

ABSTRACT

Vibratory angioedema (VA) is a rare, inherited type of physical urticaria characterized by acute onset of mucosal and / or cutaneous edema that is triggered by vibration. We report a case of a 63-year-old woman with VA elicited by use of mechanized (vibratory) dental equipment. To our knowledge, this is the first report of VA induced by mechanical dental equipment.

KEY WORDS: Vibrational angioedema, dental

Vibrational angioedema: considerations for oral health care providers

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In 1888, hereditary angioedema (HAE) was first reported and described by William Osler.¹ The disorder was initially termed hereditary angio-neurotic edema (HANE) and subsequently changed to its current terminology. HAE is characterized by a deficiency in functional C1-esterase inhibitor (C1-INH) due to mutations in one of the two alleles of C1-INH gene, SERPING1.² HAE follows an autosomal dominant inheritance pattern and is associated with significant morbidity and mortality. The prevalence of HAE is unknown, but is estimated to range from 1: 50,000 in the general population without any known sex, ethnic, or racial differences.^{1,2}

HAE is commonly misdiagnosed due to low awareness of this condition and similarity of HAE symptoms to other disorders.³ In 1977, the average time between the onset of symptoms and HAE diagnosis was 22 years.⁴ Additional research into the genetics, pathogenesis, biochemical mechanisms and clinical management of HAE has enabled health care providers to diagnose this condition earlier and by 2005, the average time from symptom onset to diagnosis decreased to approximately 10 years.^{3,4}

HAE is typified by recurrent episodes of intense, erythematous, non-pruritic, non-pitting edematous, cutaneous and subcutaneous lesions, which may be localized or generalized, as a response to identifiable triggers.^{5,6} Recurrent episodes of laryngeal edema and abdominal pain may also be observed.⁵ HAE typically involves the face, tongue, larynx, extremities, trunk, bowels, and / or genitalia.⁷ Patients may be at risk for airway obstruction, which can result in a profound impact on

quality of life and lead to a life-threatening situation.⁵ HAE may also cause difficulty swallowing and change in voice quality. Edema typically progresses slowly, peaks over the first 24 to 36 hours, and usually resolves within 72 hours or in some cases, may persist for as long as 7 days. HAE may also affect the abdomen and cause abdominal symptoms such as intra-abdominal swelling, cramping, vomiting, nausea, diarrhea, dehydration, pain and intestinal obstruction, and may potentially lead to hypovolemic shock.⁸

Although the exact pathophysiology is not fully understood, it is recognized that histamine typical of allergic edema is not a factor in this condition.⁹ Abnormal levels of C1-INH results in an inability to regulate complement activation and excessive generation of pro-inflammatory mediators. The acute onset of edema is thought to be the result of temporary excessive activation of vasoactive substances that cause dilatation and increased permeability of small blood vessels. Eventually, edema develops by

temporary allowing fluid to travel into deeper layers of cutaneous and mucosal tissues.¹⁰

HAE is categorized into three types: 1) Type I, which represent 85 % of the cases, is caused by low levels of C1-INH antigenic protein and functional activity; 2) Type II, representing 15% of cases and in this category, while C1-INH protein level is normal or elevated, C1-INH function is low and 3) a rare type of HAE can result from normal levels of C1-INH protein associated with mutations in the coagulation factor XII gene, referred to as type III HAE. (Table 1)

A wide variety of environmental stimuli play a role in triggering HAE such as skin pressure, elevated core body temperature, exercise, vibration, sunlight, and water.¹¹ The most common cause of HAE is dermatographism or urticaria factitia. This is characterized by rapid onset of a cutaneous wheal and flare after pressure is applied to the skin. Cholinergic HAE is the result of an increase in core body temperature, which may be triggered by exercise and bathing in hot water. Solar HAE is caused by direct exposure of the skin to sunlight.

