ABSTRACT

The most commonly identified causes of angioedema are medications, allergens and physical agents, but most cases of angioedema are idiopathic. Treatment depends on identification of the causative agent and, especially when the mechanism is not identified, on the clinician’s knowledge and experience with innovative therapeutic regimens.

Case report: A 48-year-old man presented with a 3-month history of recurrent severe episodes of angioedema affecting the lips, tongue and throat. A fiberoptic examination revealed laryngeal edema during some episodes. He did not report abdominal pain, nausea or vomiting. No precipitating factors were identified. The patient was not receiving angiotensin-converting enzyme inhibitors. For the previous 4 years, the patient had been receiving levothyroxine for autoimmune thyroiditis. There was no history of facial palsy or hereditary angioedema.

Allergy study: Skin prick test with aeroallergens, food, latex, Anisakis and patch test to a standard series (true test) were negative. Laboratory investigations revealed normal complete blood count (CBC), erythrocyte sedimentation rate, urinalysis, blood biochemistry, serum protein electrophoresis and serum immunoglobulins. IgE concentration was 30 UI/ml. Antiperoxidase antibodies were positive (535 UI/ml). Antinuclear antibodies serum immune complexes and rheumatoid factor were negative. Complement study during acute and asymptomatic periods revealed normal values of C1 esterase inhibitor, C1q, C3, C4, functional activity of C1 inhibitor and CH50.

No pathologic findings were observed in a lip biopsy. The patient was treated with sedating and nonsemiting H1 antihistamines and corticosteroids (prednisone 30 mg/day for 3 months) with no clinical improvement and treatment with 50 mg of dapsone daily was started. Glucose 6 phosphate dehydrogenase deficiency had previously been ruled out. The patient improved and antihistamine and corticoid treatment was withdrawn 1 month after starting the dapsone regimen. No episodes of angioedema appeared during the subsequent year. No reductions in hematologic parameters or adverse events were detected.

Dapsone may be an alternative drug in extreme cases of idiopathic angioedema in patients with poor response to conventional therapy.


RESUMEN

Los elementos más frecuentemente implicados en la etiología del angioedema son fármacos, alérgenos y agentes físicos; sin embargo, la mayoría de los casos son de carácter idiopático. El tratamiento se basa en la identificación del agente causal y en la experiencia del clínico en el manejo de estos cuadros, siendo preciso en algunas ocasiones recurrir a regímenes terapéuticos novedosos.

Idiopathic angioedema treated with dapsone

P. González*, V. Soriano*, T. Caballero* and E. Niveiro*

*Sección de Alergología, Hospital General de Alicante, Alicante. \Servicio de Alergia, Hospital Universitario La Paz, Madrid, Spain.

Correspondence: P. González Delgado
Servicio de Alergología. Hospital General de Alicante
Maestro Alonso, 109
03010 Alicante. Spain
E-mail: gonzalez_gva.es

INTRODUCCIÓN

Angioedema is a constellation of syndromes that present a challenge to the clinician. The most commonly identified causes of angioedema are medicaments, allergens, and physical agents, but most cases of angioedema are idiopathic.

The most effective treatment depends on the identification of the causative agent and specially when the mechanism is not identified on the clinician’s knowledge and experience with innovative therapeutic regimens.

CASE REPORT

A 48 year old man, presented to our Allergy Unit in May 02, because recurrent severe episodes of angioedema affecting the lips, tongue, and throat. He often presented at the Emergency room (once or twice a week for the last 3 months) with tongue and lips swelling, dysphonia and dysnea. A fiber optic examination revealed mild laryngeal edema during some episodes, that resolved within a few hours after treatment with epinephrine, antihistamines or corticosteroids. The patient did not related episodes of abdominal pain, nausea or vomiting. No precipitating factor was identified. He had not been taken angiotensin-converting enzyme inhibitors. The last 4 years he was receiving levothyroxine, because an autoimmune thyroiditis. There was no history of facial paralysis or hereditary angioedema.

Physical examination revealed edema limited to the lower lip, the remainder of his examination was unremarkable.

