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CLINICAL AND LABORATORY CHARACTERISTICS OF A GROUP OF PATIENTS WITH HEREDITARY ANGIOEDEMA

Introduction

Hereditary angioedema (HAE) is a genetic disorder characterized by recurrent episodes of angioedema affecting submucosal and subcutaneous tissues, potentially life-threatening when localized in the upper respiratory tract. It is caused by a deficiency in C1-esterase inhibitor (C1-INH), with a prevalence of 1:10,000 to 1:50,000 in the population [1].

The pathophysiology typically involves a quantitative or functional deficiency of C1-INH, which regulates the complement cascade and kinin system [2]. HAE attacks can be triggered by stress, surgical procedures, and hormonal changes, though many occur spontaneously. These attacks are linked to increased vascular permeability due to excessive bradykinin, making standard treatments (by histamine and other mast cell mediators, such as systemic glucocorticosteroids, antihistamines, and epinephrine) ineffective [3].

The clinical presentation of HAE is characterized by a high degree of individual variability regarding the location, frequency, and severity of attacks, both between different patients and in the same patient throughout life. Of particular clinical significance are edema of the larynx, pharynx, and neck, which can lead to airway obstruction and death due to asphyxia. Abdominal attacks of HAE often mimic acute surgical conditions of the abdominal cavity, such as appendicitis, which can lead to diagnostic errors and unnecessary surgical interventions [4]. Current management guidelines recommend first-line therapies such as C1-INH concentrate, bradykinin receptor antagonists, and plasma kallikrein inhibitors. Alternatives like solvent-detergent treated plasma may be used when first-line drugs are unavailable, while antifibrinolytics and androgens are not recommended due to low efficacy [5].

Thus, hereditary angioedema represents a relevant clinical problem due to difficulties in timely diagnosis, the need for specialized treatment, and the significant impact of the disease on various aspects of patients' lives.

Goal

To provide a clinical-laboratory and therapeutic characterization of a group of patients over 18 years old from Belarus with Hereditary Angioedema.

Material and methods of research

The study included data from 35 patients over 18 years old (Aged 21–71 years, median age 41 years) in a non-randomized uncontrolled trial. The inclusion criterion for the study group was the presence of a diagnosis of hereditary angioedema (HAE) confirmed according to

the diagnostic standards accepted in the Republic of Belarus [6, 7]. Clinical and laboratory data of patients with a confirmed diagnosis of HAE, observed by immunologist-allergists at the «Republican research center for radiation medicine and human ecology» from 2014 to 2025, were retrospectively analyzed. All patients included in the study were divided into two groups based on gender. The male patient group consisted of 11 individuals, while the female group consisted of 24.

A descriptive and comparative analysis was conducted based on the following parameters: average age; number of patients with clinical manifestations of the disease; average age at the onset of first symptoms; frequency of occurrences of edema in various locations; family history; number of patients taking long-term prophylactic medications; as well as levels of complement components C3, C4, and C1-inhibitor. Using statistical data processing software Statistica 12.0, descriptive and comparative statistical analyses of the data were performed.

The results of the research and their discussion

During the analysis of clinical data from patients with hereditary angioedema (HAE), we found that the onset of the disease occurred between the ages of 4 and 30 years (median age 8 years). In the first decade of life, the disease began in 21 out of 35 patients (60%), while the remaining 40% experienced onset at an older age, between 13 and 30 years. It is likely that early manifestations of HAE in these patients were not recognized as symptoms of the disease and were therefore missed. However, the diagnosis was established only after 4 to 55 years (median 25 years). This long interval between the appearance of the first symptoms and diagnosis indicates significant difficulties in diagnosis. The prolonged delay in diagnosis leads to serious consequences: 17.1% of patients lost at least one relative due to clinical manifestations of HAE. Medical history reveals that close relatives of 17 patients (48.6%) also have clinical signs and a diagnosis of HAE. The disease was genetically confirmed in 14 patients (40%).