Aquagenic HAE is a rare condition that is triggered by direct skin contact with water.¹¹ Riding a vehicle, a horse, or mountain bike, snoring, walking, handling a jackhammer, toweling, mowing the lawn, clapping, massaging are common triggers for vibratory angioedema (VA).^{12,13} In this article, we report a patient with VA describing dental procedures as a trigger for the condition due to the vibration of mechanized dental instruments, which, to our knowledge, has not been reported previously.

Case report

A 63-year-old woman was referred by her general dentist for evaluation of possible oral lesions and chronic burning sensations of the tongue. The patient reported a chronic history of multiple food sensitivities that caused oral discomfort, which she related to her underlying angioedema. She reported having VA, a specific type of

Table 1. Three major types of hereditary angioedema.

Type I	Low level of C1-INH antigenic protein and functional activity	85% of cases
Type II	Normal or elevated level of C1-INH protein but low C1-INH function	15% of cases
Type III	Normal level of C1-INH protein associated with mutations in the coagulation factor XII gene	Rare
Adapted from Bowen <i>et al.</i> ⁵		

physical urticaria, and when queried about triggers for this disorder, she stated it was induced by riding in a vehicle and with the use of (vibratory) dental equipment. The patient utilized a standard subcutaneous injection of Icatibant Acetate 30 mg/3 ml solution as prophylaxis for VA before each dental procedure that utilized mechanized (vibratory) equipment. Her past medical history included asthma, sleep apnea, anemia, mitral valve prolapse, stroke, liver disease, diabetes, multiple sclerosis, hiatal hernia, chronic back pain, urinary frequency, ocular hypertension and HAE. Medications included acetaminophen, albuterol Sulfate, azelastine-fluticasone, cetirizine, diphenhydramine HCl, fexofenadine HCl, fluticasone-salmeterol, Icatibant Acetate, icosapent, metformin, montelukast, nortriptyline, olopatadine HCl, prednisone, ranitidine, tramadol, and tranexamic acid. Past surgical history was significant for sinus surgery and childbirth x 3. The patient reported true allergies to alcaïne, cinryze, kalbitor, tetracaine, alcohol, gadolinium, iodine, banana, chocolate, coconut, food color yellow, red, tartrazine Dye, mold extract [Trichophyton Mentagrophytes], nuts, pineapple, shellfish-derived products, spinach, strawberry C [Ascorbate], sulfites and watermelon. Family history was positive for HAE and social history was unremarkable. Review of systems includes shortness of breath, generalized muscle weakness and anxiety.

Detailed physical exam revealed a well-nourished, well-developed female in no apparent distress. Extraoral and intraoral examination showed no overt clinical evidence of angioedema at the day of the visit. However, dry oral

mucosa, fissured / hairy tongue and moriscatio buccarum were observed on clinical examination. Diagnoses consisted of xerostomia, glossodynia, hairy tongue and parafunctional habit. A gram stain of the dorsal tongue revealed budding yeast consistent with candidiasis. The patient was recommended to avoid food and / or oral hygiene products that may exacerbate her current oral symptoms, maintain oral hygiene and to initiate use of over-the-counter salivary substitutes. She was also advised to self-regulate her oral parafunctional habit. The oral candidiasis was treated with clotrimazole troches 10mg, 5 times daily, for 14 days. The patient was instructed to monitor for acute onset of HAE with use of this medication or over-the-counter products and proceed immediately to her local Emergency Department for urgent care, if needed. The patient was lost to follow-up and the status of her oral conditions are unknown at this time.

Discussion

The oral findings in this case are common to patients taking multiple medications and with parafunctional habits, therefore, the relationship of these oral conditions with VA can only be considered speculative. In the authors' opinion, it is important to consider aspects of dental management of a patient with VA, as this is a rare disorder encountered in the dental setting. The most devastating consequence of VA is risk of upper airway obstruction, which has been reported in approximately 1% of angioedema-related swelling cases and is associated with significant morbidity and mortality.⁶

Table 2. Treatments for hereditary angioedema.

