

Allergic urticaria and hereditary angioedema

Independent association in the same patient

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Summary

A patient presented with both allergic urticaria and hereditary angioedema. The two conditions occurred independently, the urticaria being associated with allergy to food (which could be managed by control of the diet), whereas the angioedema was associated with C₁ esterase inhibitor deficiency.

Introduction

The incidence of atopy in the population is at least 15% (Van Arsdel & Motulsky, 1949), and although there is some evidence for HLA linkage of atopy (Turner *et al.*, 1977), it is known that the gene for C₁ esterase inhibitor is not HLA-linked but is an autosomal-dominant disorder. The genetic predisposition for the two diseases should segregate independently. Thus, specifically considering hereditary antioedema (HAE), it would be expected that 15% would be atopic.

We present here a family with HAE and allergic urticaria in which the propositus had clear evidence of both diseases.

Case description

Patient RR, a male of 50 years presented with chronic urticarial eruption covering any area of his body. Interspersed with these attacks which were extremely itchy were swellings which would appear on his face and lips, these being painful and tender rather than itchy. Treatment with cimetidine and chlorpheniramine was ineffective, indeed the former made the angioedema worse. Associated with the skin lesions the patient had frequent attacks of abdominal pain which were often associated with the appearance of the skin lesions and lasted for up to 48 hr. Latterly, when it became clear that foods induced his urticaria, and he had received treatment with danazole for his hereditary angioedema, he became completely symptom-free.

In addition to the urticaria, the patient also had chronic rhinitis and asthma for

which he took sodium cromoglycate (Intal, Fisons Ltd). Housedust and cat were potent precipitating allergens of his asthma.

Family history

The patient has two children. The son aged 21 has chronic rhinitis and recurrent abdominal pain for which he has had a number of operations with no abnormal pathology being found. The daughter aged 19, has rhinitis and has had two attacks of angioedema affecting the lips. Recently she has had two periods of surgical observation for severe colicky abdominal pain which has settled within 72 hr. These were thought to be due to intestinal angioedema. The patient's father (Fig. 1a) had recurrent swellings of his tongue and foot. His brother had swelling of the tongue and penis and his two children (aged 10 and 12) are so far unaffected. His sister had asthma but no urticarial lesions.

The patient's two children have C₄ levels which were consistently below 80% of normal and C₁ esterase inhibitor levels below 50%. The daughter was treated with methandienone and became symptom-free. The son, although with a low level of inhibitor, had only allergic symptoms and no clinical evidence of angioedema.

Investigations

Patient RR

Skin tests to several inhalent allergens showed positive responses to housedust mite, grass pollen and cat dander. Full blood count and stool culture showed no abnormality. Total IgE was 180 U/ml and RAST showed positive responses to milk (grade 4), cheese (3) and rice (2).

Complement studies

Before treatment for C₁ esterase inhibitor deficiency, three serum samples showed total

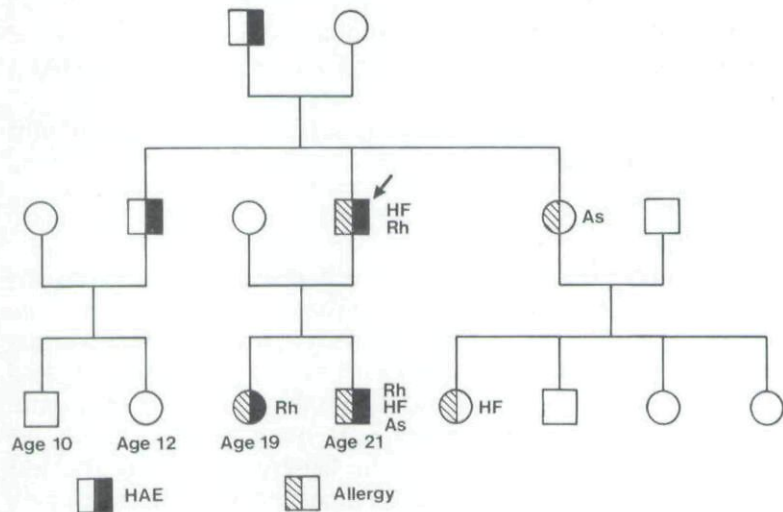


Fig. 1. Family tree of propositus RR. Allergy and HAE segregate independently (arrow points to propositus).

haemolytic complement 80–89% of normal, C₄ 74–102% of normal, C₃ 100–106% of normal and C₁ esterase inhibitor levels of zero, 34 and 55% of normal. Similar inhibitor levels were found when measured by either functional or antigenic assays. After starting danazole, the haemolytic complement, C₄ and inhibitor levels rose to normal and remained there. When his treatment was changed to methandienone the levels stayed within the normal range.

Clinical progress

The positive RASTs indicated that the urticaria could have been due to a food allergy. On this assumption the patient was treated by diet alone. With this management, the itchy urticarial lesions disappeared but could be provoked by dairy produce and rice. However, dietary management did not affect the frequency or severity of the angioedema. Eventually it was decided to treat the angioedema with danazol which resulted in cessation of the angioedema and also the attacks of abdominal pain. He remained symptom-free and was eventually changed to treatment with methandienone which we have found a cheap and reliable therapy in nine other patients.

Discussion

Atopy is a frequent condition in the population, such that in any unrelated condition it would be expected that about 15% of those suffering would be atopic. We have found other examples of patients with an atopic history who presented with angioedema associated with C₁ esterase deficiency, but none in which the simultaneous appearance of symptoms from both sources was so confusing and striking. The ability to relieve one set of symptoms with one remedy, and to leave the other unaffected added strength to the view that both conditions were contributing to his overall state. It could otherwise be argued that urticaria and angioedema were simultaneous manifestations of the same allergic state.

We advised him to take danazol initially which is a proven, effective agent for the treatment of hereditary angioedema (Hosea *et al.*, 1980). The disadvantages of this drug in our hands are 2-fold: firstly, it is a potent contraceptive, preventing ovulation, and secondly the cost of treatment is about £1000 for a woman and about £1500 for a man. In contrast, treatment with other anabolic steroids costs about 2% of this.

There is also interest in the treatment of angioedema associated with deficiency of C₁ esterase inhibitor, both because of an acquired form seen in some patients with tumours (Cohen *et al.*, 1978) and that seen in association with the use of cyclosporin A (Isenberg *et al.*, 1980). The use of anabolic steroids has largely superseded cyclokapron as treatment except for the patient with very infrequent attacks. It is, however, unclear whether anabolic steroids are effective in the acquired angioedema mentioned above.

It is about 100 years since the first descriptions of HAE by Quincke (1882) and Osler (1888), and we present this case to re-emphasize the differences between the urticarial lesions associated with allergy (IgE-mediated?) and those associated with C₁ esterase inhibitor deficiency.

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