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Pathogenetic mechanisms of affiliation generalized parodontal diseases and anorexia nervosa

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Abstract

Introduction. Diseases of parodontal tissues occupy a leading place in the structure of dental diseases. Early diagnosis of the initial degree of generalized parodontitis (GP) is an effective way of secondary prevention. This is due to the complexity of understanding the etio-pathogenetic mechanisms of the development generalized parodontal diseases (GPD) and the high association of them with a number of diseases of the internal organs and systems with common points of contact between interdependence and mutual influence, in particular with anorexia nervosa (AN). Recently, the incidence of AN has increased significantly and poses a serious state, social, psychological and medical problem. There are serious changes on the axis hypothalamus - pituitary - amygdala, genital and thyroid glands, which cause a decrease in thyroid hormone metabolism, cause hypoestrogenia, hypogonadism, secondary hyperparathyroidism due to AN. The detection of tissue sensitization to bone antigen can be an adequate specific reaction for early diagnosis of GP. **Objective.** To establish the features of configuration of generalized parodontal diseases and their clinical manifestations in the format of basic characteristics of anorexia nervosa. **Material and methods.** Clinico-radiological, immunological, analytical and statistical methods were used. Objects were 75 patients with AN, aged 18-36 years (average age 26 ± 3.8) - the main group (M), and 60 patients with GPD without signs of anorexia of the same age - comparison group (C). For a detailed analysis of the clinical manifestations of clinical manifestations of GPD in patients with AN, all patients in the main (M) and comparative (C) groups were divided into several subgroups. M_1 subgroup - patients with various forms of gingivitis. The M_2 subgroup was presented with patients with generalized parodontitis (GP) with AN as the basic pathology. The comparative (C) group consisted of two subgroups (C_1), (C_2) with different forms of gingivitis and GP, respectively. The control group consisted of 30 people similar to the age and sex without clinical signs of periodontal disease. Diseases of internal organs and systems, including the osteoarticular apparatus, in these examined people were excluded. **Results.** A high incidence of GPD up to 100% was diagnosed, including both independent parodontal soft tissue disease and all components of the paroodontal complex, which had characteristic of all age groups and varied with patient age, duration of AN and its stages. Among the independent forms of gingivitis, the most common was chronic catarrhal marginal gingivitis (86.7 ± 8.8%), with some cases of exacerbation on the background of the overwhelming absence of complaints with single manifestations of agrarian, complexity of psychological alliance. GP was predominantly I-II degree, with chronic course prevailing over other forms of GPD (80 ± 4.6%). Radiographically, in all patients, regardless of the severity of GP, there was an extension of the parodontal cleft and osteoporosis of the bone component of the parodontal complex, horizontal type of resorption. Advantages and priorities of different segments of parodontal complex lesions in patients with AN were not observed. For all patients with GP, a high degree of tissue sensitization to the bone antigen, characterizing significant changes in the bone component of the parodontal complex with AN, was finalized. **Conclusions.** Thus, direct correlation and interdependence of generalized parodontal diseases in the format of basic characteristics of anorexia nervosa were established.

Key words: *generalized parodontal diseases, generalized parodontitis, hypersensibilisation, anorexia nervosa, osteoporosis,*

Introduction

Diseases of parodontal tissues, including generalized parodontitis (GP), consistently occupy one of the leading places in the structure of dental diseases (1). Thus, according to recent epidemiological studies, the prevalence of GP is 60-100% with a persistent tendency to increase the frequency of GP in young and employable people with gender and population preferences (2). This circumstance causes serious concern of state, social, medical and scientific institutions.

Despite the increase in dental culture of the population, which has been trending lately and prompts the early treatment of patients, the result of treatment of generalized parodontal diseases (GPD) is often unsatisfactory. This is due to some extent because of the complexity of understanding the etio-pathogenetic mechanisms of development of these diseases, and the high association of GPD with a number of diseases of the internal organs and systems with common points of contact between interdependence and mutual influence (3).

A great number of researchers point to the high probability of pathogenetic communication of GPD with endocrine pathology, systemic diseases of human connective tissue, infraction vitamin, protein and lipid metabolism, emphasizing the thesis of associativity, affiliation and, even, the comorbidity of these diseases in patients with such basic pathology (4, 5, 6, 7). But in literature there are only fragmentary science articles that suggest a possible correlation of anorexia nervosa (AN) and GPD and offer a specific approach to the features of their treatment, which, in our opinion, is a major drawback (8, 9, 10, 11).

