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Age Characteristics and Concomitant Diseases in Patients with Angioedema

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Abstract

BACKGROUND: Angioneurotic oedema (AE) is an unpredictable and dangerous disease directly threatening the patient's life due to a sudden onset of upper respiratory tract obstruction. The disease is associated with various causes and triggering factors, but little is known about the conditions that accompany AE.

AIM: The study aims to determine the age-specificities and the spectrum of concomitant diseases in patients with AE.

MATERIAL AND METHODS: The subjects of observation were 88 patients (53 women and 35 men) with angioneurotic oedema who underwent diagnostics and treatment in the Department of Occupational Diseases and Clinical Allergology of University hospital "Saint George"-Plovdiv.

RESULTS: The highest level of disease prevalence was found in the age group over 50 years, both in males (45.71%) and females (54.72%). We found that the most often concomitant diseases in our patients with AE are cardiovascular (33%). On second place are the patients with other accompanying conditions outside of the target groups (27.3%). Patients with AE and autoimmune thyroiditis were 14.8%, and those with AE and skeletal-muscle disorders-10.2%. Given the role of hereditary factors in this disease, the profession of the patients is considered insignificant.

CONCLUSION: Angioedema occurs in all age groups, but half of the cases are in people over 50 years of age. The most common concomitant diseases in angioedema are cardiovascular diseases.

Introduction

Angioneurotic oedema (AE) is an unpredictable and dangerous disease directly threatening the patient's life due to a sudden onset of upper respiratory tract obstruction. Hereditary angioedema (HAE) is a rare form of AE. The disease is associated with various causes and triggering factors, but little is known about the conditions that accompany AE [1], [2], [3], [4].

The study aims to determine the age-specificities and the spectrum of concomitant diseases in patients with AE.

Material and Methods

The subjects of observation were 88 patients (53 women and 35 men, 1.5:1) with angioneurotic oedema who underwent diagnostics and treatment in the Department of Occupational Diseases and Clinical Allergology. We accepted as a technical unit of observation the Department of Occupational Diseases and Allergology at the University General Hospital for Active Treatment "Saint George"-Plovdiv, and as a logical unit-every patient hospitalised in the ward. The study is complete and covers all the patients hospitalised in the ward.

The study is retrospectively longitudinal, with AE patients being monitored throughout 4 years (from 01.01.2013 to 31.12.2016).

Signs of observation are divided into two groups:

• factorial - age, sex, place of residence, region, social group, occupation;

• resultant - leading diagnosis, diagnosis at the point of discharge, outcome of the disease during hospitalization, consecutive hospitalizations, etiology, other accompanying diseases, family history, occupational nature of the disease, determined diagnosis, how many attacks have been documented, criteria for acceptance of the diagnosis, localization and dynamics of swelling, treatment and outcome, laboratory tests.

Two basic methods of medical sociology are used to collect the primary statistical information - questionnaire and documentary.

The questionnaire contains 56 open, semi-open and closed questions, grouped into 5 sections:

1. Socio-demographic characteristics of the patient

2. Hospital treatment

3. Aetiology

4. Clinical diagnosis

5. Laboratory diagnostics

In the documentary method, the main document was the history of the disease from the archive of the primary documentation. The necessary information from the document was imported into a database. The individual survey was conducted on the day of the patient's discharge from the clinic. A basic element of the documentary sociological method was the study of the history of the disease, the registered stage epicrises, outpatient consultations, clinical and paraclinical data.

Statistical processing of information

The collected primary information was translated, coded and entered into a computer database. A primary grouping was precisely performed. On this basis, by combining the factorial and resultant signs, a second group was established to address the specific needs of the study. Statistical data processing utilised abundant methods of medical statistics.

- Variation analysis-to handle quantifiable signs. The normality of the distribution was determined by the λ criterion of Kolmogorov-Smirnov. For comparison of the mean values, u-criterion for normal distribution was used. Existing differences were considered statistically significant and confirming H1 when they exceeded the critical value of Δ for λ = 0.05.

- Alternative analysis-for processing qualitatively measurable signs. Depending on the type of signs, the classic method and Fischer's transformation were applied. For relative shares corresponding to the requirements of the classical methodology, the Van der Waerden criterion was used.

- Correlation analysis-to reveal a cause and effect relationship between some of the factorial and resultant signs. Regression analysis could be used to quantify the relationship.

- The nonparametric analysis-in need of hypothesis verification, for distributions different from the normal Gauss-Laplace, and analysis of complex composite tables.

- Dispersion analysis-the Tukey's method was used to compare more than two averages.