Skin prick tests to a battery of inhalants, foods, latex, Anisakis simplex and patch test to a standard series (True test, Abelló, Spain) were negative.

Laboratory investigation revealed normal complete blood count (CBC), erythrocyte sedimentation rate, urinalysis, blood biochemistry (liver and renal function tests), C reactive protein, serum protein electrophoresis, serum immunoglobulins. Total IgE was 30 UI/ml. Antibodies anti-peroxidase were positives: 535 UI/ml. Antinuclear antibodies and rheumatoid factor were negative. (normal values up to 34). Serum immune complexes, antinuclear antibodies and rheumatoid factor were negative.

Complement study during acute and asymptomatic periods revealed normal values of C1 esterase inhibitor, C1q, C3, C4 and CH50. Functional activity of C1 inhibitor was higher than 90 %.

Three different stool samples were negative for parasites. X-ray studies of thorax and paranasal sinuses showed normal findings.

A biopsy of the lip was performed to exclude a cheilitis granulomatosa. No pathologic findings were observed in such specimen.

The patient was treated with sedating and nonseminating H1 antihistamines and corticosteroids (prednisone: 30 mg every day during 3 months) with no improvements. The patient was then treated with dapsone 50 mg/day, presenting no episodes of angioedema, and was able to suspend the treatment with corticosteroids. The patient did not present any adverse effects with this treatment, and was discharged with instructions to continue with dapsone 50 mg/day.
clinical improvement. So we decided to start treatment with dapsone 50 mgs daily (previously a deficiency of glucose 6 phosphate dehydrogenase was excluded). Clinically the patient improved and during the subsequent year, no episodes of angioedema appeared. Corticosteroids and antihistamines were stopped one month after starting treatment with dapsone. CBCs were performed weekly during the first month of therapy, monthly for the next 6 months and every 6 months thereafter. No reduction in leukocytes, platelets, or hematopoiesis was detected. No others adverse effects were observed during treat-ment with dapsone.

DISCUSSION

The term angioedema describes the localized, transient episodic edema of the deeper layers of the skin or of the mucosa of the gastrointestinal tract. Angioedema affecting the throat, may lead to obstruction of the airways and death from asphyxiation. The most commonly identified causes of angioedema are medications, allergens and physical agents, but most cases of angioedema are idiopathic1. Rare forms of angioedema associated with either hereditary or acquired faulty activation of the complement and kallikrein-kinin systems have been extensively described2,3.

After excluding the most probable causes of angioedema, we conclude that our patient presented an idiopathic angioedema. In spite of treatment with antihistamines and a daily scheme of oral corticos-teroids for 3 months, the patient continued with re- current episodes so therapy with dapsone was ad- ministered.

Dapsone, a sulfone is an antibacterial drug for susceptible cases of leprosy. It is also a primary treat-ment for dermatitis herpetiformis and has been used with slightly greater success in urticarial vasculitis4, bullous eruptions5, and it has been proposed in cases of severe chronic urticaria to taper off prednisone or in cases of unacceptable side effects of steroids6.

The mechanism of action of dapsone is poorly un-derstood, its anti-inflammatory effects include reduc- tion in lymphocyte responses to mitogens, suppres- sion of neutrophil chemotaxis, and inhibition of the alternate pathway of complement activation The drug also appears to inhibit spontaneous and induced syn-thesis of prostaglandin E2 by polymorphonuclear leukocytes7.

Since dapsone induces severe hemolysis in pa- tients with glucose –6-phosphate dehydrogenase deficiency, this serum enzyme should be measured prior to initiation of such therapy. Others less fre-quent side effects include headaches, a mild non-he-molytic anemia and most importantly, agranulocyto-sis. Thereafter a complete blood counts should be monitored periodically in patients treated with dap- sone.

As in chronic urticaria perhaps some patient with recurrent episodes of idiopathic angioedema may have a good response to dapsone, but the response may be unpredictable in each patient, and side ef-fects must be monitored.

We conclude, that dapsone may be an alternative drug in extrem cases of chronic urticaria or idiopath-ic angioedema that precise corticosteroids for ex- tended periods as a steroid-sparing drug or in cases with poor response to conventional therapy.

REFERENCES