Hereditary angioedema: death after a dental extraction

Hereditary Angioedema: Death after a Dental Extraction

Abstract

Hereditary angioedema (HAE) is a group of three uncommon and potentially fatal conditions, each of which is transmitted as a somatic dominant trait. A recognised trigger to attacks is dental treatment, with tooth extraction frequently reported in the literature. The clinical symptoms may not manifest for many hours or even days after the procedure. We describe a recent case in Australia in which death resulted from HAE following dental extraction, and we discuss its post-mortem presentation and diagnosis, highlighting the need for dental practitioners to be aware of this condition.

Keywords: Forensic Odontology; Forensic Pathology; Dentoalveolar Surgery; Dental Extraction; Hereditary Angioedema; HAE; Dental Treatment

Introduction

The first formal description of angioedema should probably be attributed to Robert Graves in 1843[1], and for a brief time it became known as "Quincke's disease" after Heinrich Quincke, who identified that the swelling in the condition resulted from increased vascular permeability[2]. Soon afterwards, the name "angioneurotic oedema" was adopted because of an anecdotally observed correlation between exacerbations of the condition and "mental stress". William Osler, in 1888, published a case report about Mrs H. and her related family members in which he described the clinical manifestations of what we now understand to be hereditary angioedema (HAE)[3]. He was the first to recognise its autosomal pattern of transmission. Today, we know that the condition does not relate to any "neurotic" or nervous disease, so we refer generally to the group of conditions it describes as "angioedema" rather than "angioneurotic oedema".

In 2014, the European Academy of Allergy and Clinical Immunology classified angioedema in a clinically relevant manner[4]. They proposed four types of acquired angioedema, but they also recognised three different types of hereditary angioedema (HAE), all of which are transmitted by autosomal dominant genes.

Angioedema is a condition in which small blood vessels leak fluid into the tissues, causing swelling (oedema)[5]. HAE is characterised by recurrent and potentially fatal episodes of oedema of subcutaneous and submucosal tissues in skin, facial tissues, upper airways, limbs, genitals and the abdomen due to inadequate control of bradykinin generation[6] which causes the local blood vessels to become permeable to fluid. Bernstein[7] points out that, where the structure is not central, the oedematous attacks are typically unilateral. For HAE Types 1 and 2, symptoms occur as early as 2 years with a mean age of onset of 8-12 years[8], and the swelling usually lasts for 2-5 days[9]. The age of symptom onset in HAE Type 3 has been reported as 27±14 years[10]. There are no ethnic or gender differences in HAE patients[11] except for the very rare HAE Type 3, which is far more common in females[9]. Classification and disease expression in angioedema including HAE have recently been reviewed by Wu et al.[12].

The major concern to dental practitioners is that dental treatment can provide a trigger for an episode of HAE. Van Sickels et al. report that this treatment can be as simple as obtaining dental impressions or pulpal excavation[11]. It can result in potentially fatal laryngeal swelling, commonly occurring 24-48 hours post-treatment, with airway obstruction leading to death. Not every episode of dental extraction, results in an acute attack however[13].

We discuss a case where a patient suffered fatal airway obstruction as a consequence of HAE following dental extractions, and its presentation at post-mortem examination.

Case Report

A 50 year-old Caucasoid female was transferred to the mortuary for post-mortem examination. An initial external examination was undertaken by the Forensic Pathologist, who noted some facial swelling and lividity of the facial tissues. Hospital charts were available, and they revealed that the deceased had attended the Emergency Department two days after having had two dental extractions. An opinion was therefore requested from the Forensic Odontologist as part of the post-mortem investigation.

Examination of the hospital record indicated that the deceased had presented at the Emergency Department of her local hospital with her husband two days post-extraction complaining of breathing difficulties. At presentation, she was noted to have been distressed and agitated, and had exhibited cyanosis and facial swelling. While still at the hospital she suffered respiratory arrest, but the hospital emergency team was unable to revive her. She was subsequently transferred to the state mortuary for a Coroner's autopsy.

Written treatment notes from the dentist of the deceased indicated that the deceased had presented at the dental surgery complaining of pain and some swelling on the right side of her mouth. They went on to say that the dentist had performed a limited examination, and had noted that teeth 46 and 47 (lower right first and second molars) were "badly carious" with a slight buccal swelling adjacent to tooth 46. A pre-operative discussion of the risks of damage to the deceased's right inferior alveolar and lingual nerves occurred, followed by agreement on behalf of the deceased to undergo dental extractions. Local anaesthesia was obtained with 4.0 mL Scandonest 3% (Mepivacaine hydrochloride) (Specialties Septodont Pty Ltd) administered as a mandibular block, and 0.8 mL Scandonest 3% as an infiltration. Scandonest 3% does not contain a vasoconstrictor. Teeth 46 and 47 were recorded as having been extracted, with one 4/0 "catgut suture" being placed and post-operative instruction given. Amoxicillin 500mg tds (20 caps) was prescribed together with Panadeine Forte 1 or 2 tabs qid as needed (20 tabs). An ante-mortem radiograph was supplied which indicated that two teeth had been removed.