- Analysis of dynamic changes.

- Graphical analysis-to illustrate the observed processes and phenomena and to illustrate the existing regularities.

Data were processed by SPSS (SPSS Inc., IBM SPSS Statistics) 20.0 and Microsoft Office 2010 statistical analysis programs.

Results and discussion

During the study, a total of 2,198 patients were admitted to the department. Due to incomplete data, 87 (3.8%) patients were excluded from the study. Only 8 out of 88 were suspected for hereditary angioedema due to family history (most often the father had episodes of AE): 3 underwent treatment in the department, and 5 were observed ambulatory.

Age characteristics and sex of AE patients

The total number of patients with AE for the studied period was 88. Table 1 shows the distribution of patients by sex and age. The highest level of disease prevalence was found in the age group over 50 years, both in males (45.71%) and females (54.72%).

No statistically significant difference in disease prevalence levels between the two sexes was found. Women with AE slightly prevailed-53 (60.23%) then men-35 (39.77%). The nonparametric analysis confirmed that there is no significant difference between patients with AE treated in the ward by sex. The same-sex dependency was also observed in individual age groups ($\chi 2 = 5.702$, $P = 0.127$) (Table 1).

Table 1: Distribution of patients with AE by age and sex

Age group	Male			Female			Total	
	Number	%	Sp	Number	%	Sp	Number	%
Up to 30 year old	7	20.00	6.40	4	7.55	4.15	11	12.50
30-40 year old	9	25.71	7.39	9	16.98	5.16	18	20.45
40-50 year old	3	8.57	4.74	11	20.75	5.58	14	15.91
Above 50 year old	16	45.71	8.42	29	54.72	6.84	45	51.14
Total	35	100.00	-	53	100.00	-	88	100.00

Concomitant angioedema diseases

The published literature on the relationship of AE to other concomitant diseases and syndromes is scarce. There is no clear answer to the question whether some non-allergic diseases and combinations of these are more common in AE patients or there are other factors involved that determine the onset and progression of the disease besides the harmful habits. The study results concerning the most often found concomitant diseases in our AE patients are listed in Table 2.

Table 2: Concomitant diseases in patients with AE

Disease	Data obtained on the patient's anamnesis						Total	
	No			Yes				
	Number	%	Sp	Number	%	Sp	Number	%
Autoimmune thyroiditis	75	85.2	3.78	13	14.8	3.78	88	100
Diabetes mellitus	84	95.5	2.22	4	4.5	2.22	88	100
Neoplasm	87	98.9	1.13	1	1.1	1.13	88	100
Hematological diseases	85	96.6	1.93	3	3.4	1.93	88	100
Parasitoses	87	98.9	1.13	1	1.1	1.13	88	100
Systemic diseases of the connective tissue	87	98.9	1.13	1	1.14	1.13	88	100
Diseases of the musculoskeletal system	79	89.8	3.23	9	10.2	3.23	88	100
Cardiovascular diseases	59	67.0	5.01	29	33.0	5.01	88	100
Respiratory system diseases	84	95.5	2.22	4	4.5	2.22	88	100
Cerebrovascular disease	85	96.6	1.93	3	3.4	1.93	88	100
Diseases of the peripheral nervous system	85	96.6	1.93	3	3.4	1.93	88	100
Kidney disease	86	97.7	1.59	2	2.3	1.59	88	100
Other	64	72.7	4.75	24	27.3	4.75	88	100

In the observed cases, besides the type of concomitant diseases, we also studied their number in each patient. We found that the most often concomitant diseases in our patients with AE were the cardiovascular (33%). On second place were the patients with other accompanying conditions outside of the target groups (27.3%). Patients with AE and autoimmune thyroiditis were 14.8%. The patients with AE and skeletal-muscle disorders were 10.2% among the most often: myalgia, myositis and tendovaginitis. Only one of the patients was with the systemic disease of the connective tissue (Lupus erythematosus), 2 with chronic myeloid leukaemia and 1 with polycythaemia vera (hematologic diseases).

Our data concerning the association of AE with other allergic conditions are shown in Figure 1. The results confirm the statement that urticaria is often found in patients with AE.

