**Intermittent swelling of the eyelids and mild urticaria in a young man**

O. M. SCHOFIELD

---

**Presenting problem**

A 35-year-old man presents with a 6-week history of intermittent swelling of the eyelids. The swelling is not itchy or painful, and each episode lasts for about 3 days. It is not associated with any other ocular symptoms. The patient also describes an itchy rash that he describes as being ‘like a nettle rash’, which has been occurring intermittently over the last 2 months. Oral antihistamines have not been helpful. At no time has he had any swelling of his mouth or tongue. He is otherwise well, except for hypertension for which he takes enalapril. He has no history of any allergies. Direct systems enquiry also reveals that more recently he has developed intermittent abdominal pain associated with the eyelid swelling. He has a sister who has systemic lupus erythematosus and who he thinks has also had problems with eyelid swelling.

**What would your differential diagnosis include before examining the patient?**

Intermittent eyelid swelling is usually due to angioedema. This can be associated with urticaria and/or dermographism, or can occur in isolation. Angioedema most often occurs as a result of an immunoglobulin E (IgE)-mediated allergic response and in these cases there is usually a history of associated urticaria and a potential trigger for the attacks. The triggers can include allergens such as animals or specific foods, or physical stimuli such as exercise or heat. Certain drugs (e.g. aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), penicillin, angiotensin-converting enzyme (ACE) inhibitors and radiocontrast media) can cause angioedema. When angioedema occurs without urticaria, one has to include the differential diagnosis of hereditary angioedema, in which the attacks start in the second decade, and acquired angioedema (AAE). AAE1 is a rare disorder associated with B cell lymphoproliferative disorders, and AAE2 is an autoimmune condition. Alternative diagnoses to angioedema as a cause of eyelid swelling include lymphoedema and connective tissue disorders such as dermatomyositis. In these situations the eyelid swelling is chronic rather than intermittent.

In this man’s case the eyelid swelling is intermittent and associated with some mild urticaria and a family history of both connective tissue disease and possible eyelid swelling. One would therefore consider angioedema to be the most likely diagnosis but the cause needs to be investigated.
Swelling of the eyelids and mild urticaria

**Examination**

He appears well and has significant swelling of his eyelids, the left more marked than the right (Fig. 2.1). There is no evidence of any urticarial eruption and general examination is unremarkable. His blood pressure is well controlled at 115/70 mmHg.

**Further investigations**

Blood tests are performed for a full blood count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), urea and electrolytes, liver function tests, creatine kinase (CK) level, thyroid function tests, serum immunoglobulins including IgE, complement levels, antinuclear antibody, anti-double-stranded DNA antibody and C1 esterase inhibitor (C1-INH). The results of these investigations are all within the normal range.

**Does this narrow down your differential diagnosis?**

The investigations are all within the normal range and therefore have brought us no further forward in terms of establishing the cause of this man’s urticaria. The normal CK and C1-INH levels all but rule out diagnoses of dermatomyositis and hereditary angioedema.

**How will you treat this patient?**

Looking back through his history, it is apparent that temporally his symptoms started soon after commencing enalapril for hypertension. This is an ACE inhibitor and this class of drugs is well known for causing both urticaria and angioedema. In addition a careful history has revealed that he has abdominal pain in association with the attacks of eyelid swelling. Angioedema can affect three predominant sites: subcutaneous tissue (such as around the eyes), abdominal organs (stomach and intestines), and upper airway (which can result in life-threatening laryngeal oedema).

The patient was advised to change his antihypertensive medication from an ACE inhibitor to an alternative class of agent, and within a month his symptoms improved.
Global issues

- Angioedema is a potentially lethal condition if there is involvement of the tongue or throat due to airways obstruction.

- Oral antihistamines are the mainstay of treatment (both H1 and H2 antagonists).

- Angioedema occurring without any history of urticaria should lead to suspicion of hereditary angioedema.

- Neither hereditary angioedema nor drug-induced angioedema responds well to oral antihistamines.

- Around 1% of individuals on ACE inhibitors develop angioedema. If the drugs are not withdrawn, then attacks become more severe with time.

- The history and examination are the key clues to the diagnosis here. Investigations such as CK, C1-INH and double-stranded DNA antibody are expensive and probably unwarranted in resource-poor settings.

See Chapters 4 and 27 of *Davidson’s Principles and Practice of Medicine* (20th edn) for more on angioedema.