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The Many Faces of Urticaria

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Urticaria is a heterogeneous group of diseases that result from a large variety of underlying causes. It is characterized by the development of wheals, angioedema, or both. Urticaria needs to be differentiated from other medical conditions where hives and angioedema can occur as a symptom. Urticaria and angioedema may have diverse pathogenesis and clinical course and are usually the clinical consequence of vasoactive mediators derived from mast cells in the skin or mucosal tissues. Skin biopsies from lesions are important to make an appropriate diagnosis and particular therapy. Our cases demonstrate that predominance of lymphocytes and neutrophils in histological examination is important for therapeutic response. Antihistamines may not work if the infiltrate consists mainly of neutrophils. In such cases the right answer could be treatment with colchicin, dapsone or short course with steroids.

Key words: urticaria, angioedema.

Introduction

Urticaria is a disease characterized by the development of wheals, angioedema, or both. A wheal is a superficial skin-colored or pale skin swelling, usually surrounded by erythema. It may have a burning sensation or is very itchy. It has a fleeting nature, with the skin returning to its normal appearance, usually within 1-24 h. Sometimes wheals resolve even more quickly. Angioedema is deeper swelling within the skin or mucous membranes, and can be skin-colored or red. It resolves within 72 hours. Angioedema is more often asymptomatic and rarely painful.

It is very important urticaria to be differentiated from other medical conditions where wheals and/or angioedema can occur as a symptom, for example skin prick test, anaphylaxis, auto-inflammatory syndromes, or hereditary angioedema (bradykinin-mediated angioedema) [3].

It is not easy to be classified the subtype of the disease. Urticaria can be spontaneous, physical, or other, based on duration, frequency, and causes of symptoms.

Spontaneous urticaria occurs in the absence of external physical stimuli. According to the duration of the hives urticaria is: acute – when they last less than 6 weeks and often have gone within hours to days, and chronic – with a more than 6 weeks duration of the lesions.

Physical urticaria is caused by external physical stimuli. Some cases of physical urticaria may be considered chronic. However, physical urticaria is distinguished from chronic urticaria based on clear evidence that physical factors are eliciting urticaria.

Other urticaria disorders are those induced by exercise or contact, anaphylactic reactions, cholinergic mechanisms, and aquagenic factors.

We analyze five patients with hives or edema on the lips, suspected at first sight as suffering from urticaria or angioedema. After careful anamnestic and histopathological examination the diagnosis were re-examined.

Case Reports

We analyze four patients – two of them with clinical manifestations of angioedema and three patients with wheals, characterized as clinical marker for urticaria.

The patiens with angioedema had edema of lips with pain and discomfort. They were young women, aged 33 and 38. The first one had an anamnesis for lip augmentation with dermal filler before 4 days. She developed swelling of the lips 8 hours after the injection and 3 days after the procedure the conditions worsed. She refused a biopsy and was treated with parenteral steroids and antihistamins. The other patient had swelling on the lips an around the eyes. She also had lip augmentation before 6 months. A biopsy was performed and the result demonstrates labial edema with mild vessel ectazia, without granuloma or inflammatory reaction (**Fig.1**). The treatment was intravenous steroids.

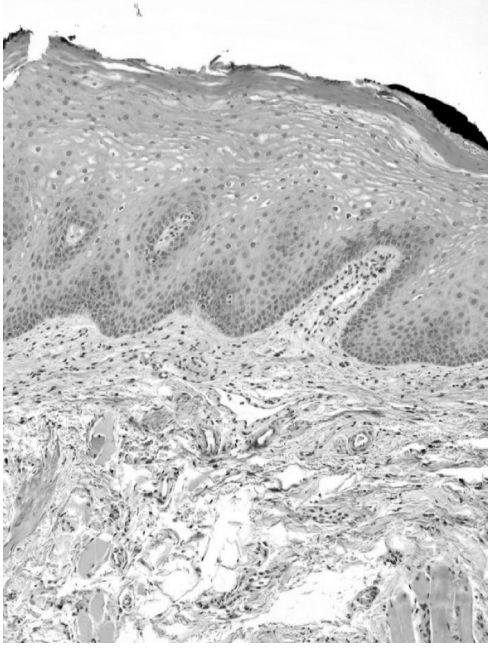

Fig. 1. Labial edema with mild vessel ectazia, without granuloma and inflammatory reaction

