Idiopathic Angioedema: A Subtle Presentation

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PATIENT HISTORY

CHIEF COMPLAINT:

A 44-year-old man presented to the community clinic complaining of:

- Localized lower lip swelling
- Onset 12 hours previous to the visit
- Gradually worsening over time
- No dyspnea, rash or pruritis
- No new creams, lotions, or meds
- No fever, tenderness, recent dental work, trismus, difficulty swallowing, or trauma.
- Works as cook; no contact with shrimp

PAST MEDICAL HISTORY:

- No previous illnesses or surgeries

Allergies:

- Shrimp consumption causes rash but no history of labial swelling.

PHYSICAL EXAMINATION

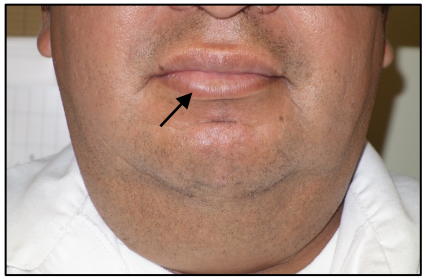

Figure 1. Subtle swelling left lower lip

VITALS: BP: 108/62 mmHg
Temp 97.1°F, HR: 70, Resp: 16

GENERAL:
Exam was noncontributory except for:

Face: mild, painless swelling of the right lower lip and surrounding tissues with no tenderness, erythema, or warmth.
Oral: good oral dentition

DIFFERENTIAL DIAGNOSES

A. Dental abscess

B. Idiopathic angioedema (AE)

C. Resolving herpes simplex virus (HSV)

D. Crohn's disease

Commentary:

- Dental abscess: No pain at infected site, trismus, or sensitivity to hot or cold stimuli; no gingival edema, erythema, fever, or fluctuant mass. Considered this as possible complication: infection of surrounding tissue
- HSV: No recent cold or vesicular rash on erythematous base at the vermilion border.
- Crohn's Disease was considered because swelling can present before GI manifestations.[1] But patient did not have oral ulcers, fatigue, weight loss, abdominal pain, diarrhea, or family history.

DISCUSSION

AE is defined as localized, transient edema of subcutaneous and submucosal tissues due to a temporary increase in vascular permeability from the release of vasoactive mediators.

Idiopathic allergic AE is the most common form and is a diagnosis of exclusion

- Focal swelling develops rapidly and peak in 5 hours
- Mostly affects the face while sparing the gastrointestinal and laryngeal mucosa[4]
- Ig-E-mediated Type 1 reaction; mast cells release histamine or vasoactive mediators
- Antihistamine and corticosteroids are the mainstay treatment of idiopathic AE

C1 esterase inhibitor deficiency (C1-INH) is the most common form of hereditary AE

- Abnormal complement cascade resulting in unregulated activity of vasoactive mediators bradykinin, kallikreins and plasmin.
- Prevalence: 1/10,000 – 100,000.[3]
- Bradykinin causes skin, upper respiratory airways and gastrointestinal tract symtpoms
- Order C1 INH and C4 for patients with family history of AE or suspect C1-INH deficiency
- Antihistamines, glucocorticosteroids, and epinephrine have little to no effect hereditary AE
- Treatment of choice is plasma-derived C1-INH concentrate

ACEI AE is a pharmaceutical side effect that initiates unregulated bradykinin production causing edema in the face, lips, eyelids, tongue, neck and upper airways

- Incidence is highest (25%) in first month of starting meds but may occur years after use.[2]
- Occurs in less than 1% of patients[4]
- Epinephrine is used for laryngeal edema and anaphylaxis.
- Definite treatment is the discontinuation of the offending agent.

CONCLUSION

- Successful AE management requires detection and avoidance of triggers, early recognition of acute attacks, and aggressive airway management.
- The most common type of AE is idiopathic and responds to antihistamine and corticosteroids.
- If the patient is not responding to treatment, consider hereditary or medication induced AE.
- Antihistamines, glucocorticosteroids, and epinephrine have little to no effect hereditary AE.
- Treatment of choice is plasma-derived C1-INH concentrate.

REFERENCES

1. Gu Y, Williams M, Poh CF. How do I evaluate a patient with a swollen lip? *J Can Dent Assoc.* 2010;76:a92.
2. Temiño VM, Peebles RS Jr. The spectrum and treatment of angioedema. *Am J Med.* 2008;121(4):282-286.
3. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy.* 2014;69(5):602–616.
4. Byrd JB, Adam A, Brown NJ. Angiotensin-converting enzyme inhibitor associated angioedema. *Immunol Allergy Clin North Am.* 2006; 26:725–737.

