

At the end of the procedure, a transitional partial denture was placed (Fig. 1d). Before installing the device, the surface condition was checked to avoid any mucosal trauma. Post-operative advices have been clarified. A stage I analgesic and an antiseptic solution were ordered. The patient remained hospitalized for the night, for observation. No laryngeal edema occurred.

At the post-operative appointment (J14), healing was satisfactory (Fig. 1e). The sutures have been removed and the transitional removable device was readjusted at this time (Fig. 1f) to avoid any trauma to the mucosa.

Discussion

HAE of type II is a rare disease [4], which can lead to life-threatening edema of the limbs and face. In order to enrich the presentation of this case, a review of the literature on the PubMed search engine was conducted from 2002 to 2019 with the following search equation: [hereditary] AND [angioedema] AND [dental]. 12 articles have been retained among 78 articles initially selected (Fig. 2). Articles were excluded if it was clear from the title of the article or abstract that the topic was not relevant or did not meet the criteria of the literature review (articles relating to cases of HAE of type II related to dental care).

The main causes of the appearance of HAE reported in the literature are dental extractions, taking certain medications, stress, pulp devitalization and taking dental impressions (Table I). Different care protocols are reported in relation to the performance of the various acts of odontostomatology.

Dental extractions appear to be the most common trigger for HAE type II, since 8 cases have been reported in the literature [6,9,10]. Among these 8 cases, two had a fatal outcome [6,9]. In both cases, the patient did not know that he was a carrier of HAE. It should be noted that in most cases the edema arrives late after the operation, sometimes more than 2 days later, which underlines the importance of post-operative follow-up [10]. In this case, the patient should be warned that edema may appear even several days after the operation. The patient must be attentive to any respiratory difficulties in order to act quickly. Dysphagia, a weak or

Table I. Summary of selected articles.

Ref	Year	Age/Sex	Risk factors	Summary
[5]	2019	24/H	Drugs (Ibuprofen, Codeine)	Angioedema triggered by taking analgesic drugs after fracture of the mandible
[13]	2019	20/H		Successful prerioperative management, with C1-INH prophylaxis
[4]	2016	26 to 54/H-F	Anxiety	Tooth extraction in 6 patients with HAE type II with C1-INH prophylaxis and anxiety management
[9]	2017	50/F	Dental extraction	Fatal laryngeal angioedema 2 days after dental extractions in a woman anaware of having HAE type II.
[12]	2015			Review of practitioners' awareness of the different treatments for perioperative management of HAE type II
[14]	2015	13/H		Management with C1-INH prophylaxis.
[11]	2011			Presentation of the clinical aspects of HAE type II, recent data of its management in emergency and perioperative. In hereditary forms, depending on the location and severity of the seizures, emergency treatment is based on the use of Icatibant, a bradykinin B2 receptor antagonist, and of the C1 inhibitor concentrate.
[7]	2011	42/F	Pulp extirpation	Angioedema triggered by pulp extirpation in a patient unaware of having HAE type II.
[15]	2010	56/H 18/F 12/F		Invasive dental care with C1-INH prophylaxis without perioperative complications
[6]	2008	28/F	Dental extraction	Angioedema several hours after tooth extraction in a patient unaware of having HAE type II
[10]	2003		Dental extraction	Four patients died from laryngeal oedema induced by tooth extraction which, after a symptom-free latency of 4 to 30 hours, caused laryngeal edema. Three of the patients died of suffocation the night after surgery and the fourth died the second night.
[8]	2002		Dental impressions	Perioral angioedema secondary to taking dental impressions

inaudible voice can also be the prodromes of a future laryngeal attack.

Certain drug treatments also appear to be a trigger. Hammond *et al.* report a case of a patient with HAE type II after taking ibuprofen and codeine [5].

Psychological stress may trigger edema [4]. For this reason, prior to tooth extraction in a patient with HAE, Rosa *et al.* describe the use of conscious sedation to reduce anxiety and thus pain perception to help prevent post-operative angioedema [4].

Baliga *et al.* described a case of HAE type II following pulp devitalization. In this case, the patient was unaware that she had this disease and no family history had been reported [7]. More marginally, a case of HAE was described following dental impression taking [8].

Short-term prophylaxis consisting of the injection of C1-Inh within 6 hours before the procedure does not completely avoid the risk of postoperative edema, which is why the use of icatibant (FIRAZYR®) or the concentrate injection of C1-Inh (20 U/kg) may be necessary postoperatively [12].

Early diagnosis of this disease is essential [11] although the lack of specificity of symptoms complicates the diagnosis [1]. In this context, most incidents during dental care have occurred in patients who were unaware of being a carrier of this disease [13,6,5,9]. HAE type II should be mentioned in the case of any clinical signs suggestive of the disease: isolated non-erythematous and non-pruritic angioedema, unexplained recurrent abdominal pain, recurrent oral edema or a family context [11]. However, only the quantitative and functional C1-INH assays and the C4 Complement Compound assay can certify the diagnosis. A concentration of C1-INH lowered on two samples allows to confirm the diagnosis. The treatment of the pathology takes place in specialized centers, the CREAKs [16].

Conclusion

This report shows the importance of early diagnosis of HAE type II, allowing effective multidisciplinary care and control of a risk management of post-operative edema.

Mobilization of practitioners to know and suspect this disease must be important in view of the fatal nature of the attacks. In the case of recurrent and transient edema, type II HAE should be mentioned and a consultation at the CREAK reference center should be considered. Studies are underway to improve the early diagnosis. The genotype-based approach should eventually allow earlier detection of this type of pathology.

Conflicts of interests: The authors declare that they have no conflicts of interest in relation to the publication of this article.

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