Case Report
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Perioperative management of a patient with hereditary angioedema (HAE) undergoing endometrial ablation: a case report and review of literature

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Introduction

HAE is a rare genetic disorder caused by deficiency of complement 1 (C1) esterase inhibitor (C1-INH). It is a rare disease with an estimated prevalence between1: 10,000 and 1:50000. HAE is an autosomal dominant disease clinically characterised by recurrent non pruritic face, skin or extremities swelling as well as gastrointestinal concerns and respiratory system failure. Since HAE is not an allergic phenomenon, pruritus does not occur concomitant with the swelling.[1] HAE manifestations in the upper respiratory system, specifically involvement of the larynx may lead to asphyxiation, which is the primary cause of death in HAE patients.[2] There are many known HAE episode inciting factors, including physical injury, medical or dental operations, psychological stress, menstruation, infections or certain medications. The list includes oestrogen containing contraceptive pills and angiotensin converting enzyme (ACE) inhibitors.[1]

Perioperative prophylaxis with Danazol and C1 inhibitor concentrate (C1-INH) are commonly used to prevent angioedema episodes. Anaesthesia management and perioperative implications have been recently commented by some authors.[3] Airway oedema and hypovolemic shock due to the tissue leak of fluids are especially significant in the perioperative period, challenging even the most experienced anaesthesiologist. We represent a patient who had previously diagnosed HEA who underwent successful elective Novasure endometrial ablation under general anaesthetic. Perioperative management and anaesthetic implications are discussed below in details.

Case report

A 24years old para 2 woman who had been diagnosed with C1-INH deficiency (HAE type I) back in 2010, was admitted to our hospital for Novasure endometrial ablation. Since her condition was diagnosed she was under the care of a consultant clinical immunologist and liaison psychiatry team for cognitive behaviour therapy to help her adjust to living with chronic disease. She was on prophylactic Danazol 200mg three times a day and a constant home supply of C1-inhibitor concentrate (Berinert) for emergency IV injection in case of swelling affecting airway, face, or causing severe abdominal pain. She came to be seen in Gynaecology outpatient clinic complaining of heavy prolonged periods for 3years. She found that her angioedema attacks coincided with the start and the end of bleeding, and when she came to see us she had already had 6 attacks of angioedema in the previous two months and needed ITU admission in one of them. She didn't find the Danazol helpful in controlling her periods, and she had previously tried the Mirena IUS but her bleeding was the same and the coil eventually fell out after 6months. Recently, she used Implanon (progestetional implant) for contraception as she was not allowed to have combined oral contraception, as oestrogen is a well-known trigger for angioedema attacks.

Her pelvic ultrasound scans showed a normal uterus and both ovaries were polycystic in appearance. Otherwise her examination was unremarkable. The patient was requesting a definite treatment to her menstrual symptoms. She confirmed that her partner and she have completed their family. She felt that her health was too poor to cope with another pregnancy and childbirth. In addition, she was concerned about the risk of transmission of her genetic disorder to her children, aware that the risk was 50%. Her elder daughter has been already tested and fortunately didn't inherit the HAE whereas her son was waiting testing. The options that were offered to the patient included the GnRh. analogue (Zoladex) injections for 6 months, but she wasn't keen on any medical treatment particularly injections which seemed to initiate her angioedema attacks. So surgical options were discussed including endometrial ablation or hysterectomy and information leaflets were given. She opted for endometrial ablation, a preoperative anaesthetic review was arranged and a perioperative prophylactic medication plan was organised by the clinical immunology team to reduce the risk of angioedema.

It was planned that the woman will require prophylactic infusion of Berinert (plasma derived human C1inhibitor concentrate) 2000IU at least an hour prior to general anaesthetic and intubation. A further 2000IU was available in theatre/Gynaecology ward for her stay in case she might experience a postoperative episode of either airway/facial angioedema, or intestinal angioedema, An extra 2000 IU was made available as 5% of the attacks require a second dose for symptomatic improvement. The C1 inhibitor was pre-ordered from the hospital pharmacy in advance to ensure that sufficient stock was available. The anaesthetic team planned for an advanced recovery and an ITU bed was secured in case it was needed. The patient was advised that she was to stay in hospital overnight for observation. Expecting some difficult airway intubation, an emergency tracheostomy kit

and 2 experienced consultant anaesthetists were present while the anaesthesia was induced. The surgical procedure was uneventful and lasted around 20minutes. Convalescence was trouble free apart from abdominal pain that eventually settled down with analgesics and the patient was discharged home the next day.