Among the causes of edema, women reported: stress (13 out of 24 patients, 54.2%); mechanical impacts (including blows, injuries) – 7 patients (29.2%); and physical activity (including prolonged walking) – 3 patients (12.5%); pregnancy – 3 patients (12.5%); heavy lifting and association with infectious-inflammations – 2 patients each (8.3%); and dental treatment was noted by 1 patient (4.2%).

In men, the causes of edema included: mechanical impacts (blows, injuries) – in 5 out of 11 patients (45.5%); stress – in 3 patients (27.3%); physical activity (prolonged walking) and dental treatment were noted by 2 patients each (27.3%). In the female patient group, edema occurred in various locations with a frequency of 1-2 times per month. Throughout their lives, edema could recur in different areas. Women reported edema in the respiratory tract (larynx) in 13 out of 24 patients (54.2%); abdomen, including abdominal attacks – in 13 patients (54.2%); upper limbs – in 12 patients (50%); face (lips, tongue, nasolabial area) – in 10 patients (41.7%); lower limbs – in 10 patients (41.7%); and chest, back, and genitals – in 2 patients for each location (8.3% each). Seven patients out of 24 (29.2%) noted the occurrence of edema along with pallor of the skin. Peripheral edema, abdominal attacks, and upper respiratory tract edema (the complete symptom triad) troubled 11 out of 24 women (45.8%).

In male patients, edema occurred less frequently than in females (from 1–2 times a month to 1-2 times a year). Men reported edema in the upper limbs – in 9 out of 11 patients (81.8%); lower limbs – in 7 patients (63.6%); abdomen (abdominal attacks) – in 7 patients (63.6%); face (lips, tongue) – in 6 patients (54.5%); respiratory tract (larynx) – in 5 patients (45.5%); and 1 patient each with edema localized to the back, neck, and genitals (9.1% each). The complete symptom triad (peripheral edema, abdominal attacks, and upper respiratory tract edema) was found in 6 out of 11 men (54.5%).

Analysis of laboratory test results in the HAE patient group revealed a significantly low level of complement component C4 at 0.048 (0.039-0.08) g/L, with a normal range of 0.1–0.4 g/L; the level of complement component C3 did not exceed reference values (0.82–1.85 g/L) and was 1.15 (1.08–1.38) g/L. The level of C1-inhibitor in HAE patients was 0.05 (0.03–0.088) g/L, which was below reference values (0.21–0.39 g/L).

To prevent the occurrence of edema, the drug Takzairo (lanadelumab) was used in 6 out of 35 patients (17.1%) with a positive effect; patients reported fewer episodes of edema and milder symptoms. For emergency treatment when edema was present, aminocaproic acid or fresh-frozen plasma was used, and since 2024, the drug Sunrise (C1-inhibitor) has been used with positive effects

Conclusion

Thus, the study of the patient sample allowed for an assessment of the population structure of hereditary angioedema (HAE) patients. This research highlights the clinical heterogeneity of HAE and the prolonged nature of the diagnostic process. The onset of the disease in childhood for a significant portion of patients often remains unrecognized for many years, leading to substantial delays in diagnosis. The clinical picture of HAE is characterized by a variety of triggers for edema, with stress and mechanical impacts being predominant, as well as a wide range of localizations, including life-threatening laryngeal edema and abdominal attacks. Gender differences in the frequency and localization of edema, as well as in provoking factors, have been noted. Laboratory confirmation of the diagnosis is based on a pronounced decrease in levels of C4 and C1-inhibitor, aligning with the classic presentation of HAE. The introduction of modern medications, such as lanadelumab and C1-inhibitor, demonstrates potential for improved disease control. However, the main issue remains the late detection of HAE. To improve the quality of life for patients and reduce the risk of fatal complications, it is essential to focus on increasing awareness among physicians of various specialties about the clinical manifestations of HAE, especially in children and adolescents, as well as to expedite the implementation of modern diagnostic and treatment methods into clinical practice.

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