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Original contribution

Perioperative course in patients with hereditary or acquired angioedema☆,☆☆,★

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Abstract

Purpose: Two types of bradykinin-mediated angioedema, hereditary angioedema (HAE) and acquired angioedema (AAE), result from deficiency or dysfunction of C1 esterase inhibitor, leading to an overproduction of bradykinin, which can lead to vascular permeability and life-threatening angioedema of the airway. The objective of this study was to review perioperative outcomes in a series of patients with HAE and AAE and to review current knowledge about anesthetic complications in patients with HAE or AAE.

Methods: Medical records were retrospectively reviewed for perioperative complications in patients with HAE or AAE who underwent general anesthesia from January 1, 2000, to December 31, 2014, at our institution.

Results: Twenty-four patients (13 with HAE, 10 with AAE, and 1 with unspecified angioedema) underwent 38 instances of general anesthesia with airway manipulation. All except 4 received prophylactic therapy. One patient, a 67-year-old woman who was pretreated with stanozolol and fresh frozen plasma required reintubation after postoperative airway edema developed.

Conclusion: Life-threatening episodes of angioedema of the airway occur infrequently, but they can occur in patients who received pretreatment and in patients who have previously undergone anesthesia uneventfully. Anesthesiologists must be ready to emergently manage a difficult airway and must be familiar with recommendations provided in consensus guidelines for the treatment of HAE and AAE patients.

1. Introduction

Bradykinin-mediated angioedema can occur in patients with hereditary angioedema (HAE) or acquired angioedema (AAE) and with the use of angiotensin-converting enzyme inhibitors. HAE and AAE are nearly indistinguishable clinically [1]. They are characterized by episodic edema of the skin and mucosa of the gastrointestinal tract and respiratory system as a result of bradykinin-mediated increased vascular permeability of

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capillaries and postcapillary venules [2]. Edema can involve the mucosa of the upper airway and lead to life-threatening airway compromise and asphyxia [3]. With these disorders, dysfunction of C1 esterase inhibitor (C1-INH) modulates the contact activation, coagulation, and complement cascades [4]. Uninhibited, these pathways lead to an overproduction of bradykinin, increasing vascular permeability and resulting in edema (Figure 1) [5,6].

HAE is a rare, autosomal dominant disorder with a prevalence of approximately 1 in 50,000 people. Patients with type I HAE (85%) have deficient levels of C1-INH, whereas patients with type II HAE (15%) may have normal or even elevated levels of dysfunctional C1-INH [2,5]. The cause of type III HAE is unrelated to the production and function of C1-INH; instead, a mutation of factor XII leads to overproduction of bradykinin through increased production of kallikrein, which cleaves high-molecular-weight kinin to bradykinin [5,7].

AAE is associated with autoimmune and lymphoproliferative disorders and malignancies of the gastrointestinal tract [1,8]. In AAE, C1-INH is rendered dysfunctional by consumption mediated by immune complexes or autoantibodies against the inhibitor [9]. The Figure 1 shows relevant pathways in patients with HAE or AAE and therapeutic interventions that may interrupt this unwanted cascade.

The development of edema can be unprovoked [6] or triggered by innocuous stimulation such as vibrations from a power mower or motorcycle [10], snoring [11], or minor trauma from dental procedures [12], and the frequency of attacks seems to be increased by stress. Risks for the development of angioedema include the perioperative setting (with the potential for upper airway trauma from airway management), oral surgery, and psychologic and physiologic stress [13]. Triggers vary between patients and within patients, so that the prediction of complication is not possible and management of the disorder may be difficult.

The purpose of this study was to review the perianesthetic course and outcomes in patients with HAE or AAE undergoing general surgery at a single academic medical center and to review current knowledge about anesthetic complications in patients with HAE or AAE. This analysis included patients undergoing various surgical procedures under general anesthesia, and therefore, the outcomes reflect the range of routine clinical practice.