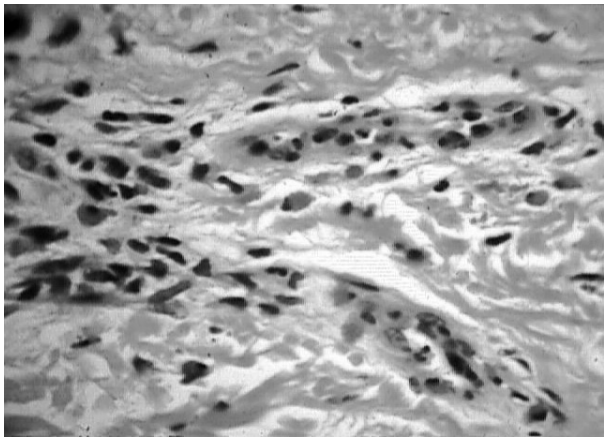

Fig. 2. Dermal edema, slight dilatation of superficial dermal vessels and slender perivascular infiltrate of macrophages, lymphocytes and granulocytes

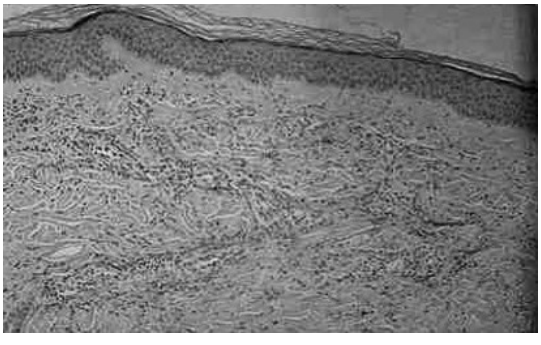

Fig. 3. Leucocytoclastic vasculitis with distroyed blood vessels and neutrophilic infiltrate

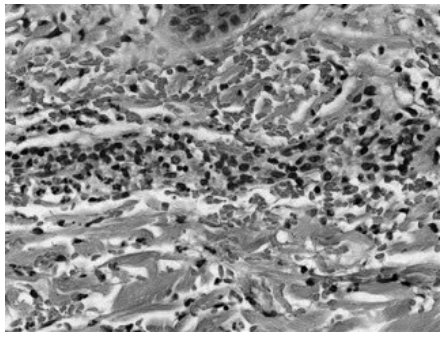

Fig. 4. Mixed inflammatory infiltrate in upper derma composed mainly of neutrophils and eosinophils

Three other patients were with hives all over the skin without mucosal involvement. Histopathological investigations were performed. One patient showed characteristic features of the urticaria with dermal edema, slight dilatation of superficial dermal vessels and slender perivascular infiltrate of macrophages, lymphocytes and granulocytes. (**Fig.2**). The biopsy specimens from the other two patiens were quite different from the typical picture for urticaria. They showed leucocytoclastic vasculitis with distroyed blood vessels and neutrophylic infiltrate (**Figs. 3, 4**).

Results and Discussion

The both patients with lips swelliing raise the question wheather the reason for mucous edema is because of the filler. Some transient swelling in the immediate postprocedural period is normal and occurs with all dermal fillers. This type of edema happens shortly

after injection and is related to injection volume and technique. It is so called short-term posttraumatic edema.

Another subtype of angioedema is antibody-mediated edema. This may occur after initial or repeated exposure to dermal fillers, which are essentially foreign bodies. Some patients may develop hypersensitivity to injected products due to an immunoglobulin E-mediated immune response (Type I hypersensitivity reaction). IgE stimulates mast cells to degranulate, releasing proteases, heparin, histamine, cytokines, prostaglandins, leukotrienes, and platelet-activating factor, which result in the edema, erythema, pain, and itching characteristic of an allergic response. Angioedema occurs within hours of exposure. Reactions can be severe and can last for several weeks [4].

Nonantibody-mediated (delayed) edema is characterized by induration, erythema, and edema, and are mediated by T lymphocytes rather than antibodies. They typically occur 1 day after injection, but may be seen as late as several weeks after injection and may persist for many months [1]. Delayed hypersensitivity reactions are nonresponsive to antihistamines. The allergen should be removed. In the case of HA, this will involve treatment with hyaluronidase.

We think our first patient had a severe short-term posttraumatic edema even the clinical picture was supposed to be angioedema. The second one had typical angioedema despite the anamnesis for dermal filler in her lips, which was confirmed with the histopathological findings. The biopsy was very important in this case as this reaction could be assosiated also with granuloma but fortunately this was rejected with the morphology.

The other three patiens with the clinical manifestation of urticaria with wheals involving all over the skin were diagnosed as urticaria. The interesting finding is that two of them had leucitoclastic vasculitis on the biopsy speciments and only one of them was confirmed to have real urticaria with dermal edema and without vessel involment. The presence of leukocytoclastic vasculitis in persistent lesions indicates an underlying immune complex disease[2]. The patients were reexamined as suffered from urticaria vasculit. It was very important for the therapy for these patients, where corticosteroids are indicated. Cytotoxic drugs may be required for adequate treatment in such cases.

According to the latest guidelines, urticaria pigmentosa, urticarial vasculitis, familial cold urticaria and nonhistaminergic angioedema are no longer considered to be subtypes of urticaria [5].

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