ANGIOEDEMA

Typically affects the skin and mucosa of the face, lips, mouth, and throat, larynx, often in an asymmetric pattern.

- Bowel wall angioedema is occasionally seen in patients on ACE inhibitors and frequently in those with hereditary or acquired C1 inhibitor deficiency.

Types of angioedema

- Mast cell-mediated, also called histaminergic angioedema
- Bradykinin-mediated angioedema
- Idiopathic

Mast cell-mediated -histaminergic angioedema

- Symptoms begin within minutes of exposure to the allergen, builds over a few hours, and resolve in 24 to 48 hours.
- Often but not always presence of other signs and symptoms of mast cell mediator- histamine release.
    - Urticaria, flushing, generalized pruritus, bronchospasm, and/or hypotension.
- Etiology
    - Triggered by allergen such as foods, insect stings, latex, drugs including NSAID, narcotics, radiocontrast, thienopyridines (Clopidogrel/Plavix and and Prasugrel/Effient)
        - Of note, non-thienopyridines such as Ticagrelor/Brilinta does not have cross-reaction with (Clopidogrel/Plavix and and Prasugrel/Effient).

Bradykinin-mediated angioedema

- Contrary to mast cell mediated it is more typical to present with symptoms over a longer period of time (hours to days) and not associated with urticaria, bronchospasm, or other symptoms of allergic reactions.
- Etiology
    - ACE inhibitors and angiotensin receptor-neprilysin inhibitor (ARNIs)
        - Symptoms typically begin during the first week of treatment, although some cases develop after years of uneventful therapy.
        - There are no laboratory tests to diagnose ACE inhibitor-induced angioedema. Resolution following discontinuation of the ACE inhibitor confirms the diagnosis.
        - Their use can unmask previously asymptomatic hereditary and acquired angioedema disorders.
            - So, in patients taking ACE-I with risk factors for alternate etiologies C4 screening is recommended
    - Hereditary and acquired angioedema due to C1 inhibitor deficiency
        - In patients with risk factors for hereditary or acquired angioedema C4 screening is indicated and if f the C4 level is low
            - Testing for C1 inhibitor levels
            - Referral to allergist/immunologist
        - Hereditary angioedema
            - Typically present in childhood or early adolescence
        - Angioedema may follow trauma, infection, dental procedures, or emotional stress
        - Risk factors for hereditary angioedema
            - Family history
            - Lymphoma or MGUS
    - The acquired angioedema
        - Typically occurs at an older age

        - Most patients have an associated lymphoproliferative or autoimmune disorder
- **Idiopathic**
    - Infections
        - Although more common in children can be seen in adults specially after viral infection and streptococcus pharyngitis.
    - Several drugs
        - Calcium channel blockers, amiodarone, metoprolol, risperidone, paroxetine, sirolimus, inhaled cocaine, several herbal medicines
    - Rare causes of angioedema
        - **Disorders with eosinophilia**
            - Hypereosinophilic syndromes
            - Gleich syndrome
        - Urticarial vasculitis

Treatment:

- Immediate intubation if evidence of impending airway obstruction.
- Oxygen via facemask as needed if no need for intubation.
- Angioedema with anaphylaxis
    - Epinephrine IV infusion at 0.1 mcg/Kg/min and titrate according to BP, HR, and oxygenation.
- Management of mast cell-mediated-histaminergic angioedema
    - Diphenhydramine 25 to 50 mg IV q12h
    - Famotidine 20 mg IV q12h
    - Methylprednisolone 125 mg IV followed by 60 mg q12h initially
        - Replace with prednisone 40 mg/d and tapered over five to seven days
- Management of bradykinin-mediated angioedema
    - It does not respond to epinephrine, antihistamines, or glucocorticoids.
    - Patients with C1-inhibitor deficiency can be treated with:
        - C1-inhibitor concentrate
        - Kallikrein inhibitor ecallantide
        - Bradykinin β_2-receptor antagonist Icatibant
        - Fresh frozen plasma if these agents are not available
    - Patients taking ACE-I or ARNIs the treatment is largely supportive.
        - If severe consider treatment as in patients with C1-inhibitor deficiency.
        - Consider tranexamic acid 1 gr IV over 30 min.