Familial angio-oedema—a particularly severe form

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Summary

A case of hereditary angio-oedema is described together with the family history and manifestations in the father of the patient. The problems encountered in his management are discussed, including tracheostomy and genetic counselling.

Introduction

Angio-oedema was first described by Quincke in 1882; a familial variety by Sir William Osler in 1888 and subsequently by other authors.

The condition behaves as an autosomal dominant factor and so far only heterozygotes have been described. It has three common major manifestations, oedema of the larynx, causing stridor, oedema of the gut, causing vomiting and colic, or oedema of the limbs giving painless non-inflamed swelling. The onset is usually in childhood but can be at any stage of life. Each attack is self-limiting, clearing in 1-4 days, but the life-threatening aspect of the illness is the laryngeal oedema. This may manifest in a mild or devastatingly serious manner, requiring urgent tracheostomy. A rare manifestation is with epilepsy due to angio-oedema of the brain.

Interest in the condition has revived following the discovery of a deficiency of inhibitor of the activated first component of complement ($\bar{C}_1$), levels of less than 30% of normal being diagnostic. The $\bar{C}_1$ -inhibitor activity is spared to some extent by the antifibrinolytic agents (e.g. aminocaproic acid) and these form the basis of prophylaxis. Acute attacks usually respond to infusions of fresh frozen plasma which supplies this heat labile $\bar{C}_1$ -inhibitor (Pickering *et al.*, 1969, 1973; Landerman *et al.*, 1962; Leading Article, 1973). The case described is of unusual severity and illustrates the problems of management of this condition.

Case report

A 28-year-old builder's labourer presented in March 1975 with a 6-hr history of swelling of the lower face and neck and developing stridor. He was very hypoxic on reaching the Casualty Department and an emergency tracheostomy was performed. He

had already received steroids and antihistamines and these were continued intravenously.

Since childhood the patient had had recurrent attacks of vomiting and abdominal pain lasting 1-4 days and at intervals of about 1 month. They had always been self-limiting. During his in-patient stay he developed one such attack which was treated conservatively.

From the age of 20 years he had intermittent swellings of the hands or feet, lasting 1-4 days, always painless, non-itchy and not inflamed. Resolution always left full function.

When the patient's laryngeal oedema had settled it emerged that his father had died at home from a similar attack in 1965. The details of the father's illness were obtained from the hospital notes of his admission in 1947 with swelling of the face and a little blood in the urine but no proteinuria. This was diagnosed as 'nephritis' but he had two unexplained attacks of 'colicky vomiting' whilst in hospital then.

Assay of the $\bar{C}_1$ -inhibitor level in the present patient showed an enzymic level of only 28% thus confirming the diagnosis of hereditary angio-oedema. The patient has two sisters, and has been twice married, so his offspring and siblings were all

FIG. 1. Family tree. Figures represent the assay of $\bar{C}_1$ in Professor Lachmann's department.

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investigated. He seems to be the only member of his family manifesting the condition (Fig. 1).

During the in-patient stay the patient was commenced on ϵ -aminocaproic acid 3 g/4 hr. Ten days later he developed the signs and symptoms in the calf of the left leg that on clinical grounds could only be interpreted as a deep venous thrombosis. It was untimely that this coincided with a breakdown of X-ray screening facilities and a venogram could not be arranged immediately. He was anticoagulated and the leg improved. The venogram 5 days later failed to demonstrate venous occlusion. However, this prompted the change of therapy to the more potent tranexamic acid taken 6 hourly in tablet form.

Discussion

It is assumed that the patient's father had hereditary angio-oedema, on the basis of his 'nephritis' of 1947, which seems to have been facial hereditary angio-oedema, and his recurrent attacks ending with a fatal attack involving the larynx. There is no accurate account of the health of the next generation back.

Kagen and Becker (1963) showed that patients with hereditary angio-oedema had a low level of $\bar{C}_1$ -inhibitor. This has been further characterized as a heat labile fraction available therapeutically in fresh frozen plasma. An enzymic assay should detect all cases (Rosen *et al.*, 1965; Donaldson and Rosen, 1966).

Antifibrinolytic agents have been shown by clinical trials to offer some prophylaxis by sparing $\bar{C}_1$ -inhibitor (Beck *et al.*, 1973; Champion and Lachmann, 1969). The patient described developed a clinical deep venous thrombosis on aminocaproic acid in full dosage, and although extensive muscle necrosis has been described with aminocaproic acid therapy (Korson-Bengtsan *et al.*, 1969), it was felt that anticoagulant therapy could not be withheld.

Tranexamic acid has been reported to be of greater prophylactic value (Blohmé, 1972), and is more convenient to take and this patient is now on tranexamic acid. He feels his attacks are less frequent and less severe, but in 6 months he had had two attacks of facial oedema and each has rapidly responded to an infusion of 2 u of fresh frozen plasma.

In view of the near fatal attack of laryngeal hereditary angio-oedema, the patient was offered a permanent tracheostomy, but he declined and, so far, by presenting to the same casualty department immediately any signs of facial swelling develop, serious attacks have been aborted.

There is also little mention in the literature of

genetic counselling for this condition. The patient has four children by two marriages and only the newborn male infant has a low assay. This child will be followed-up with much care and interest. With such a severe form of the condition and an expected incidence of 1 in 2 in the offspring it seems reasonable to caution the patient of the risks involved for further children.

It has been suggested (Rosen and Austen, 1969), that fresh frozen plasma may initially worsen the condition by supplying not only the required inhibitor but also the substrate parts of the complement cascade allowing the production of vaso-active components of the complement system. This has not so far been observed in the treatment of this patient.

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