Plenary Lecture

Angioedema in adults and children

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Angioedema is a diffuse swelling of deeper skin layers. Under the heading of angioedema in a broader sense, swellings of other organs are subsumed, including self-limiting edema attacks of the tongue and other parts of the gastrointestinal tract, and laryngeal edema. Angioedema belongs to various disease entities with different causes and pathogenesis.

Angioedema may occur with or without urticaria. Little is known about the pathogenesis of angioedema associated with the clinical subtypes of urticaria. Histamine may play a major role. Many patients with angioedema associated with chronic spontaneous urticaria (CSU) respond to antihistamines, partially or completely. This confirms that histamine is involved at least in a part of angioedema in patients with CSU. Other types of angioedema are not associated with an urticaria. Some of them are clearly bradylinin-mediated and do not respond to antihistamines or corticosteroids. Those types include hereditary angioedema (HAE) due to C1 inhibitor (C1-INH) deficiency (HAE-C1-INH) and acquired angioedema due to C1-INH deficiency (AAE-C1-INH).

Clinically, HAE-C1-INH is characterized by recurrent swelling of the extremities, face, genitals, by gastrointestinal attacks (painful abdominal cramps, mostly accompanied by circulatory symptoms, sometimes vomiting, and diarrhea), and by edema of the larynx and other organs. Death by asphyxiation is most likely to occur in patients whose symptoms have not been diagnosed. HAE-C1-INH occurs for the first time most often early in the second decade of life, also frequently in the first, and in a few patients in the third decade or even later. Recurring HA attacks follow, the frequency of which varies greatly from patient to patient. Some attacks are triggered by trauma, pressure, psychological stress situations, menstruation, ovulation, or infectious diseases.

In AAE-C1-INH the C1-INH deficiency is due to an increased C1-INH catabolism. Accordingly, C1q is usually decreased. The symptoms are similar to those of HAE-C1-INH. In a significant proportion of these patients there is an underlying B-cell disorder, e.g., monoclonal gammopathy of unknown significance or

malignant lymphoma, and it can happen that these are discovered through the angioedema diagnosis. In some patients auto-antibodies against C1-INH are found.

Other types of recurrent angioedema include several forms of HAE with normal C1-INH, solitary angioedema with unknown cause (so-called idiopathic angioedema, histamine-mediated or bradykinin-mediated), and angioedema induced by ACE-inhibitors.

An exact diagnosis and a clear assignement to one of the forms of angioedema are mandatory. Treatment differs within the various forms of angioedema. HAE is the most threatening form of angioedema. Therefore nation-wide patient registries for patients with HAE-C1-INH have been established in the last years. Large steps forward have been achieved in the treatment of HAE-C1-INH. At present C1-INH concentrate, icatibant, recombinant C1-INH, ecallantide and fresh frozen plasma are used for treating acute HAE attacks. For the prevention of attacks C1-INH concentrate and attenuated androgens are available.