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CLINICAL MANIFESTATIONS OF DIFFERENT ETIOPATHOGENETIC VARIANTS OF CHRONIC NASOPHARYNGITIS

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The study was devoted to evaluating the clinical manifestations of different etiopathogenetic variants of chronic nasopharyngitis in children, depending on the predominant trigger factors of exacerbations under different associated conditions of the nasopharyngeal zone. A total of 214 children with confirmed chronic nasopharyngitis were divided into three groups: 62 with isolated chronic nasopharyngitis, 41 with chronic nasopharyngitis associated with pharyngeal tonsil hypertrophy, and 111 with chronic nasopharyngitis associated with allergic rhinitis. The comparison group included 35 children with recurrent respiratory infections and complete recovery between episodes. Retrospective and prospective assessment, clinical examination, videoendoscopic otorhinolaryngological evaluation, allergological testing, cytological analysis, and microbiological study of nasopharyngeal mucus were performed. Children with isolated chronic nasopharyngitis most commonly demonstrated frequent acute viral rhinosinusitis followed by prolonged bacterial activation; those with pharyngeal tonsil hypertrophy showed bacterial predominance in both disease periods; and those with allergic rhinitis exhibited viral-allergic exacerbations with allergic-bacterial persistence between exacerbations.

Key words: chronic nasopharyngitis, rhinosinusitis, recurrent respiratory infections, microbiome, dysbiosis, allergic rhinitis, pharyngeal tonsil hypertrophy, immunological status.

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КЛІНІЧНІ ПРОЯВИ РІЗНИХ ЕТІОПАТОГЕНЕТИЧНИХ ВАРІАНТІВ ХРОНІЧНОГО НАЗОФАРИНГІТУ

Дослідження було присвячене оцінці клінічних проявів різних етіопатогенетичних варіантів хронічного назофарингіту у дітей залежно від переважаючих факторів, що провокують загострення, при різних супутніх захворюваннях назофарингеальної зони. Усього 214 дітей з підтвердженим хронічним ринофарингітом було розділено на три групи: 62 з ізольованим хронічним ринофарингітом, 41 з хронічним ринофарингітом, асоційованим з гіпертрофією глоткових мигдаликів, та 111 з хронічним ринофарингітом, асоційованим з алергічним ринітом. До контрольної групи увійшли 35 дітей з рецидивуючими респіраторними інфекціями та повним одужанням між епізодами. Було проведено ретроспективну та проспективну оцінку, клінічне обстеження, відеоендоскопічне отоларингологічне дослідження, алергологічне тестування, цитологічний аналіз та мікробіологічне дослідження слизу носоглотки. У дітей з ізольованим хронічним ринофарингітом найчастіше спостерігалися часті гострі вірусні риносинусити, за якими слідувала тривала бактеріальна активація; у дітей з гіпертрофією глоткових мигдаликів у обох періодах захворювання переважали бактерії; а у дітей з алергічним ринітом спостерігалися вірусно-алергічні загострення з алергічно-бактеріальною персистенцією між загостреннями.

Ключові слова: хронічний назофарингіт, риносинусит, рецидивуючі респіраторні інфекції, мікробіом, дисбіоз, алергічний риніт, гіпертрофія глоткового мигдалика, імунологічний статус.

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The main characteristic of chronic nasopharyngitis (CNP), in contrast to recurrent respiratory infections (RRI), in addition to its persistence over a long period of time, is the absence of complete recovery during the inter-exacerbation periods [6, 8, 10]. In childhood, when rhinitis develops or worsens, the question always arises whether it is acute viral rhinosinusitis (AVRS), acute nasopharyngitis (or an exacerbation of chronic nasopharyngitis), acute bacterial rhinosinusitis (ABRS), or a manifestation of allergic rhinitis (AR) [9]. Clearly, these diagnoses alternate with varying frequency in most children. However, in our opinion, such variability is more typical of children without associated conditions of the nasopharyngeal zone [4]. Comorbidity accompanies most chronic diseases, both provoking and maintaining the persistence of pathological factors.

