A Case of Angioedema Refractory to Conventional Treatment

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Introduction

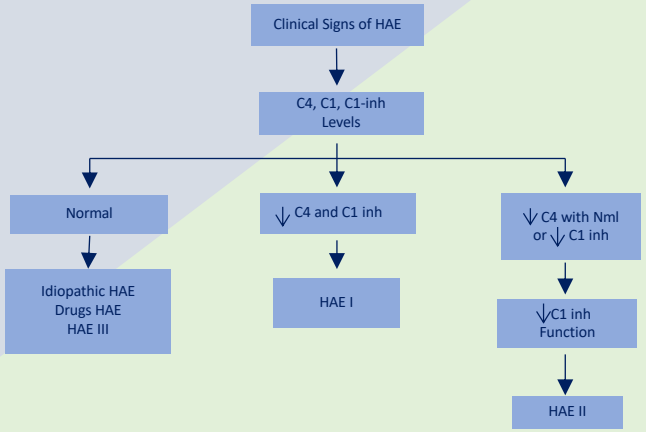
- Angioedema is defined as intermittent episodes of subcutaneous/submucosal swelling affecting the skin, GI tract, and upper airways and is mediated by either mast cell or bradykinin activation.
- Mast cell activation makes up the majority of cases and can be characterized clinically by the presence of urticaria and elevated inflammatory markers.
  - Treated by mast cell- targeted treatment or antihistamines.
- Angioedema caused by bradykinin, labelled as Hereditary Angioedema (HAE), is diagnosed with abnormal C1- inhibitor studies and treatment is problematic due to the many variants that exist.
- Mortality for bradykinin-related angioedema has 45- fold higher mortality than the mast cell counterpart of angioedema.
- In this case, the authors present an adolescent female who presented with antihistamine and steroid refractory angioedema in the presence of normal C1-inhibitor tests.

Case Presentation

- Patient is a thirteen-year-old female with anxiety and ADHD who was initially admitted one year ago with histaminergic angioedema that was responsive to antihistamines.
- During her most recent three-day admission, she presented with angioedema and severe bilateral jaw/cheek pain which showed minimal improvement in her pain and facial swelling even at discharge.
- The patient returned two days later with three episodes of vomiting and another episode of increased subcutaneous swelling of her face.
- She also had return of her jaw pain now causing a limited range of motion opening her mouth.

Results

Lab	Patient Value	Reference Range
C1 esterase quantitative	28 mg/dL	(21-39 mg/dL)
C1 esterase function	93%	(> or = 68%)
C1q binding assay	7.5 mcg Eq/mL	(< or = 25.1 mcg Eq/mL)
C4 level	21.7 mg/dL	(14-46 mg/dL)



Management

Initial presentation-

- IV Methylprednisolone 1 mg/kg (60mg) q6h
- Hydroxyzine 50 mg q4h
- Cetirizine 10 mg QD
- Famotidine 20 mg BID for GI ppx
- Due to significant trismus, patient was given Toradol with as needed Lortab for pain

Readmission-

- Same regimen as initial presentation
- Cromolyn 200 mg QID for new GI symptoms
- IV Diphenhydramine 50 mg q8h, Montelukast 10 mg QD, Fexofenadine 60 mg BID
- Pain control: scheduled Ibuprofen with PRN Oxycodone and Morphine
- Initiated on 0.35 mg progesterone oral contraceptive pill and C1 esterase inhibitor to take during future acute angioedema attacks
- Discharged on a steroid taper, antihistamines, progesterone-only OCP, and instructions to follow up with an angioedema specialist

Discussion

- Diagnosis of HAE with normal C1-inhibitor levels presents a conundrum in conventional hospitalist medicine.
- This patient was refractory to conventional treatment with antihistamines and steroids, which was further made difficult by normal C1-inhibitor levels, which rules out histaminergic/conventional HAE.
- Patient falls into a category of HAE Type III.
- There are genetic mutations of bradykinin-type of angioedema, one of which is present in females corresponding to estrogen fluctuations in menstrual cycle with normal C1- inhibitor studies.
- Progesterone - only oral contraception in these females can help to reduce severity of angioedema episodes.
- This case shows that there are variants of angioedema that are refractory to conventional treatment.
- Expert consultation should be warranted for genetic testing and initiation of unconventional treatment modalities.

Conclusion

- Angioedema mediated by either mast cells or bradykinin activation requires prompt recognition and treatment with antihistamines and steroids.
- There exist subsets of HAE that result in atypically normal C1 esterase levels and are refractory to conventional treatment.
- Treatment with standardized therapy is minimally effective and this requires expert consultation and referral.

References

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