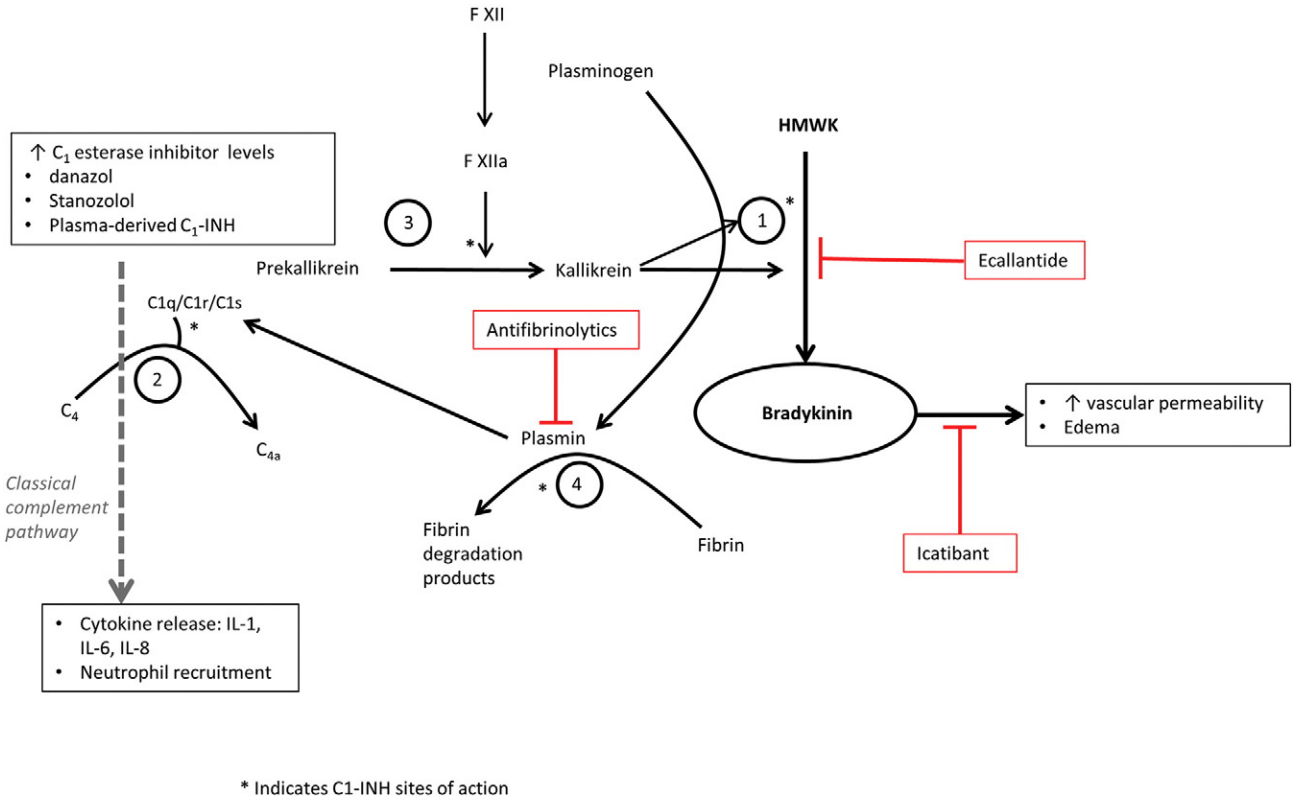

Figure 1 With deficiency or dysfunction of C1-INH, the complement cascade, fibrinolysis, and contact activation proceed uninhibited, leading to overproduction of bradykinin and episodes of edema. The function of C1-INH includes inhibition of (1) kallikrein-mediated conversion of high-molecular-weight kinin (HMWK) to bradykinin; (2) C1 esterase–mediated activation of C4 in the classical complement pathway; (3) activated factor XII (FXIIa)–mediated cleavage of prekallikrein to kallikrein; and (4) plasmin-mediated fibrinolysis. The mechanism of action of pharmacologic therapy for bradykinin-mediated angioedema includes inhibiting the action of kallikrein with ecallantide, bradykinin with icatibant, and plasmin with antifibrinolytics (eg, tranexamic acid or ε-aminocaproic acid). In addition, C1-INH levels can be increased with attenuated androgens (danazol or stanozolol), C1-INH concentrate, or FFP (not depicted). Asterisk indicates site of activity of C1-INH; FXII, factor XII; IL, interleukin; upward arrow, increased.