Whereas previously nasopharyngeal obstruction [1, 3, 11], impairing nasal breathing, was considered the main trigger for chronicity of upper respiratory tract diseases in children, current concepts also include infectious burden caused by representatives of the opportunistic microflora of the pharyngeal biocenosis (streptococci, staphylococci, Haemophilus influenzae, etc.), respiratory and lymphotropic viruses [7, 11, 12], and/or the child's predisposition to allergy [1, 2]. Thus, persistence of the inflammatory process within the lymphoid tissue and mucous membrane, together with recurrent episodes of acute inflammation, contributes to the development of CNP and requires correction of the child's immunological status as a preventive measure for controlling the incidence of RRI, achieving complete recovery, and avoiding complications of

bacterial inflammation, including acute and chronic rhinosinusitis, acute and chronic otitis, etc. [4].

Based on the studies performed, we confirmed the role of comorbid conditions which, in CNP, determine the predominance of the same causes of exacerbations in a given patient, each characterized by an individual set of conditions and features: pharyngeal tonsil hypertrophy (PTH), AR, viral and bacterial burden, and the microbiome (the state of the commensal microflora) of the nasopharyngeal zone.

The purpose of the study was to investigate the clinical characteristics of different variants of chronic nasopharyngitis in children depending on the predominant etiological factor of exacerbations under different associated conditions of the nasopharyngeal zone, for the further substantiated modulation of nasopharyngeal immune system activity.

Materials and methods. From November 2023 to November 2025, during the first visit, 315 parents of frequently ill children (more than 8 episodes of recurrent respiratory infections (RRI) per year) were asked to choose one of the three above-mentioned variants describing disease exacerbations before referral. If the parental characterization coincided with the results of the analysis of the submitted medical documentation (284 patients), the child was invited to further participation in the study. In 35 of the 284 children, CNP was not confirmed, since during the inter-exacerbation period all indicators (medical documentation data before inclusion in the study, complaints, examination findings, and laboratory results after exacerbation) were within normal limits; these children were included in the control group (CG) as children with RRI without CNP. The parents of 35 of the 249 children with a confirmed diagnosis of CNP were unable to confidently choose one of the proposed variants describing the course of the disease before referral. The parents of 31 of the 315 children refused participation in the study, or the children did not meet other inclusion/exclusion criteria.

Thus, 214 patients with CNP rather than RRI, whose parents confidently described the course of the disease before the study with documentary confirmation, formed three main groups:

1. Main group 1 (MG I): 62 children with CNP without comorbidity of the nasopharyngeal zone;

2. Main group 2 (MG II): 41 children with CNP associated with pharyngeal tonsil hypertrophy (PTH);

3. Main group 3 (MG III): 111 children with CNP associated with allergic rhinitis (AR).

Patients of all study groups were representative in terms of age and sex.

The study was conducted at the Department of Otorhinolaryngology of Odesa National Medical University with the participation of the Clinical Diagnostic Laboratory of the University Medical Center of Odesa National Medical University and the Educational and Research Laboratory of Molecular Pathology of Odesa National Medical University (Certificate No. 04-0053/2023 on compliance of measurement systems with the requirements of DSTU ISO 10012:2005 dated December 29, 2023).

The study was performed in accordance with the principles of the Declaration of Helsinki. The examinations provided for in the study were generally accepted and approved for use. Each patient involved in the study was informed of its purpose and objectives, and written parental consent for participation was obtained. The study used medicinal products and devices registered by the relevant state authorities of the Ministry of Health of Ukraine and approved for use in medical practice. The Biomedical Ethics Commission of Odesa National Medical University (Protocol No. 17 dated November 1, 2023) established that this scientific study complied with ethical and moral-legal requirements in accordance with Order of the Ministry of Health of Ukraine No. 281 dated November 1, 2000.

The study used current adapted clinical guidelines of the Ministry of Health of Ukraine: Order No. 499 dated July 16, 2014 (acute respiratory infections), Order No. 1793 dated October 13, 2023 (chronic rhinosinusitis), and Order No. 181 dated March 24, 2009 (chronic pharyngitis).