Drug / dose	Potential indications
Plasma-derived nanofiltered C1 inhibitor (Cinryze); 1000 U IV	Acute attacks Short/long-term prophylaxis
Plasma-derived C1 inhibitor (Berinert-P); 20 U per kg IV	Acute attacks Short/long-term prophylaxis
Recombinant human C1 inhibitor (Rhucin); 50–100 U per kg IV	Acute attacks Short-term prophylaxis
Ecallantide (Kalbitor); 30 mg SC	Acute attacks
Icatibant (Firazyr, Jerini); 30 mg SC	Acute attacks
Adapted from Zuraw BL, ⁴ and Bowen <i>et al.</i> ⁵	

Avoidance of vibration is the most appropriate recommendation to prevent episodes of VA; however, it is difficult to achieve this completely for patients with this condition when receiving dental care. Therefore, various prophylactic treatments have been suggested for this purpose. (Table 2) Several therapeutic options are available such as Cinryze, Icatibant, Berinert-P, Rhucin, Ecallantide.

Cinryze is C1-esterase inhibitor therapy indicated for routine and long-term prophylaxis against HAE. It is the first FDA-approved therapy in the U.S. for treating unpredictable recurrent attacks of HAE (more than one episode/month).¹⁴

Icatibant is a small peptide, bradykinin B2 receptor (antagonist) blocker approved by U.S. FDA (in 2011) and by the European Union (in 2008) for use in treatment of acute attack of HAE in adults.⁵ This therapy is recommended for self-injection.¹⁵ Berinert-P is a human plasma-derived C1-INH approved for the treatment of acute attacks and for prophylaxis of HAE. This drug is recommended for intravenous use and was used for more than 30 years in over 400,000 treatments with a significant safety record.^{16,17}

Rhucin is a recombinant human C1-INH. It is conestat alfa that is made from the milk of transgenic rabbits. Conestat alfa has shown similar functional effectiveness to plasma-derived C1-INH in terms of inhibiting C1, plasma kallikrein, Factor Xa and Factor XIIa. This drug is recommended for intravenous use for acute attacks and short-term prophylaxis of HAE.¹⁸

Ecallantide (DX-88) is a potent and specific inhibitor of plasma kallikrein. It is a recombinant small protein which was identified through phage display technology. It exerts its beneficial effects in treating acute attacks of HAE and is recommended for subcutaneous use.^{18,19}

In addition to prophylaxis, appropriate use of dental hand instruments is recommended to avoid attacks of VA. Use of a spoon excavator for caries removal, files instead of rotary instruments for endodontic therapy and scalers and curettes for periodontal maintenance should be considered to decrease the risk of inducing VA attacks. If a patient with VA has an acute reaction during and / or following dental treatment, airway assessment and immediate referral to a medical center is essential for continued monitoring and supportive care, such as early intubation or tracheostomy in the case of airway compromise.²⁰ Patients with severe and / or poorly controlled VA may require dental care in an outpatient hospital dental clinic or in an operating room in order to manage potentially life-threatening complications that may occur during treatment.

Based on the authors' opinion, modifications to home oral hygiene care should be considered for patients with VA. Manual home oral hygiene aids, such as a toothbrush and flosser, are encouraged rather than electric oral care devices, such as electric toothbrushes and water picks/flossers, due to the risk of inducing an acute attack. Oral health care professionals should demonstrate

appropriate oral hygiene techniques for patients using manual devices. Moreover, preventive measures such as use of prescription fluoride toothpaste and / or use of fluoride trays should be considered on an individual basis. Patients with medication – induced xerostomia are generally advised to maintain adequate hydration and to consider use of salivary substitutes to maintain oral comfort and reduce risk of infection. Increased frequency of recall visits should be considered in order to maintain optimal oral health for patients with VA.

Conclusion

VA is a condition that is not commonly encountered in routine dental practice. It is important for oral health care providers to recognize this disorder in order to provide appropriate care for patients with this condition. Modifications to provision of routine dental care and interdisciplinary management is often required for successful management of patients with VA.

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