Hey Hey HAE
(Hereditary Angioedema)

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38-year-old ASA III woman with a history of Grave’s disease complicated by bilateral exophthalmos presenting for the second of a two-stage orbital decompression.
History

**PMHx:** Grave’s Disease, Hypertension, Obesity, **Type III Hereditary Angioedema**

**PSHx:** Total thyroidectomy, Stage 1 orbital decompression, C-section, Tonsillectomy

**FHx:** Negative for angioedema

**Allergies:** ACE inhibitors (AE), Estrogens (AE), Cardizem (AE), Sulfa (AE), Penicillin (rash), Tegaderm (rash), Norco (N/V)

**Airway Hx:**
- ED (7/2014) Grade 1 w/ glidescope, significant arytenoid swelling bilaterally, distortion of laryngeal tissue.
- OR (8/2014) Grade 1 mask, Grade 1 view w/ MAC 3

**Studies:** Basic & CBC wnl, TSH/T3/T4 wnl, EKG (7/16/2014) NSR, ECHO (7/16/14) EF 70%, normal chambers, normal valves, unable to calculate RVSP
Monitoring: Standard ASA, arterial line

Access: 18G R hand, 16G R foot

Airway: normal dentition, >3cm mouth opening, Mallampati III, TM distance >6cm, good head extension/flexion, normal neck anatomy, no appreciable facial or oropharyngeal edema

Exam: T 37, BP 157/60, HR 73, SpO2 100%, Ht. 66in, Wt. 83kg, BMI 35
- no murmurs
- lungs clear bilaterally
- no neurological deficits

Medication/Products: 2 units FFP, Midazolam 2mg
Intra-op

**Induction**: Fentanyl, Propofol, Rocuronium

**Airway**: Grade 2 mask, grade 2a view with a MAC 3 blade, 7.5 oral RAE

**Maintenance**: Propofol/Remifentanil gtt, 0.5 MAC Isoflurane

**Emergence**:
- No evidence of swelling, cuff leak present
- Extubated over 14Fr Cook airway exchange catheter
- New onset lip and facial edema
- Sedated and reintubated over airway exchange catheter with a 7.0 cuffed ETT
- Kalbitor 30mg SQ
- Additional unit FFP
Learning Objectives

• Categorize and describe angioedematous disease
• Review the underlying pathophysiology of HAE
• Describe the different types of Hereditary Angioedema (HAE)
• Discuss management of acute HAE attacks
• Identify anesthetic considerations for patients with HAE
Types of Angioedema

Angioedema

Without urticaria

C1-inhibitor activity
< 30-50 %

Congenital

Hereditary angioedema type 1
(reduced C1-inhibitor concentration)

Hereditary angioedema type II
(dysfunctional C1-inhibitor)

Acquired
C1-inhibitor deficiency
(increased C1-inhibitor catabolism)

Normal C1-inhibitor activity

Congenital

Hereditary angioedema with normal C1-inhibitor (also called familial oestrogen dependent angioedema)

Unknown genetic cause

Acquired

Idiopathic angioedema

Drug-induced angioedema
(e.g. angiotensin converting enzyme inhibitor, non-steroidal anti-inflammatory drugs)
Hereditary Angioedema

- 2% of clinical angioedema cases
- Incidence: 1:10k-50k people
- Average HAE patient has 20+ attacks per year
- 15,000 - 30,000 ED visits per year in the US attributed to HAE
HAE: Clinical Presentation

Facial: Most often affects lips, eyelids, and tongue; swelling may migrate or extend to the upper airways

Abdominal: Common site affected; intestinal obstruction causes pain, nausea, and vomiting; may lead to hospitalizations and unnecessary surgeries

Laryngeal: May lead to death from asphyxiation; often requires intubation and tracheotomy

Urogenital: May result from intercourse/local trauma; bladder involvement causes painful and difficult urination

Extremity: Most common site affected; swelling of the hands or feet is functionally disabling
Learning Objectives

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HAE: Inflammatory Pathway

Contact activation (intrinsic) pathway
Damaged surface

XII XIIa

XI XIa

IX IXa VIIIa

Prothrombin (II)

Xa V

Active Protein C

Protein S

Protein C + thrombomodulin

Tissue factor (extrinsic) pathway

Trauma

TFPI

VIIa VII

Tissue factor

Antithrombin

Common pathway

Fibrinogen (I)