Cytological examination of nasopharyngeal secretions was performed using imprint smears obtained from the mucosal surface of the posterior nasopharyngeal wall and from the nasal cavity mucosa. Biomaterial delivery conditions were as follows: no later than 48 hours at a temperature of 20 to 25°C. Cytological micropreparations were stained according to the Romanowsky–Giemsa method. Microscopic examination included counting cells of different layers of the stratified squamous epithelium of the pharynx and nasal cavity. The assessed parameters included the number of leukocytes (absolute count, %), erythrocytes, basophilic granulocytes, eosinophilic granulocytes, band neutrophils, segmented neutrophils, monocytes, lymphocytes, squamous/cylindrical epithelium, coccal flora, and yeast-like fungi.

The microbiocenosis of nasopharyngeal secretions was determined using standard bacteriological and microscopic methods. The study procedure included endoscopically controlled sampling of material from the nasopharynx for bacteriological examination before and after treatment. The obtained material was inoculated onto a set of standard culture media. Cultivation was performed under aerobic, anaerobic, and reduced-oxygen conditions. Microbiological examination

included identification of all species of microorganisms persisting on the nasopharyngeal mucosa. The population level of microorganisms was expressed as the number of colony-forming units in 1 mL of washings (CFU/mL) according to the formula $X = 20 \times M \times N$, where X is the number of CFU/mL, 20 is the constant coefficient for inoculation of 0.1 mL of the sample, M is the number of colonies grown, and N is the dilution factor.

To characterize the clinical pattern of CNP exacerbations before enrollment, three anamnestic variants of disease onset were identified.

Variant 1 of the onset of CNP exacerbations was usually characterized by exacerbation of rhinitis without prodromal manifestations and without hyperthermia at disease onset; exacerbation of rhinitis after routine attendance of a children's group; exacerbation of rhinitis without contact with patients with AVRS; onset of rhinitis exacerbation immediately with colored nasal discharge; subfebrile temperature 3–5 days after the onset of CNP exacerbation, or exacerbations of CNP occurring without an increase in body temperature; nasal discharge accompanied by postnasal drip and/or cough; predominance of nocturnal cough during exacerbations of rhinitis; and frequent complications such as acute purulent otitis media, acute bacterial rhinosinusitis (ABRS), bronchitis, pneumonia, cervical lymphadenitis, etc.

Variant 2 was usually characterized by exacerbation of rhinitis after contact with patients with AVRS; the autumn-winter period being the most intense with regard to the frequency of CNP exacerbations; and exacerbations beginning with prodromal manifestations and hyperthermia from the first hours of the disease, sometimes with complications.

Variant 3 was characterized by a burdened allergic history; no dependence of exacerbation occurrence on attendance of a children's group and only moderate dependence on contact with patients with AVRS; presence of exacerbations depending on contact with the causative allergen; exacerbations often occurring without hyperthermia, with possible short-term subfebrile temperature; exacerbations being rarely complicated by purulent otitis or bacterial rhinosinusitis; and effective antiallergic therapy of CNP exacerbations.

Statistical processing of the results was performed using parametric and nonparametric statistical methods. For the assessment of numerical indicators, the arithmetic mean (M) and the standard error of the mean (m) were calculated using Student's t-test for independent and dependent samples. The Shapiro–Wilk test was used to assess the distribution of quantitative data. Differences were considered statistically significant at $p<0.05$ [5].

Results of the study and their discussion. Among 48 (77.4 %) patients with CNP (MG I), frequent episodes of acute viral rhinosinusitis (AVRS) were identified with a very high probability ($p<0.01$) as the cause of exacerbations. Patients with CNP associated with pharyngeal tonsil hypertrophy (PTH) (MG II), namely 31 (75.6 %), demonstrated the highest dependence on the bacterial component of inflammation, with almost no AVRS, at $p<0.05$. In patients with CNP and allergic rhinitis (AR) (MG III), the pattern was less clear, and none of the factors showed a statistically significant predominance, although in a fairly substantial number of patients, 51 (45.9 %), exacerbations depended on frequent AVRS. The leading factors of CNP exacerbation according to anamnestic, questionnaire-based, and retrospective documentary data in the study groups are presented in Fig. 1.