Recently, the incidence of AN has increased significantly and poses a serious state, social, psychological and medical problem. According to WHO in the general population, the prevalence of AN ranges from 0.37 to 1.0 per 100,000 population, with a frequency of 0.9- 4.3% in women and 0.3% in men and tends to increase significantly (12, 13, 14, 15). A particularly high risk of death was found with critically low body weight and later onset (16, 17, 18, 19, 20).

There are significant changes, associated with AN, in the neuro-endocrine system, including the axis of the hypothalamus - pituitary - amygdala - genital and thyroid gland (21, 22, 23, 24). These changes are accompanied by a decrease in estrogen production, leading to pre-menarcheal amenorrhea and potentiating cortisol levels, abnormal secretion of insulin-like growth factor-1 and decreased thyroid hormone metabolism (25, 26, 27, 28). Hypoestrogenia can be a trigger for the development of osteopenia and osteoporosis, which leads to a decrease in bone mineral density (29, 30, 31). Emerging hypogonadism and secondary hyperparathyroidism, as a result of disorganizing eating behavior in AN, low calcium intake, and vitamin D deficiency and hypercorticism, may also be one of the important components that predispose GPD in patients with AN (32, 33, 34, 35, 36, 37).

Absence of clear ideas about interaction and interaction do not allow to develop adequate methods of treatment of GPD in patients with AN.

It should be noted that clinical, radiologic, as well as laboratory diagnostics of advanced degrees of GP is not a problem. At the same time, the diagnosis of GP at the initial degree presents certain difficulties. Thus, the absence of clear markers which identify initial changes in the key moment of initiating the debut of the pathological process in GP, makes it difficult to diagnose and, as a result, to conduct opportune in full and adequate treatment. This circumstance often leads to the fact that the initial degree of GP is accepted and identified with different forms of gingivitis. As a result, the current treatment is directed to stopping, first of all, the inflammation process in the parodontal tissues in order to reduce the activity of osteoclasts without the inclusion of funds that normalize the metabolism of the bone tissue of the alveolar process.

Standard indicative criteria for the condition of the alveolar process, for example, the level of calcium, copper, strontium in blood plasma, bone-specific alkaline phosphatase, cholesterol, triglycerides of blood serum, oxyproline plasma, bone mineral density are quite burdensome for patients and are nonspecific indicators under impact of many components of the body, which makes it difficult to use, complicates the interpretation of the facts. In our opinion, the determination of tissue sensitization to bone antigen can be that adequate specific reaction that could help for early diagnosis of GP.

Aim: To establish the features of the configuration of generalized parodontal diseases and their clinical manifestations in the format of basic characteristics of anorexia nervosa.

Tasks:

1. To establish frequency, clinical and radiological markers of generalized parodontal diseases in patients with anorexia nervosa.
2. To study the degree of cooperation of age, gender, duration and form of anorexia nervosa with generalized parodontal diseases.
3. To determine tissue allergy to bone antigen in patients with generalized parodontal diseases and anorexia nervosa.
4. To present our view of the paradigm of interaction of affiliation and comorbidity of generalized parodontal diseases and anorexia nervosa.

Materials and methods: to achieve this goal, clinical and radiological methods of parodontal assessment were used to verify the diagnosis (according to the systematics of parodontal diseases after M.F. Danilevsky, 1994) as well as immunological tests (inhibition of migrating leukocytes) by M. George method as a first type screening reaction and statistical methods which were performed in the SPSS STATISTICA 6.0 and MS Excel 2010 (license number K9366093I 2016). Statistical analysis of the data included the calculation of mean values, standard deviation, and mean error.

Evaluation of tissue sensitization to bone antigen was determined in the inhibition of leukocyte migration (RILM). In RILM reaction, water-salt extract of bone tissue of group 0 (I) Rh (D) was used. The migration index was calculated by the formula:

$$IM = \frac{\text{migration area with antigen}}{\text{migration area without antigen}}, \quad (1)$$

where IM, equal to 0.1-0.5, was corresponded to a high degree of sensitization. The reaction was taken 24 hours after blood collection.

The use of RILM was due to its high specificity and informativeness. It is included in the list of reactions recommended by WHO. Taking into account that the reaction was carried out outside the body (in vitro), conditions were created for multiple examination of the patient for diagnosis and at the stages of treatment.

The research was carried out in compliance with the principles of bioethics and the rights of the patient in accordance with the Helsinki Declaration (2000) and the Fundamentals of Ukrainian legislation on health care (1992).

The object of our research, with informed consent, included 75 patients with AN, 18-36 years (average age 26 ± 3.8) - the main group (M), and 60 patients without AN of the same age - the comparison group (C). For a detailed analysis of the clinical manifestations of GPD all patients in the main (M) and comparative (C) groups were divided into several subgroups. M_1 subgroup - patients with various forms of gingivitis. The M_2 subgroup included patients with generalized parodontities (GP), associated with AN as the basic pathology.