Discussion

In 1888, William Osler, published the first article which had described a hereditary form of angioneurotic oedema. However discovery of the biochemical basis for the disease did not occur until several decades later. A study published in 1963 by Donaldson and Evans first described the biochemical abnormality responsible for HAE which is the absence of C1-INH in patients with this disease. Since that study, the body of knowledge regarding the clinical manifestations, spectrum, pathophysiology and genetic basis of the various forms of angioedema has broadened considerably.[4,5] The underlying cause of HAE is attributed to autosomal dominant inheritance of mutations in C1-INH gene, which is mapped to chromosome 11(11q12-9 13.1), but the absence of family history does not rule out the possibility of HAE and 15% of cases are due to spontaneous gene mutation.[6] The C1-INH gene (SERPING-1) is responsible for the production of a plasma protease (C1-esterase inhibitor) that functions to block the activation of complement and the formation of bradykinin at multiple sites in the sequence.[7]

Lack of this enzyme allows the complement to cascade to proceed relatively unimpeded resulting in clinical angioedema. Historically, 2 types of HAE have been described. Type 1 has low level of C1 INH (80%) while type II has normal level yet malfunctioning C1 esterase inhibitor (15%).[8] However, a variant possibly X linked inherited angioedema has recently been described, and tentatively it has been named "type 3"/HAE.[8] Worth to mention that signs and symptoms are identical in all types of HAE. Skin and visceral organs may be involved by the typically massive oedema. The most commonly involved viscera are the respiratory and gastrointestinal systems.[9] Involvement of the upper airways can result in severe life threatening symptoms, including the risk of asphyxiation, unless appropriate interventions are taken. Quantitative and functional analysis of C1 esterase inhibitor and complement components C4 and C19 should be performed when HAE is suspected.[10] Hormonal factors play a significant role in the precipitation or worsening of the condition in women. There appears to be variation in overall frequency of angioedema symptoms according to the different female life stages of childhood, puberty, menses, pregnancies and menopause.[11] Combined contraceptive pills exacerbate symptoms in 63-80% of women.[12] This method of contraception is therefore contraindicated in women with HAE. Progestagen pills should be advised in this situation. Similarly, Oestrogen replacement therapy must not be used for the menopause.

Most reports revealed that menses might precipitate acute episodes as seen in our case. In PRE HAEAT studies, menses and ovulation provoked attacks in 35.3% and 14% of cases respectively.[12] A study of pelvic ultrasound scans performed in 13 patients with HAE-C1-INH reported an increased frequency of PCOS and multifollicular ovaries with rates of 38.4% and 53.8% respectively.[13] The episodes might occur without any apparent cause, although anxiety, stress, or minor trauma can trigger such an attack. Our patient reported a tendency to coincide with the onset of menstrual bleeding or with any episode of infections. The long term prophylactic treatment is usually done with Danazol and C4, and tranexamic acid (anti-fibrinolytic), probably its action on the C1 inhibitor activity depends on the anti-plasmin action that regulates the release of vasoactive mediators.[14] Because HAE is not an allergic condition, corticosteroids and anti-histamine administration doesn't constitute an effective therapy.[15] First line drugs for emergency treatment of laryngeal oedema can be done with C1-INH as well as contact system modulators such as Ecallantide (acts as a potent reversible inhibitor of plasma Kallikrein) and Icatibant (a specific and selective competitive antagonist of bradykinin B2 receptor). If first line drugs are not available fresh frozen plasma (FFP) or solved detergent treated plasma (SDP) is the next choice. Although FFP is a good source of C1-INH, it also contains kinins and uncleaved C2 and C4 which may exacerbate acute attacks.

The C1-INH preparation is available as both human plasma derived (Berinert) and recombinant human protein (Rhucin in north America and in Europe it is known as Ruconest: Pharming Technologies BV, Leiden, the Netherlands). The use of this preparation is indicated for the treatment of acute episodes of angioedema and as preoperative prophylaxis.[16] After administration most patients experience relief after 15-20minutes. Swelling responds more quickly when treated early in course of the attack. In the current case, the patient received a dose of 2000U slow IV Berinert one hour before general anaesthetics in addition to her routine long term prophylaxis of Danazol before and immediately after the operation. After surgery it was recommended that these patients should be transferred to ICU for at least 24hours for monitoring and early treatment in case of angioedema or other complications to happen. However our case didn't need an ICU admission. But she stayed in the hospital overnight. Endometrial ablation procedure can be done under local anaesthetic but the anaesthetic team opted for general anaesthetic technique in order to secure the airway by tracheal intubation in case of laryngeal oedema might be triggered. Because of the rarity of the occurrence, reports of perioperative management of HAE are very limited in the literature.[15] However international consensus guidelines have emerged in the year 2012 elucidating an algorithmic approach to the management of HAE.[17]

