

Case report



IDIOPATHIC ACQUIRED NONHISTAMINERGIC ANGIOEDEMA – A case report

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SUMMARY

Angioedema is a self-limited, localized swelling that involves subcutaneous tissue or mucosa of the face and other areas. It affects males and females equally, usually during the 3rd and 4th decades of life.

We present a patient with angioedema of the head and neck with a typical clinical picture of an acquired type and with a normal level of C1-INH. Initially the patient was treated with a combination of drugs for allergy. However the swelling did not respond to the therapy and fresh frozen plasma was added. After the 10th day, the edema began reducing progressively.

Despite the controversies in the literature we demonstrate that FFP is useful not only to ameliorate the acute attack but also for prophylaxis.

Keywords: angioedema, allergy, fresh frozen plasma,

INTRODUCTION

Angioedema is a self-limited, localized swelling that involves subcutaneous tissues or mucosa of the face and other areas. Skin colour is usually unchanged. [1] The main reason for the angioedema is the loss of vascular integrity allowing fluid to escape into soft tissues. Exposure of the vasculature to inflammatory mediators causes dilatation and increased the permeability of capillaries and venules. [2-4]

Angioedema without urticarial flares (hives) is poorly understood. Its causes are diverse, and little is known about its pathogenic mechanisms. [5] Angioedema occurs without urticaria, and does not respond to drugs against allergies. Depending on the underlying mechanism, Hallak et al. (2012) subdivided angioedema into three types: mast cell mediated, bradykinine mediated, and unknown etiology. [6]

Lack of response to therapies including antihistamines, steroids, and epinephrine suggested the possibility of angioedema related to a deficiency in the C1-inhibitor protein. The first case of the acquired form of angioedema (AAE) related to a deficiency in C1-inhibitor was published in 1972 by Caldwell et al. [7] The angioedema related to a hereditary or acquired deficiency in protein C1-inhibitor has bradykinine as a mediator.

We present a patient with angioedema of the head and neck with a typical clinical picture of an acquired deficiency in the protein C1-inhibitor activity but with a normal level of C1-INH.

CASE REPORT

A 43-year-old woman presented to the ophthalmology clinic with mild eyelids swelling and foreign body sensation, mainly in the left eye. The history of the patient showed only working in a dusty environment and recurrent episodes of mild eyelids swelling. The patient was in good health and had an allergic predisposition to some foods and drugs. The allergic reaction was suspected, and recommended treatment of corticosteroid was administered. On the next day, no clinical response was noted and the edema extended to the right eye. Antihistamine was then added to the therapy, but without improvement. The swelling involved the eyelids of the eyes, the left side of the face, and mild edema of the tongue and the neck. The patient was in poor general condition, with ataxia and dysarthria, and tracheostomy was done (Figure 1). Routine laboratory blood and urine tests were normal. Immune status (C1, C3, ANA, ANCA, SS-A./RoEIA) was also normal.

Fig. 1. 43-year-old woman with swelling of eyelids, left side of head and neck. 3 days after first signs of swelling (a). 4 days of the beginning (b).





Fig. 2. After 10 days edema began to reduce (a). Recovery of the woman after 43 days (b).



The patient was treated with a combination of drugs: serum NaCl (saline solution 0,9%) 200 ml iv, serum Glucose 250 ml iv, Ca gluconici + Vit C x 1 amp.iv, Urbason 160+80+60mg iv, Gentamycin 80 mg, 2x1 i.v., adrenalin 1 amp. s.c., Allergosan amp. iv, Quamatel 20 mg. iv, Tobradex ung., oxygen therapy and cold compresses.

However the swelling did not respond to the therapy and phlegmon of the face was suspected. Therefore diflucan 200 mg and flagil 2x500 mg were given. On the next day, no obvious improvement was noted, and fresh frozen plasma (FFP) and immunovenin intact were added to the therapy.

The laboratory findings showed a level of C1 – inhibitor 0.329 (normal quantitative analysis between 0.21–0.39 g/L).

Consultation with a neurologist was conducted, and it established that the patient had a normal neurological status and no computer tomography changes.

