Management of a Dentigerous Cyst in a Child with Hereditary Angioedema

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ABSTRACT

The purpose of this paper was to report the case of an 8-year-old girl with hereditary angioedema (HAE) who underwent 2 oral surgeries for removal of a dentigerous cyst without any significant episode of angioedema. One week after routine radiographic examination revealed an odontogenic cyst, short-term prophylactic therapy (Danazol 600 mg/day) was initiated to avoid an angioedema attack. The cyst was carefully removed under general anesthesia without life-threatening complications. Postoperative prophylactic therapy also was performed. Histopathological exam confirmed the diagnosis of a dentigerous cyst. Nine months after surgery, the cyst recurred and it was successfully removed once more under general anesthesia. The same prophylactic therapy was used, this time with fresh frozen plasma. The case presented showed that the oral management of a pediatric patient with HAE is a high-risk procedure. It can be performed successfully, however, when the involved health professionals are aware of both the risks and preventive strategies.

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Hereditary angioedema (HAE) is a rare autosomal dominant disorder with incomplete penetration, characterized by a deficiency or functional anomaly in complement C1 esterase inhibitor (C1-INH).[1] C1-INH protein is the main regulator of the activation steps of complement pathway. It operates to block C1, the first protein in the complement system.[2] Once C1 protein is activated with C1-INH deficiency, an uninhibited activation of the entire complement system will occur, resulting in increased vascular dilatation and permeability, with excessive uncontrolled edema of the affected part.[3,4]

Currently, 2 types of HAE have been described: HAE type I (C1-INH deficiency in circulating concentration), which has been reported to range from 69% to 91% of affected patients,[5-8] and HAE type II (C1-INH concentration is normal but not functional). The prevalence of this disease is unknown, but current estimates suggest that it affects 1 in 10,000 to 1 in 50,000 persons.[9]

The manifestations of HAE are multiple, transient, and often subtle. Episodes are characterized by nonpruritic, localized edema[10] of the gastrointestinal tract accompanied by abdominal pain, nausea, protracted vomiting, and diarrhea; edema of subcutaneous tissue of face, hands, arms, legs, and genitals[3,5]; or laryngeal edema, which can manifest as dysphagia, sensation of a lump in the throat, voice changes, dyspnea, or even life-threatening laryngeal edema leading to airway obstruction.[8,11,12] The condition can result in debilitation and reduced quality of life,[13] although the frequency and severity of these episodes range widely among affected individuals.[5] The symptoms seem to be more severe in women than in men, and patients with early onset of clinical symptoms seem to be affected more severely than those with late onset.[14]

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Angioedema can result from some stimulus[5] or it can appear spontaneously without any apparent reason, which occurs in the vast majority of cases.[5,8] Factors reported as a trigger for angioedema are psychological stress, menstruation, and trauma (direct or indirect).[5] It is important to emphasize that the trauma factor includes: surgery[13]; intubation to general anesthesia[8]; and dental procedures such as prophylaxis, impressions, restorations, endodontics, and oral surgery.[12,15-18]

HAE treatment is usually classified into 3 types: (1) long-term prophylactic therapy; (2) short-term prophylactic therapy; and (3) treatment of acute attacks. Long-term prophylactic therapy is used for patients who usually present angioedema attacks (more than once a month). Treatment is performed with: antifibrinolytic agents; synthetic anabolic androgens (Danazol and Stanozolol); and C1-INH. The choice and dosage depend on frequency and severity of attacks and on patient characteristics. Short-term therapy is used before procedures that can result in an angioedema episode such as intubation and dental treatment and is similar to long-term prophylactic therapy with the addition of fresh-frozen plasma. Treatment of acute attacks is performed with C1-INH concentrate,[10,17]

The aim of this paper was to report the case of an 8-year-old Brazilian girl with hereditary angioedema who underwent 2 oral surgeries for dentigerous cyst removal.

CASE REPORT

An 8-year-old Brazilian girl was referred from her immunologist to the handicapped patients unit of the Department of Pediatric Dentistry, School of Dentistry, of Federal University of Rio de Janeiro, Brazil, due to a swelling on the right side of her face (Figure 1a and b).