The comparative (C) group consisted of two subgroups (C_1), (C_2) with different forms of gingivitis and GP, respectively.

All patients with AN had a treatment in the neuropsychiatric department of Kiev Clinical Hospital on railway transport №1 (head of the Department – O.V. Moskalenko). Note, that all examined patients had a restrictive form of AN. We did not have patients with the cleansing form of AN.

The control group consisted of 30 people similar to the age and sex without clinical signs of parodontal disease. Diseases of internal organs and systems, including the osteoarticular apparatus, in these examined people were excluded.

Results of own research.

The research, as a whole, established a high incidence of GPD in patients with AN, including both independent soft parodontal tissue diseases and diseases of the entire parodontal complex (table 1).

Table 1 - Basic design of generalized parodontal diseases in patients in the main and comparative groups

Groups of patients	Independent forms of gingivitis (without detailing the form and a course of disease), number of patients (%)	Generalized parodontities (without detailing the degree and a course of disease), number of patients (%)
The main group	15 patients 20±4,6%	60 patients 80±4,6%
The comparative group	48 patients 80±5,2%	12 patients 20±5,2%

In the result of the research, independent parodontal soft tissue diseases of various forms and the course of gingivitis were diagnosed in 20±4.6% cases, while GP of different degrees and course was observed in 80±4.6% in the main group.

It should be noted that patients of the comparative group without manifestations of anorexia nervosa had a higher incidence of independent forms of gingivitis - 80 ± 5,2%, while GP of different degrees and course was diagnosed less frequently and was observed in 20 ± 5,2% of cases.

Analyzing the data of patients of the subgroup M_2, catarrhal gingivitis prevailed among the independent diseases of the soft parodontal tissues, while other forms of gingivitis were not diagnosed.

It was found that the majority of patients had catarrhal gingivitis in 86.7±8.8% cases, which had exclusively chronic course, and exacerbation of the process was observed only in 13.8±8.8% cases.

It is fair to note that the collection of a detailed anamnesis in patients of the main group and the identification of complaints was difficult due to the lack of a psychological alliance, which was accompanied by a lack of willingness to participate in voluntary contact during the examination. This is due to the fact that people with AN are unreliable "informants". Only a further structured interview helped gather information to evaluate anamnestic features and complaints.

While examination patients of the (C) group collection of anamnesis and complaints had no difficulties. Such patients were ready for dialogue. There was an open desire to participate in a therapeutic alliance.

We believe that the absence of any connotative dental complaints in patients of (M) group, in our opinion, could be due to the full focus only on the paradigm of their appearance, pathological concern about their own weight, figure and low level of all components of compliance. But in 20±10.3% of cases there was a so-called symptom of aeration, manifested by complaints of the inability to chew food, unbearable pain when trying to bite off a piece of fresh bread, "pathological tooth mobility" and a feeling of tooth loss that did not respond to clinical changes.

It should be noted that in the majority of patients of M_1 subgroup chronic gingivitis was characterized by involvement in the pathological process of only the marginal part of the gums. In most cases (66.7±12.2%) with a background of stagnant hyperemic and dense gums, a marked narrow band of stagnant hyperemia was noted in the area of the cervical teeth. In 20±10.3% cases areas of congestive gum hyperemia were replaced by zones with marked pallor. It was found that only 13.8±8.8% cases of chronic inflammation covered all components of the soft tissues of the periodontium.

Patients in M_1 subgroup had typically supragingival dental calculus, and in 26.7 ± 11.4% cases it appeared as a whole layer.

In all patients of the M_1 subgroup according to the radiological examination, the extension of periodontal fissures was established throughout, while maintaining the cortical plate. They noted osteoporosis of the apex of the alveolar bone ridge and bone components of the parodontal complex.

It can be assumed that the enlargement of the periodontal cleft and osteoporosis, on the one hand, was due to chronic inflammatory process in the soft tissues of the parodontum, and on the other - the existing osteoporosis could be a manifestation of systemic osteoporosis caused by a decrease in estrogen production, abnormal secretion of insulin secretory factor and decreased thyroid hormone metabolism, resulting hypogonadism, and secondary hyperparathyroidism.

Patients of the C_1 subgroup, unlike pations of the M_1 subgroup, were diagnosed with all forms of gingivitis, including catarrhal, atrophic, desquamative, ulcerative-necrotic and hypertrophic, accounting for 77.1±6.1% cases, 4,2±2.9% cases, 6.3±3.5% cases, 2.1±2.1% cases, 10.4±4.4% cases, respectively.