There is no known contraindication related to the use of any of the available intravenous or volatile anaesthetics and neuromuscular blocking agents, including succinyl choline. Although tracheal intubation is not contraindicated, it is important to reduce airway manipulation to the minimum. Intubation is always the first choice in the case of acute airway compromise and should be done as early as possible. While performing laryngoscopy and intubation the presence of difficult airway equipment and the provision for urgent tracheostomy is mandatory.[18] This was the first gynecology patient diagnosed with HAE and operated for dysfunctional uterine bleeding by endometrial ablation in our Gynaecology department. Surgery was a success with appropriate evaluation and anaesthetic management. We conclude that, in patients with HAE, it is very important to use appropriate preoperative prophylaxis for oedema during an acute attack using C1 inhibitor and have some extra doses ready in case of needing it perioperatively. Finally, the importance of a multidisciplinary and aggressive anaesthetic approach in cases of HAE cannot be stressed enough and yields successful results in these critical patients.

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None.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper."

References

1. Nzeako UC, Frigas E, Tremaine WJ. Hereditary angioedema a broad review for clinicians. *Arch Intern Med*. 2001;161(20):2417–2429
2. Bork K, Barnstedt SE. Laryngeal oedema and death from asphyxiation after tooth extraction in four patients with hereditary angioedema. *J Am Dent Assoc*. 2003;134(8):1088–1094
3. Spyridonidou A, Iatrou C, Alexoudis A, et al. Peri-operative management of a patient with hereditary angioedema undergoing laparoscopic cholicystectomy. *Anaesthesia*. 2010;65(1):74–77
4. Osler W. Heriditary angioneurotic oedema. *Am J Med Sci*. 1888;95:362–367.
5. Donaldson VH, Evans RR. A biochemical abnormality in hereditary angioneurotic edema absence of serum inhibitor of C1-esterase. *Am J Med*. 1968;35(1):37–44
6. Beleña JM, NúñeZ M, Vidal A. Perioperative management of a patient with hereditary angioedema undergoing lumbar interbody arthroclesis. *Int J Clin Anaesthesiol*. 2013;1(2):1011
7. Bowen T, Cicardi M, Farkas H, et al. Canadian 2003 international consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. *J Allergy Clin Immunol*. 2004;114(3):629–637
8. Bova M, Petraroli A, Loffredo S, et al. A unique case of angioedema with anti-C1 inhibitor antibodies and normal C1 inhibitor levels. *J Investig Allergol Clin Immunol*. 2016;26(2):111–112
9. Trigganese P, Guarino MD, Pellicano C, et al. Recurrent angioedema: occurrence, features, and concomitant diseases in an italian single centre study. *Int Arch Allergy Immunol*. 2017;172(1):55–63
10. Nzeako UC, Frigas E, Tremaine WJ. Hereditary angioedema a broad review for physicians. *Arch Intern Med*. 2001;161(20):2417–2429
11. Yip J, Cunliffe WJ. Hormonally exacerbated hereditary angioedema. *Australas J Dermatol*. 1992;33(1):35–38
12. Bouillet L, Longhurst H, Boccon-Gibod I, et al. Disease expression in women with hereditary angioedema. *Am J Obstet Gynecol*. 2008;199(5):484 e1–e4
13. Perrocone R, De Carolis C, Giacomello F, et al. Impaired human ovarian follicular fluid complement function in hereditary angioedema. *Scand J Immunol*. 2000;51(1):104–108
14. Wintenberger C, Boccon-Gibod I, Launay D, et al. Tranexamic acid as maintenance treatment for non-histaminergic angioedema: analysis of efficacy and safety in 37 patients. *Clin Exp Immunol*. 2014;178(1):112–117
15. Bork K, Sven-Erik Barnstedt. Laryngeal edema and death from asphyxiation after tooth extraction in four patients with HAE: Review and case report. *Oral Surg Med Oral Path Oral Radiol Endod*. 2003;96(5):540–543
16. Riedl MA, Bernstein JA, Li H, et al. Recombinant human C1-esterase inhibitor relieves symptoms of hereditary angioedema attacks: phase 3, randomized, placebo-controlled trial. *Ann Allergy Asthma Immunol*. 2014;112(2):163–169.e1.
17. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012;109(6):395–402
18. Narayanan A, Date RR, Birur S, et al. Anaesthesia management of a patient with hereditary angioedema with prophylactic administration of C1 esterase inhibitor. case report and literature review. *Sultan Qaboos Univ Med J*. 2003;13(3):E467–471.