During anamnesis, the patient's mother reported that the child had HAE type 1, which was diagnosed when she was approximately 5-years-old, after her father was diagnosed. She also mentioned a strong family history of HAE: 1 aunt and 2 cousins had the condition. The mother also reported that the patient probably had an angioedema attack in her legs at 2-years-old, which was diagnosed and treated as a urinary infection; the condition had already presented sporadic episodes of abdominal pain.

The patient had not received any long-term prophylactic therapy to avoid angioedema episodes until the time of this dental appointment. According to the immunologist, she did not need treatment because the angioedema attacks were not frequent and the specific medicine for treatment, synthetic anabolic androgens, is not indicated for children.

Extra- and intraoral examination revealed a swelling on the right side of the face and an enlarged mass in the region of the maxillary right canine (Figures 1a and b and 2). Dental examination revealed a mixed dentition with various treatment needs (restorations and extractions).

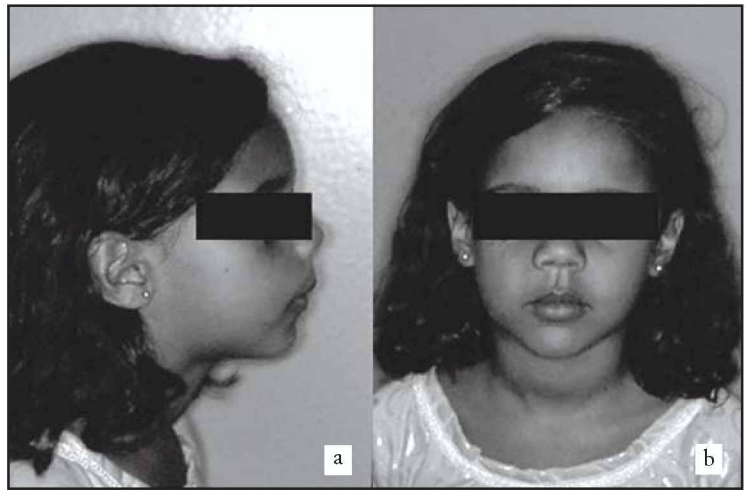

Figure 1. (a and b) Swelling on the right side of the face.

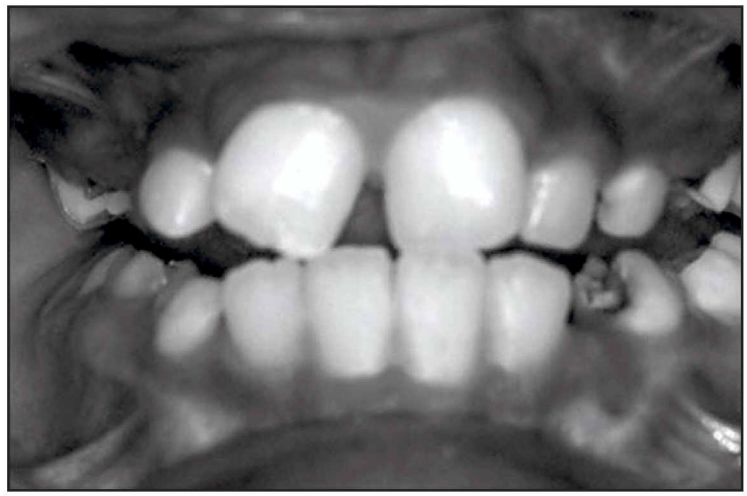

Figure 2. Enlarging volume in the permanent maxillary right canine region.

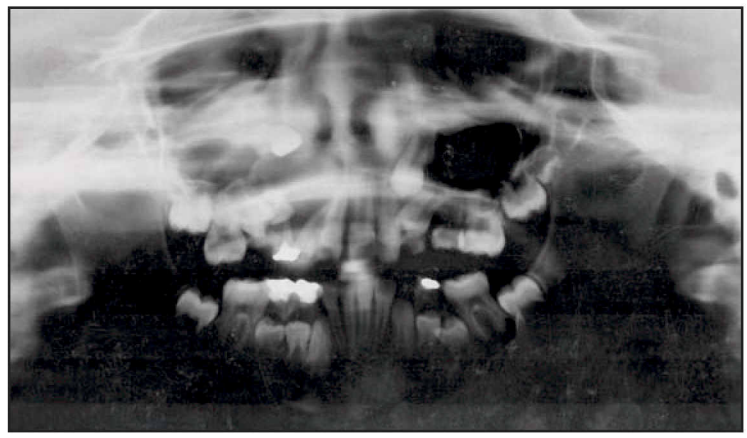

Figure 3. Image suggesting the presence of a cyst related to the permanent maxillary right canine's crown.