After allergological, hematological and gastroenterological consultations, the possibility of a lymphoproliferative syndrome and gastrointestinal carcinoma were rejected. After the 10th day the edema began reducing progressively, and disappeared completely within 43 days (Figure 2).



DISCUSSION

Angioedema is a rare disease that affects males and females equally, usually during the 3rd and 4th decades of life.

Our patient, aged 43, presented with recurrent cutaneous and mucosal angioedema without urticaria, without an evident triggering factor, and without a family history of angioedema. The clinical picture of angioedema showed an absence of allergy.

Prada et al. (1998) describe the primary biologic roles of C1 inhibitor (C1-INH) in the regulation of activation of the classical complement pathway and of the

contact system of kinin formation. [8] We identified our patient to have idiopathic nonhistaminergic angioedema having clinical symptoms and a pathogenetic mechanism similar to that of C1-INH deficiency and bradykinin as mediators of symptoms but with a normal level of C1-INH. [9, 10] Hereditary angioedema (HAE) is based on deficiency or dysfunction of C1-INH. Hallak et al. defined two subtypes of HAE and three subtypes of AAE. Type II HAE resulted from the presence of a dysfunctional C1-INH, which is present in normal or elevated amounts and Type II AAE due to inactivation of C1-INH by autoantibodies. [6]

Given the normal level of C1-INH in the patient described here, we suppose inactivation of C1-INH in the result of the formation of autoantibodies directed against C1-INH [11], like in type II AAE due to neutralization of C1-INH by autoantibodies. [10, 12]

The results of complete physical exam, laboratory testing for complete blood cell count with differential, serum protein electrophoresis, chest X ray and abdominal ultrasound assessing lymphoid tissue are normal. The recommended standard testing for lymphoproliferative and autoimmune disease [12] in our patient was negative

When laryngeal edema presents angioedema can progress to asphyxiation and death. Initially we suggested a possible diagnosis of anaphylaxis and infection, and treatment involved antihistamine, steroids, epinephrine, and antibiotics therapy. However, laryngeal edema occurred a few hours after onset of AAE and tracheostomy was performed. The literature suggests that application of C1-INH concentrate is highly and rapidly effective in the treatment of laryngeal edema of HAE and AAE. [13] The laboratory test for C1-INH deficiency was normal, but we performed replacement therapy in the emergency way with fresh frozen plasma, also contains C1 inhibitor, in reverting laryngeal edema. We applied 3000 U of FFP. The same approach has been useful for HAE and AAE. This treatment lasted for three weeks with good results. The success of this treatment approach with FFP in our patient confirms findings of other studies, although this effect is not examined given the nature of disease [12]. There are no studies evaluating its effectiveness, but multiple case

reports appear to support its use in acute attacks. [13-19] Despite the risk of blood borne infection, worsening the severity of the attack because of the inclusion of other biologically active molecules [20], FFP can be used as an alternative where C1 inhibitor concentrate is not available.

Preventing attacks with long term prevention with antifibrinolytics or androgens, or by curing the associated disease [21, 22] is an effective way to prevent new swelling. Although androgen therapy, in vivo, results in an increase in C1-INH plasma levels, a direct effect of androgens on C1-INH synthesis has not been convincingly demonstrated. [7, 11]. We followed up the patient for one year and did not find recurrence or other complications; therefore no preventive treatment was recommended.

CONCLUSION

Angioedema is a potentially life threatening condition, and it is the end result of a variety of pathophysiological processes. Diagnosis is based on specific clinical criteria, and in addition, analysis of immunoglobulin levels and various mediators should be carried out. For successful therapy the differentiation of bradykinin induced angioedema to allergic is crucial. In our case, severe angioedema occurred without urticaria and did not respond to anti-allergy, steroids, and epinephrine drugs. Then the choice of treatment remained FFP. Despite the controversies in the literature we demonstrate that FFP is useful not only to ameliorate the acute attack but also for prophylaxis.

Abbreviation list :

FFP - fresh frozen plasma

C1-INH - C1 inhibitor

AAE - acquired form of angioedema

HAE - Hereditary angioedema

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