Fibrin (Ia)

XIIIa XIII

Cross-linked fibrin clot

Type I & II Hereditary Angioedema

- **Type I**
  - 75% of all HAE cases
  - Autosomal dominant inheritance
  - Deficiency of C1-INH

- **Type II**
  - 20% of all HAE cases
  - Autosomal dominant inheritance
  - Dysfunction of C1-INH
Type III Hereditary Angioedema

- **Type III**
  - 5% of all HAE cases
  - Normal plasma C1-INH
  - Activating mutation in the gene for Factor XII
  - Autosomal dominant but with less penetrance

- **Diagnosis**
  - Recurrent angioedema in the absence of urticaria or medications known to trigger angioedema
  - Documented normal lab C1-INH levels and function
Acute Angioedema Attack
Learning Objectives

• Broadly categorize angioedematous disease
• Review the underlying pathophysiology of HAE
• Describe the different types of Hereditary Angioedema (HAE)
• Discuss management of HAE acute attacks
• Identify anesthetic considerations for patients with HAE
Management of an Acute Episode

1. Increase C1-INH levels
   - Plasma-derived C1-INH (Berinert)
   - Recombinant C1-INH
   - Fresh Frozen Plasma

2. Ecallantide (Kalbitor)
   - Selectively, reversibly inhibits activity of plasma kallikrein

3. Icatibant (Firazyr)
   - Selectively antagonizes bradykinin (B2) receptors
Management of an Acute Episode

<table>
<thead>
<tr>
<th>cutaneous swellings</th>
<th>abdominal attack</th>
<th>laryngeal attack</th>
</tr>
</thead>
<tbody>
<tr>
<td>other than face, neck</td>
<td>face, neck</td>
<td></td>
</tr>
<tr>
<td>Wait and see (spontaneous resolution)</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>Plasma-derived C1 INH (pdC1INH)(^1) Icatibant(^1); Ecallantide(^1,2,3)</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>ICU (intubation(^4), tracheotomy)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Table 2 Summary of recommendations**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Evidence and Strength of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment of Acute Angioedema Attacks</strong></td>
<td></td>
</tr>
<tr>
<td>1. Effective therapy should be used to treat acute attacks of angioedema to reduce duration and severity of attacks.</td>
<td>High, Strong</td>
</tr>
<tr>
<td>2. pdC1-INH is an effective therapy for the treatment of acute attacks.</td>
<td>High, Strong</td>
</tr>
<tr>
<td>3. Icatibant is an effective therapy for the treatment of acute attacks.</td>
<td>High, Strong</td>
</tr>
<tr>
<td>4. Ecallantide is an effective therapy for the treatment of acute attacks.</td>
<td>High, Strong</td>
</tr>
<tr>
<td>5. rhC1-INH is an effective therapy for the treatment of acute attacks.</td>
<td>High, Strong</td>
</tr>
<tr>
<td>6. Attenuated androgens should not be used to treat acute attacks.</td>
<td>Low, Strong</td>
</tr>
<tr>
<td>7. Tranexamic acid should not be used to treat acute attacks.</td>
<td>Low, Strong</td>
</tr>
<tr>
<td>8. Frozen plasma could be used for treatment of acute attacks if other recommended therapies are not available.</td>
<td>Low, Strong</td>
</tr>
<tr>
<td>9. We recommend early treatment of attacks to reduce morbidity (Level of Evidence: Moderate) and mortality (Level of Evidence: Expert Opinion).</td>
<td>Moderate, Strong/Expert Opinion, Strong</td>
</tr>
<tr>
<td>10. All attacks of angioedema involving the upper airway are medical emergencies and must be treated immediately. (Level of Evidence: Low) In addition, we recommend emergency department assessment. (Level of Evidence: Expert Opinion).</td>
<td>Low/Expert Opinion, Strong</td>
</tr>
</tbody>
</table>
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Anesthetic considerations

**Preop**
- PMHx / FHx
- Obtain 1st line medications/products (FFP)
- Anxiolytic premedication
- Type and Screen
- Use all resources available (ENT, pharmacy, airway team, PCP)

**Intraop/Postop**
- Consider sedation or regional if appropriate
- Smooth wakeup
- Consider Cook Exchange Catheter
- Detailed PACU handoff
Back to our patient...
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Take home
References

Thank you