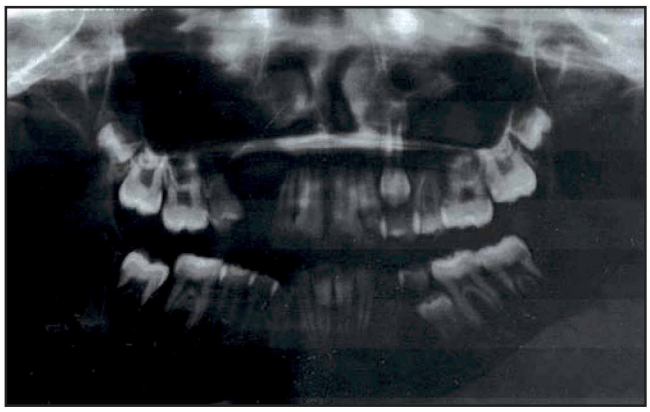

Figure 4. Follow-up panoramic view, 9 months after cyst removal, showing dentigerous cyst recurrence.

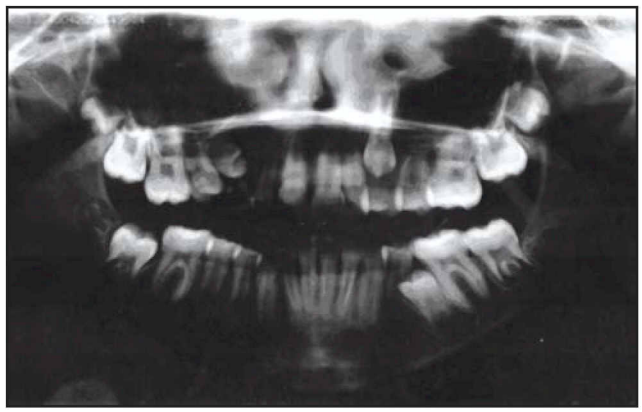

Figure 5. Follow-up panoramic view, 3 months after recurring cyst removal, showing lack of a dentigerous cyst image.

Radiographic examination was requested (periapical and panoramic) to formulate a treatment plan. The panoramic view showed an image suggesting a cyst related to the crown of the permanent maxillary right canine (Figure 3).

After an unsuccessful effort to find someone to remove the cyst under general anesthesia (all requested dentists refused to perform the treatment because of the patient's life-threatening condition), a member of the oral surgery staff consented to perform the treatment. Physical examination and review of systems were unremarkable, and laboratory tests were all within normal limits to administer general anesthesia. One-week, short-term prophylactic therapy was planned, to be followed by another week of postoperative treatment of 600 mg/day of Danazol (an attenuated androgen) in an effort to avoid an angioedema attack.

The patient was subjected to a cyst enucleation that also involved removing the permanent maxillary right canine and attending to all necessary restorations and extractions under general anesthesia. On the day after surgery, when the patient was still in the hospital, a facial angioedema developed on the right side, lasting 4 days but without further complication. Histopathological exam confirmed the diagnosis of dentigerous cyst.

Nine months after cyst removal, a follow-up panoramic X ray revealed a recurrence of the cyst (Figure 4). The surgery was repeated using the same general anesthesia and type of medication, this time with fresh frozen plasma (to replace C1-INH). It was decided to use plasma because of its duration and intensity and the patient's history of angioedema during the first surgery. The maxillary right first premolar also was removed because its position would have prevented its eruption. One day postsurgery while the patient was still in the hospital, she had another angioedema attack on the right side of her face. Despite the prophylactic therapy, the attack was more severe than that of the first surgery, however, no life-threatening complications occurred.