On external examination at the post-mortem procedure, swelling of face and neck was apparent, and post-mortem lividity was present on the right side of the face extending into the neck (Figure 1). The cheek on the right side was rigid on palpation. Intra-orally, the maxilla appeared to be edentulous, and we noted extensive cervical caries on teeth 43 and 44. A post-extraction socket was visible and contained a blood clot, which appeared consistent with normal healing. Further anteriorly, additional blood clots indicated the presence of a second extraction socket (Figure 2). A post-mortem radiograph of the extraction area did not reveal any abnormality other than the expected post-extraction features. The tongue appeared somewhat swollen, but the floor of the mouth was not raised on either side and the tongue was not displaced.

Initially it seemed likely that the patient had suffered from Ludwig's angina after extraction, given the recency of extraction, the manner of death and the presence of facial swelling. However, the cheek rigidity, the absence of swelling in the floor of the mouth and the absence of tongue displacement on the affected side did not accord well with that diagnosis.

On opening into the right submandibular tissue space, we observed no evidence of inflammatory exudate or pus, but all of the soft tissues in the region were clearly oedematous, and quantities of fluid were expressed from the soft tissues during dissection. We noted no evidence of infective exudate in the sublingual tissue space on either side, or in any of the other tissue spaces when we extended the dissection into the neck, but the wetness of the tissues in this area due to oedema persisted.

We also noted swelling of the soft palate and uvula, the pharynx, and significantly, the larynx, with narrowing of the laryngeal inlet due to soft tissue swelling (Figure 3). A large amount of fluid was present in the trachea, bronchi and lungs.

On this basis, it was clear that any diagnosis of Ludwig's angina was inconsistent with the findings; no evidence of infection was present. The medical history, however, suggested hereditary angioedema, disclosing that the patient had attended hospital on two occasions, thirteen years and ten years prior to death, complaining of swelling of the face and throat on both occasions. On the second occasion, she was advised to stay in hospital but chose not to. Four years prior to death, she was diagnosed with angioneurotic oedema when attending hospital for a further episode of throat swelling and she was referred to an immunologist for monitoring and treatment. She failed to attend. On two further occasions, she attended hospital for facial swelling, and the incidences of swelling were increasing. Her final hospital attendance was for the fatal episode.

Further investigations revealed that the patient's brother and father also suffered from HAE, establishing the hereditary nature of the condition.

The dentist's medical history as completed by the patient indicated that she suffered from a "nervous condition where she swells up". It did not specifically mention hereditary angioedema. The dentist asked the patient whether she was nervous about going to the dentist, and the patient responded "Yes".

The patient herself seems to have encountered the term "angioneurotic oedema" in connection with her diagnosis, and this term appears in her hospital notes. It seems that she may not have understood the diagnosis and may have believed it related to a nervous condition, leading her to describe it to the dentist in this way. It seems that the dentist has thus acted in good faith on the information received. Had the patient attended the immunologist to whom she had been referred, a greater degree of understanding may have eventuated and this may have saved her life.

Discussion

There are many recent references in the literature to dental treatment as a trigger for HAE[14-16]. It is important to the dentist to be aware of HAE, because there is a possibility of life-threatening laryngeal swelling leading to airway obstruction or asphyxia after routine dental care[15]. This may occur hours or even days after the trigger treatment, by which time the dental appointment will be long over[17-19]. In the present case, the dental treatment occurred early one afternoon, but the episode of swelling began in the morning two days later. A dentist may therefore be unaware of the exacerbation of the patient's condition following treatment, and is unlikely to be able to play a role at the critical time.

Sanuki[15] states that HAE attacks can be triggered by physical or psychological stress, and points out that dental appointments abound with such potential triggers. It is also a possibility that the local anaesthetic used in the present case may have contributed to the outcome. The Company Core Product Information document for Mepivacaine hydrochloride indicates that angioedema is listed as a potential adverse reaction to the drug, albeit rarely[20].

In Australia, the Australasian Society of Clinical Immunology and Allergy published a position paper on HAE; they estimated there were approximately 480 cases of HAE in Australia in 2012[21], but only 66 of these were registered on the Australasian Society of Clinical Immunology and Allergy's Primary Immunodeficiency Register. This suggests that the majority of such cases remain unrecognised or undiagnosed, although a careful and thorough medical history should be sufficient to detect such individuals. The probability of any given practitioner unknowingly treating such a patient is therefore statistically low. Because the condition is hereditary and multiple members of the same family may attend the same dental practice, it is possible that a single practitioner may treat several family members with the condition.

If a patient presents with a diagnosis of HAE, management of the patient in consultation with their medical practitioner is appropriate. HAE can be treated (see Bork[17]), and acute attacks controlled, but this is a medical responsibility. If HAE is suspected following the taking of a medical history, consultation with the patient's medical practitioner to discuss management would be appropriate.

In conclusion, we believe that HAE is a condition with which every dental practitioner should be familiar. While the risk of encountering such a patient is relatively low, the consequences of uninformed treatment may be severe. We suggest that dental practitioners might consider adding a question to their medical history forms asking about previous recurrent episodes of swelling of the face with difficulty in breathing as a filter to prevent further fatal outcomes. An alternative might be for practitioners to be alert to the condition when asking a patient about their general and medical histories so that they recognise cues that might be disclosed and act accordingly.

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Human Ethics

The Chair of the Health Support Queensland Forensic and Scientific Services Human Research Ethics Committee has verified that the case materials used in this paper have been adequately de-identified.

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Figure Legends:

Figure 1: Swelling on the right side of the face and neck with post-mortem lividity.

Figure 2: Extraction sockets present in the lower right quadrant.

Figure 3: Swollen tissues narrowing the laryngeal inlet.