

Angioedema associated with *Helicobacter pylori* and type 2 diabetes

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ABSTRACT

Angioedema without wheals with duration of symptoms over six weeks is relatively rare. This applies especially for the chronic forms of angioedema associated with metabolic, infectious, malignant, and systemic connective tissue disease. Described in the literature cases are rare, especially when the etiology of isolated angioedema associated with *Helicobacter pylori* and type 2 diabetes. We report a case of a 66-year-old male patient with recurrent isolated angioedema without wheals, affecting the upper lip, with a disease duration of one year and no symptoms of respiratory and gastrointestinal tract. Laboratory, immunological and serological studies we found only elevated blood sugar and elevated Anti *Helicobacter pylori* IgG antibody. In patients with type 2 diabetes mellitus etiology of angioedema may be associated with *Helicobacter pylori* and poor metabolic control. To be an effective treatment, the etiology of such phenomena should be precisely clarified with the respective set of immunological and serological tests.

Key words: Angioedema; *Helicobacter pylori*; Type 2 diabetes

INTRODUCTION

Chronic urticaria/angioedema is defined as wheals, angioedema or both with daily or almost daily symptoms lasting for more than 6 weeks [1]. Angioedema is characterized by localized, self-limiting, nonpitting swelling of the skin and/or of the mucous membranes of the upper respiratory and gastrointestinal tracts [2,3]. Most guidelines include isolated angioedema as a subtype of chronic spontaneous urticaria [4-6]. About 10% of patients with chronic spontaneous urticaria do not show wheals and exclusively develop angioedema [7]. Angioedema without wheals with duration of symptoms over six weeks is relatively rare. The most common forms of chronic and isolated angioedema are induced by medications such as angiotensin-converting enzyme inhibitors (ACE inhibitors), nonsteroidal anti-inflammatory agents and antibiotics. Hereditary angioedema with different types is also part of the chronic isolated forms of angioedema, and their diagnosis is important for proper treatment [1]. On the other

hand, isolated angioedema associated with metabolic abnormalities, and laboratory evidence of infection with *Helicobacter pylori* is more rarely [7,8]. Various etiologic factors, the broad range of immunological and non-immunological changes reflecting the pathogenetic mechanisms and defining forms of urticaria and angioedema often create diagnostic and differential diagnostic difficulties for dermatologists and allergists. This is especially true for the chronic forms, the more that they sometimes establish an association with a number of accompanying metabolic, infectious, malignant, systemic connective tissue diseases and others.

CASE REPORT

We present a case of 66-year-old male patient with recurrent isolated angioedema without wheals, affecting the upper lip (Fig. 1), with disease duration of one year and without symptoms of respiratory and gastrointestinal tract. The patient reported only numbness of the upper

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lip a few hours before the start of angioedema. With a history of acute episode of angioedema with wheals 7 years ago, drug induced by a single dose of ACE-inhibitor (enalapril maleate). Without family history of atopy and other allergic diseases. He suffers from type 2 diabetes and hypertension. His daily treatment included diet for type 2 diabetes and chlorthalidone 0,15 mg/day for hypertension. Except angioedema localized to upper lip (Fig. 1), findings from the physical and dermatology examination and are unremarkable.

The hematology and blood differential tests were in reference ranges. Total bilirubin, total protein, albumin, urea, ALT, AST and electrolytes in blood were normal except blood glucose levels was elevated 8,18 mmol/l (reference ranges 3,3-6,0 mmol/l). Anti-thyroglobulin (anti-TG) and anti-peroxidase (anti-TPO) antibodies, TSH and FT4 were normal. C1 inhibitor levels, C4 serum complement levels, IgA, IgG, and total IgE were in reference ranges. Anti-Toxoplasma gondii IgM and IgG titer were negative. Anti Helicobacter pylori IgG antibody titer was positive 55 IU/ml (reference ranges < 20 IU/ml), but the Helicobacter pylori stool antigen was negative. Stool tests for enteroparasites (Giardia lamblia, Amoebiasis and Blastocystis hominis) were negative. Abdominal ultrasound was normal.

We started treatment with levocetirizine dihydrochloride 10 mg/daily for 6 months and Metformin 1000 mg/daily. Attacks of angioedema disappeared. After discontinuing treatment with an levocetirizine dihydrochloride patient is in complete remission, asymptomatic and without recurrence of angioedema (Fig. 2).

DISCUSSION

Type 2 diabetes is one of the diseases often associated with the etiology of chronic urticaria. As unlockable clinical manifestations of urticaria factors indicating unsatisfactory metabolic control and received antidiabetic drugs, many of which rash and itching are cited as more frequent or rare side effects. Hypertension is a common comorbidity in patients with diabetes. The American Diabetes Association guidelines recommend the use of either ACE inhibitors or angiotensin receptor blocker (ARB) as initial therapy to achieve the blood pressure target in patients with type 2 diabetes mellitus [9,10]. One of the most common causes of drug-related angioedema is from ACE inhibitor [1]. Our patient had a medical history of drug-related angioedema from ACE inhibitor. Angioedema is also seen with ARB therapy but much less frequently than with ACE inhibitors [11]. On the

other hand, antidiabetic drugs-Dipeptidyl peptidase-IV inhibitor are also associated with angioedema and increase angioedema risk in patients treated with ACE inhibitors [12]. In our patient, laboratory testing showed elevated blood glucose levels. Rogala et al. associated isolated angioedema with elevated blood glucose levels and impaired glucose tolerance. The reasons for this remain unclear. It may be that impaired glucose tolerance and high glucose levels contribute to the development of recurrent angioedema [7]. In our patient, serology testing showed elevated Anti Helicobacter pylori IgG antibody titer. Described in the literature cases of isolated angioedema induced from Helicobacter pylori are rare and the treatment designed to eradicate the infection shows no significant results [8].

CONCLUSION

Isolated angioedema without wheals induced by the combination of various factors presented our case is



Figure 1: Angioedema without wheals, affecting the upper lip.



Figure 2: Patient without angioedema.

a rare phenomenon. In patients with type 2 diabetes mellitus etiology of angioedema may be associated with *Helicobacter pylori* and poor metabolic control. To be an effective treatment, the etiology of such phenomena should be precisely clarified with the respective set of immunological and serological tests.

Consent

The examination of the patient was conducted according to the Declaration of Helsinki principles.

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