Three months after removing the recurring cyst, another follow-up panoramic exam was performed and no evidence of recurrence was noted (Figure 5). The patient is still being observed, and the dental treatment will be performed in the dental office under short-term prophylactic therapy for HAE.

DISCUSSION

The patient in this case report had the most frequently occurring type of HAE—type I. Although some authors[5] reported that patients with this condition usually become symptomatic within the second decade of life, in the present case the patient was 8-years-old and had already presented a probable attack when she was 2-years-old.

There are many reported cases showing late diagnosis of this condition because of its complex symptoms. This subjects patients to many hospitalizations, with the angioedema attacks often wrongly diagnosed, and the treatment sometimes results in death.[11,15,19-21] In this case, although the patient was diagnosed during childhood, a probable episode—treated as a urinary infection—had already occurred before the diagnosis.

The HAE diagnosis of this case was a due to the family history, after the patient's father's diagnosis, as previous reported.[11] But there are cases in which no similar family history is present,[6,15] making diagnosis difficult and late. The necessity of studying all family members when HAE is diagnosed has been emphasized in order to detect asymptomatic children.[7] After investigation of a whole family, a rare mosaicism case was found in the parents of the affected brothers,[22] reinforcing the importance of molecular genetic studies in family members who do not present clinical manifestations of the disease. In the present case, this was not necessary because the child's father and aunt had already been diagnosed with the condition.

Our patient had presented a dentigerous cyst with characteristics in agreement with the literature. Dentigerous cysts are the most common odontogenic cysts, frequently observed in patients between 10 and 30-years-old;

the second-most involved teeth are the maxillary canines. These cysts can remain asymptomatic until routine radiographic examination or until painless expansion of the bone appears. It is important to mention that they can displace the involved tooth for a considerable distance.[23] The present case was diagnosed after radiographic exams. In the radiograph (Figure 3), a displacement of the permanent maxillary right canine, the involved tooth, could be observed; a malpositioned maxillary right first premolar was seen that also could have been displaced by the cyst. Conversely, recurrence of dentigerous cysts is not common, so the recurrence could have been the result of a cyst associated with the maxillary right premolar which was not removed at the first surgery.

In a study performed with 53 HAE patients, 4 presented oral cysts requiring removal and none experienced angioedema after cyst removal. The authors pointed out that, although it is a high number, it is important to consider that it was just a group of patients, and it may be a coincidental finding, suggesting the need of periodic panoramic radiographs for these patients.[16]

The difficulty of treating the oral needs of patients having angioedema has already been reported. Of 57 observed patients, one third had problems obtaining oral treatment (a common cause of acute attacks), and half of this group had experienced an acute angioedema attack following dental treatment.[17] This situation was fully ex-perienced in the present case.

In agreement with the oral surgeon and immunologist physician, treatment under general anesthesia was chosen because of the controlled setting where the life-threatening angioedema could be treated if it occurred. Fortunately, no life-threatening episode occurred. Despite the fact that laryngeal edema consequent to intubation has already been demonstrated[8] and that intravenous sedation as an alternative treatment[15,24] in this setting is still more secure, some cases have already been done this under general anesthesia.[4,14,23]

Danazol (attenuated androgen), which raises the C1-NIH level, can be used before and/or after the procedure.[26,27] Fresh frozen plasma (containing a concentration of C1-NIH) can be used before or during the procedure.[15,25,26] Although some authors suggest the use of different medications, there is no definite rule in the reviewed literature for the right way to use the available medications to prevent an attack.[13,28] Currently available agents used to treat HAE prophylactically are suboptimal.[13] Although it is not possible to eradicate an acute attack during Danazol therapy and despite the high risk of adverse effects, many patients accept this medicine to avoid the distressing and sometimes life-threatening attacks.[29]

Oral management of a pediatric patient having HAE can be performed successfully if the involved health professionals are aware of both the risks and preventive strategies. A successful outcome depends on a multidisciplinary professional relationship and a careful treatment plan. Even so, health professionals must be prepared for undesirable angioedema episodes.

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