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ABSTRACT

A 44-year-old male presented to the community clinic complaining of localized lower lip swelling that started gradually last night, totaling 12 hours at time of visit. He denied any difficulty breathing, rash or itchiness. The patient did not use any new creams, lotions, or medications. He has a shrimp allergy that produces a rash but had no prior episode of labial swelling. The patient works as cook but had no contact with shrimp. He also denied fever, tenderness, recent dental work, trismus, difficulty swallowing, or trauma.

He was alert, oriented, and in no acute distress. Vital signs were within normal limits. Examination revealed a mild, painless swelling of the right lower lip and surrounding tissues with no tenderness, erythema, or warmth. The physical examination was otherwise unremarkable.

The patient was diagnosed with mild idiopathic angioedema (AE). He was started on 25 mg of diphenhydramine every six hours as needed, scheduled to return in one week, and given emergency precautions. The patient did not return to the clinic and was lost to follow up. Dental abscess, resolving herpes simplex virus (HSV), and Crohn's Disease were considered in the diagnosis. Patients with dental abscess present with pain at infected site, trismus, sensitivity to hot or cold stimuli. They also have physical exam findings of gingival edema and erythema, fever, and a fluctuant mass. Potential complications include infection and cavernous sinus thrombosis. HSV was ruled out because the patient did not have a recent cold or a vesicular rash on erythematous base on the vermilion border. Crohn's Disease was considered because lip swelling can present earlier than gastrointestinal manifestations.[1] The patient did not present with oral ulcers, fatigue, weight lost, abdominal pain, diarrhea, or family history.

AE is defined as localized, transient edema of the subcutaneous and submucosal tissue due to a temporary increase in vascular permeability caused by the release of vasoactive mediators. AE often resolves in hours to days but can be life threatening with upper airway involvement. AE occurs in approximately 15% of population.[2] The swelling is nontender, nonpitting, and asymmetric and occurs in the periorbital region, lips, tongue, extremities, genitalia and bowel wall. A careful history attempts to identify potential triggers: stress, heat, cold, trauma, UV light, allergies, family history, and medications. If suspecting AE, the first step is aggressive airway management when warranted. Afterwards, correctly identifying AE and its cause is vital to management. The main categories of AE are idiopathic, hereditary, and angiotensin-converting enzyme inhibitor (ACEI).[3]

Idiopathic allergic AE is the most common form and is a diagnosis of exclusion. These patients develop focal swelling rapidly that peak in 5 hours. It most affects the face while sparing the gastrointestinal and laryngeal mucosa.[4] It is thought to be an Ig-E-mediated Type 1 hypersensitivity reaction that causes mast cells to release histamine and other vasoactive mediators. Antihistamine and corticosteroids are the mainstay treatment of idiopathic AE.

The most common form of hereditary AE is a C1 esterase inhibitor deficiency (C1-INH) of the complement cascade resulting in unregulated activity of vasoactive mediators bradykinin, kallikreins and plasmin. There is estimated prevalence of 1/10,000 – 100,000.[3] It causes an unregulated activity of the vasoactive mediators bradykinin that affects the skin, upper respiratory airways and gastrointestinal tract. Order laboratory levels of C1 INH and C4 for patients with family history of AE or suspected C1-INH deficiency. Unlike the acute attacks of idiopathic allergic AE, antihistamines, glucocorticosteroids, and epinephrine have little to no effect hereditary AE. Treatment of choice is plasma-derived C1-INH concentrate.

ACEI AE is a well-documented pharmaceutical side effect that initiates unregulated bradykinin production causing edema in the face, lips, eyelids, tongue, neck and upper airways with airway obstruction dangers. The incidence is highest (25%) within the first month of starting medication but may present years after use.[2] ACEI AE occurs in less than 1% patients taking ACEI therapy.[4] Epinephrine is used for laryngeal edema and anaphylaxis. Definite treatment is the discontinuation of the offending agent.

Successful AE management requires detection and avoidance of triggers, early recognition of acute attacks, and aggressive airway management. The most common type of AE is idiopathic and responds to antihistamine and corticosteroids. If the patient is not responding to treatment, consider hereditary or medication induced AE.

REFERENCES

1. Gu Y, Williams M, Poh CF. How do I evaluate a patient with a swollen lip? *J Can Dent Assoc*. 2010;76:a92.
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