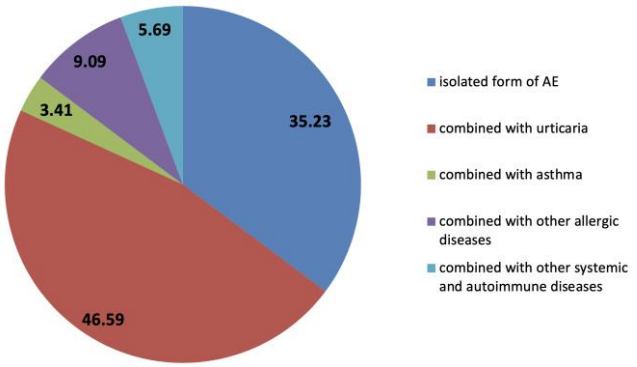

Figure 1: Association of AE with other allergic conditions in percentage (%)

Regarding the presence of concomitant diseases in one AE patient, in one third (30.68%) of the patients, we didn't prove any concomitant disease whereas in the other two thirds (69.32%) we found at least one up to five concomitant conditions (Figure 2).

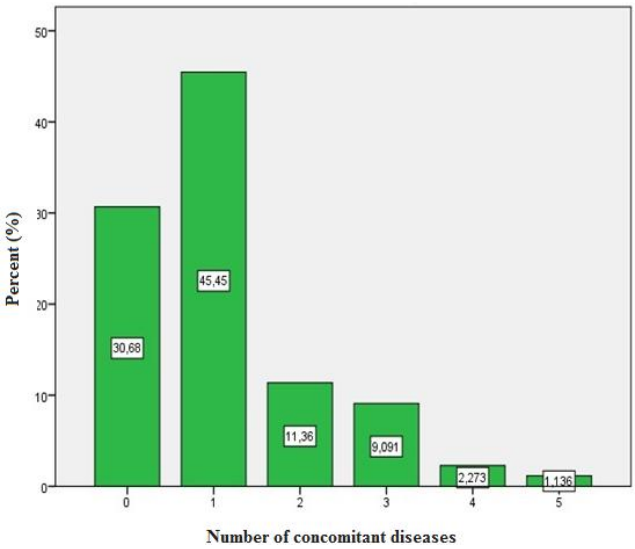

Figure 2: Number of concomitant diseases of one patient with AE

By the indicator "number of concomitant diseases" in one AE patient we found that the majority of patients with AE had only one accompanying disease (45.45%). Almost 1/3 of the studied patients have only C1 inhibitor deficiency.

Professional aetiology of angioneurotic oedema

In the majority of our AE patients (95.4%), the profession was excluded as a factor causing the onset of the disease. We consider that workplace risk factors may in some cases play the role of triggers leading to the clinical manifestation of swelling in AE patients, although such risk is objectively explored in one of our patients, and in other three is in the process of proving (Figure 3).

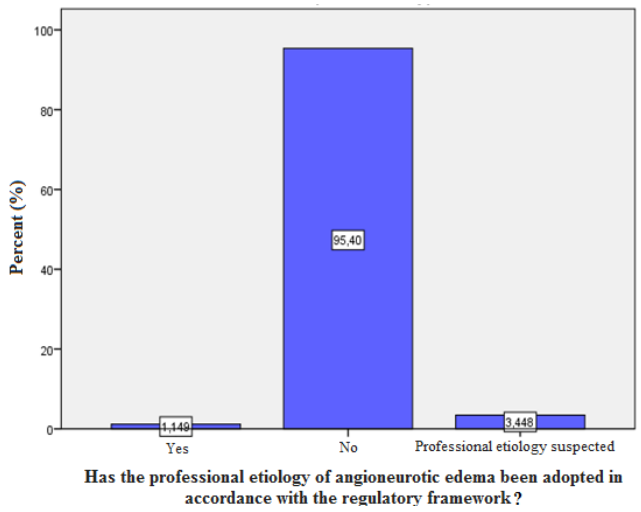

Figure 3: Professional aetiology of angioneurotic oedema

Discussion

Several literature sources discuss the association of AE with urticaria and other immune and autoimmune diseases [5], [6], [7], [8], [9], [10].

Our results correlate with the results published by Brickman CM et al., in two studies in 1986 regarding the frequency of autoimmune disorders in patients with AE (12%) [11], [12]. In 2012, Habal F. & Huang V reported a case of AE associated with Crohn's disease [13].

Half of the patients with AE have at least one concomitant disease (45.45%). The most common concomitant diseases in patients with AE are the cardiovascular (33%), followed by autoimmune thyroiditis (14.8%), musculoskeletal disorders (10.2%) and diabetes mellitus (4.5%). Given the role of hereditary factors in this disease, the profession of the patients is considered insignificant.

In conclusion, angioedema occurs in all age groups, but half of the cases are in people over 50 years of age. The most common concomitant diseases in angioedema are cardiovascular diseases, autoimmune thyroiditis and musculoskeletal system diseases.

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