It should be noted that, unlike the patients in the (M) group, in the (C) group, a high motivational component was observed, which indicated a willingness to take part in full treatment.

Finalizing the analysis of subjective and clinical manifestations of lesions of parodontal soft tissues affiliated with AN, the patients of the (M) group were characterized by:

- no complaints;
- low degree of psychological alliance with the doctor;
- had catarrhal gingivitis with a predominant lesion of the marginal gums with chronic course;
- extension of the periodontal cleft and osteoporosis of the bone component of the parodontal complex.

In 60 patients (80,0±4,6%) (out of 75) of the (M_2) subgroup on the basis of clinical and radiological examination was diagnosed GP from the initial to the second degree, chronic course with the predominant absence of complaints (table 2).

Table 2 - The distribution of parodontal lesion in patients with anorexia nervosa

Group of patients	GP, initial-I degree, chronic course	GP, I-II degree, chronic course
The main group	12 patients 20±5,2%	48 patients 80±5,2%

It should be noted that among the examined patients of the M_2 subgroup, GP had a chronic course, and only 3.3± 2.3% cases had exacerbation of the process as a result of the recently transmitted infectious process. Symptomatic catarrhal marginal gingivitis was observed in soft parodontal tissues. We believe that mainly chronic course of GP in patients of M_2 subgroup, in our opinion, could be caused by significant changes in the general

immunological reactivity of the organism due to AN, which did not allow to trigger an active inflammatory response.

As a result of radiological examination of patients of M_2 subgroup with primary –I degree GP, the extension of the periodontal fissure and osteoporosis of the bone component of the parodontal complex was revealed, the horizontal type of resorption in all patients, as well as the cortical plate dislocation in the segment of the primary degree, and 1/3 reduced in the segment I degree. The advantages and priorities of different segments of the parodontal complex in patients with AN were not observed.

In determining the hypersensitivity of the delayed action to the bone antigen in this group, all patients showed a high degree of tissue sensitization, which showed significant changes in the bone component of the parodontal complex. This could be a predictor and an indicative factor that simplifies the diagnosis of initial -I degree, GP when the radiographic picture is not yet clearly expressed (table 3).

Table 3 – The frequency of tissue sensitization to the bone antigen in patients with generalized parodontal diseases and in almost healthy people

Groups of patients	Diagnosis	Tissue allergy	
		The number of patients	Bone antigen (inhibition of migrating leukocytes*)
The main group	GP, initial -I degree, chronic course	12	16,7±4,4
	GP, I-II degree, chronic course	48	66,7±5,6
	Generalized catarrhal gingivitis, chronic course	13	5,6±2,7
The comparative group	GP, initial -I degree, chronic course	9	15±4,6
	GP, I-II degree, chronic course	3	5±2,8
	Generalized catarrhal gingivitis, chronic course	35	8,3±3,6
The control group	Almost healthy	30	0

* - % positive reactions

We would like to note, that in no case in the patients of the control group tissue sensitization to the bone antigen was not established.

Some peculiarities were established in the research of the interdependence of GPD and AN with the gender of patients, age and their peculiarities of duration, form and stage of the main disease.

Thus, no influence of gender on the peculiarities of manifestation of GPD, associated with AN was noted (fig 1).

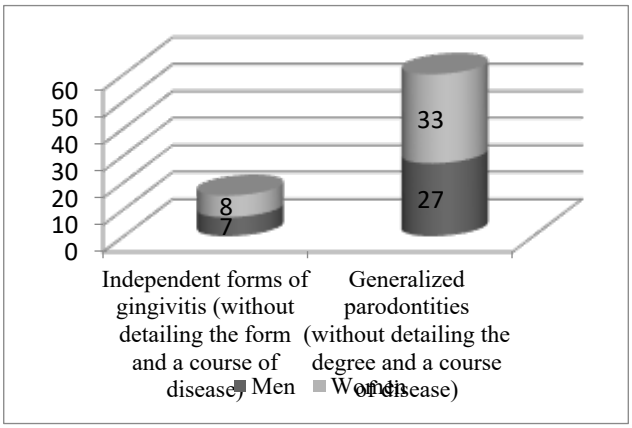

Fig. 1- The impact of patient's gender with anorexia nervosa on the features of the course of generalized parodontal diseases

It was found that high frequency of GPD was defined to all age categories of patients with AN, and the course of GP increased with age (table 4). It should be noted that since the exacerbated course of both catarrhal gingivitis and GP was observed in 2 persons, respectively, we considered it expedient to analyze the effect of patients' age on the frequency of GPD only among persons with GPD chronic course, associated with AN.

