Angioedema Causes, Symptoms and Treatment

Angioedema is a term used to describe giant wheals or wheals involving the mucous membrane surface lasting longer than urticaria. Angioedema is a deep-tissue swelling that must be distinguished from urticaria.

Angioedema is rarely itchy and tends to give discomfort from pressure. In hereditary angioedema and sometimes in idiopathic angioedema, there is often a premonitory tingling before the swelling occurs.

Any part of the body (including gut) may be involved) It may occur over the face (primary periorbital area, lips, tongue), an extremity or within a vital organ system

Causes of Angioedema

- Allergic (accompanied by other features such as urticaria, anaphylaxis,).
- Hereditary C1-esterase inhibitor or C4BP deficiency
- ACE deficiency.
- Acquired C1-esterase inhibitor deficiency (autoantibody-mediated, SLE, lymphoma). Lymphoma-associated acquired C1-esterase inhibitor deficiency is usually due to splenic villous lymphomas.
- Physical (pressure, vibration, water—often with urticaria).
- Drugs (Angiotensin-converting enzyme inhibitors, NSAIDs, statins, proton-pump inhibitors are the most common drugs).
- Idiopathic.

Pathophysiology of angioedema

Histamine and chemokine release from mast cells and basophils is the basic pathogenetic mechanism in angioedema and urticaria These chemical mediators act on the blood vessels causing vasodilatation (erythema), sensory nerve stimulation that leads to itching, increased vascular permeability and leakage of fluid into the skin leading to dermal edema.

The activation of mast cells and basophils may be both immunologic and nonimmunologic.

Immunologic activation involves Type I—Type IV hypersensitivity reactions depending upon the cause, whereas nonimmunologic activation happens due to direct degranulation of mast cells by certain agents (drugs—morphine, codeine; foods—strawberries and shellfish)

Immunological features

The mechanism is thought to involve activation of the kinin system with bradykinin production, leading to tissue edema.
ACE inhibitors inhibit bradykinin breakdown (also cause cough due to excess bradykinin).
Histamine is not involved (unless there is accompanying urticaria).

The C1-esterase inhibitor is a control protein for the kinin cascade in addition to its role in the complement and clotting systems. There are polymorphisms of this enzyme but it is not known whether they correlate with the tendency to develop angioedema.

Congenital ACE deficiency has also been associated with angioedema.

Diagnosis

History and clinical observation will give useful clues in the diagnosis of angioedema:

family history, connective tissue disease, lymphoma (may be occult), drug exposure, association with physical stimuli.

Differential Diagnoses

The differential is wide.

Angioedema with urticaria will not be due to hereditary angioedema.

In angioedema without urticaria, C1-esterase inhibitor deficiency should be excluded.

- C4 will be low, even between attacks;
- C1-inhibitor will be low in type I but high in type II.
- Levels of C2 are said to distinguish acquired from inherited C1-esterase inhibitor deficiency (low in inherited deficiency) but this test is not reliable.

If acquired C1 esterase inhibitor deficiency is suspected, check for:

- Lymphadenopathy and splenomegaly clinically
- Serum immunoglobulins
- Serum and urine electrophoresis;
- Serum-free light chains

Consider a chest/abdominal CT scan.

Check ACE level to exclude ACE deficiency.

Connective tissue disease will usually be obvious, but the detection of autoantibodies (antinuclear antibody (ANA), dsDNA, and extractable nuclear antigen (ENA) antibodies) may be necessary.

Treatment

The goal of managing urticaria is to identify and then remove the offending agent/cause.

Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) may aggravate urticaria and should be avoided.
Soothing lotions (calamine) and cool compresses are given for relieving pruritus.

A trial of elimination diet or a course of antibiotic, antifungal, and antihelmintic drugs may be useful in some cases.
H1 anti-histaminic drugs (AHD) are the mainstay of treatment.

Acquired C1-esterase inhibitor deficiency (AAE) due to lymphoma will be improved by effective treatment of the underlying disease, as will the autoimmune-associated angioedema.

Purified C1-esterase inhibitor may be required in acquired C1-esterase inhibitor deficiency; Frequent doses may be required because of the presence of inhibitory antibodies:

In severe cases, plasmapheresis and immunosuppression may be required;
FFP is less effective and may actually make the angioedema worse by providing an extra substrate.

There is no role for C1-esterase inhibitor concentrate in idiopathic angioedema without evidence of deficiency.
Icatibant (bradykinin B2 receptor antagonist) may have a role in the management of severe recurrent angioedema; it can be self-administered by subcutaneous injection.