Table 4 - Influence of age on frequency of generalized parodontal diseases in patients with anorexia nervosa

Main disease	Age of patients, years	Catarrhal gingivitis, chronic course	Generalized parodontal diseases	
			GP, initial-I degree, chronic course	GP, I-II degree, chronic course
Anorexia nervosa	18-25	7 9,9±3,5% p > 0,05	8 11,3±3,8% p > 0,05	11 15,5±4,3% p > 0,05
	25-30	4 5,6±2,7% p > 0,05	3 4,3±2,4% P > 0,05	16 22,5±5% p > 0,05
	31-36	2 2,8± 2% p < 0,01	1 1,4±1,4% p > 0,05	18 25,4±5,2% p > 0,05
Total		13 18,3±4,6%	12 17,1±4,5%	45 63,4±5,7%

*p – confidence indicator

It is established that as the stages of AN progress, in particular primary, anorectic and cachectic, the proportion of people with GP increases. Thus, if it was 14.7% at the initial stage of AN, and reached 20% at the anorectic stage, then it was already 42.7% at the cachectic stage (fig.2).

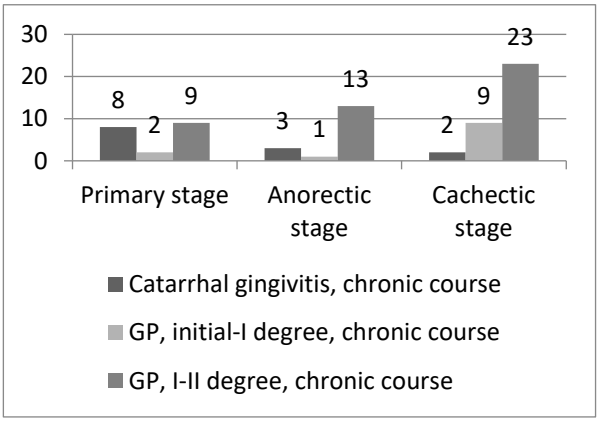

Fig 2. Influence of stages of anorexia nervosa on the frequency of generalized parodontal diseases

The results of the research showed no correlation between the duration of AN and the independent forms of gingivitis, but a direct dependence of the underlying disease and GP was found more with accentuation for the duration of 9-12 years (table 5).

Table 5 - Influence of the duration of anorexia nervosa on the manifestation of generalized parodontal diseases

Duration of anorexia nervosa, years	The number of patients	Catarrhal gingivitis, chronic course	Generalized parodontal diseases	
			GP, initial-I degree, chronic course	GP, I-II degree, chronic course
1-3	15	4 5,6±2,7% p > 0,05	3 4,2±2,4% p> 0,05	8 11,3±3,8% p > 0,05
4-8	19	5 7±3% p > 0,05	2 2,9±2% P > 0,05	11 15,5±4,3% P > 0,05
9-12	37	4 5,6±2,7% p < 0,01	7 9,9±3,5% p > 0,05	26 36,6±5,7% p > 0,05
Total		13 18,3±4,6%	12 17,1±4,5%	45 63,4±5,7%

As a result of our study, we have formed a view regarding the interaction of affiliation and comorbidity of generalized parodontal diseases and anorexia nervosa (scheme 1).

Conclusions:

1. A high incidence of parodontal disease was established, reaching 100% in patients with anorexia nervosa.
2. Among the independent forms of gingivitis, the most common was generalized chronic catarrhal gingivitis with an emphasis on the marginal gums in patients with anorexia nervosa.
3. It is established that generalized parodontitis prevails over other forms of GPD (80 ± 4.6%), mainly I-II degrees, chronic course in patients with anorexia nervosa.
4. The influence of age on the frequency of generalized parodontal diseases has been established. The severity of GP was directly dependent on the age of patients with AN.
5. The course of GP was directly dependent on the age of patients with AN.
6. The relationship between the main clinical and radiological manifestations of generalized parodontitis from the the duration and stage of nerve anorexia (primary → anorectic → cachectic) was established.
7. The revealed tissue sensitization to the bone antigen in patients with GP and AN even at the initial degree requires mandatory inclusion in the general treatment regimen of osteotropic drugs, including preparations of vitamin D_3, which provides differentiation of cells of the alveolar process, potentiation of carbohydrate, lipid metabolism.
8. The hypothesis of a probable paradigm of interdependence of GPD and AN as affiliated diseases is proposed as the first stage of further development of this direction.

Authors declare no conflict of interest.

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