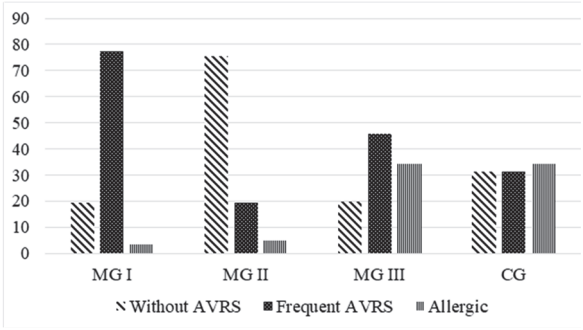

Fig. 1. Leading factors of CNP exacerbation according to anamnestic and retrospective documentary data.

Assessment of patients' complaints during different periods of CNP makes it possible to determine the further plan of investigations that may confirm or refute suspicions regarding the causes of exacerbations and chronicity in the groups depending on comorbidity of the nasopharyngeal zone. The distribution of specific complaints across all studied groups depending on the disease period is presented in Table 1.

In MG I, the combination of prodromal manifestations, hyperthermia at exacerbation onset, symptom variability, and predominance of colorless nasal discharge during exacerbation indicates an important role of respiratory viral infection. In contrast, the predominance of colored discharge in the inter-exacerbation period, compared both with CG and with exacerbation, suggests prolonged secondary bacterial pathogenization after AVRS and supports the chronic nature of the disease.

In MG II, the absence of prodromal manifestations, fever at onset, and symptom variability, together with predominance of colored discharge in both disease periods relative to CG, indicates the leading role of bacterial burden during both exacerbation and inter-exacerbation periods. The predominance of impaired nasal breathing day and night, ear fullness and pain, postnasal drip, and

nocturnal cough further confirms the substantial contribution of pharyngeal tonsil hypertrophy.

In MG III, prodromal manifestations at exacerbation onset suggest a viral trigger in 51 children (45.9 %). At the same time, low symptom variability points to an allergic origin of many exacerbations. The high frequency of nocturnal nasal obstruction in the inter-exacerbation period, 34 (82 %), the lower rate of persistent day-and-night obstruction during exacerbation, 28 (25.2 %), and the predominance of colorless discharge, 82 (73.9 %), indicate a substantial allergic component in both exacerbation and chronicity. The limited role of bacterial inflammation is supported by only 17 (15.3 %) cases of colored discharge during exacerbation; although higher than in CG during the inter-exacerbation period ($p<0.05$), this remained less pronounced than in MG I and MG II ($p<0.01$).

Table 1

Quantitative characteristics of complaints in all groups of patients with CNP during different disease periods

Complaints	DP	MG I, n=62		MG II, n=41		MG III, n=111		CG, n=35	
		abs.	%	abs.	%	abs.	%	abs.	%
Prodromal manifestations	E	48	77.4*	6	14.6*	51	45.9	16	45.7
	IE	-	-	-	-	-	-	-	-
Hyperthermia at the onset of exacerbation	E	41	66.1*	6	14.6*	33	29.7	15	42.9
	IE	-	-	-	-	-	-	-	-
Hyperthermia after the onset of exacerbation	E	21	33.9	25	40.3	5	4.5	11	31.4
	IE	-	-	-	-	-	-	-	-
Symptom variability	E	46	74.2*	14	34.1	21	18.9*	16	45.7
	IE	33	53.2	13	31.7	59	53.2	0	0
Difficulty in nasal breathing both day and night	E	22	35.5*	41	100*	22	19.8*	21	60
	IE	12	19.4*	36	87.8**	28	25.2*	0	0
Difficulty in nasal breathing only at night	E	40	64.5[a]	0*	0*	89	80.2*	14	40
	IE	21	33.9*	5	12.3	34	82**	4	11.4
Predominance of colored nasal discharge	E	8	12.9*[a]	29	70.7*	17	15.3*[a]	13	37.1
	IE	54	87.1**	30	73.2**	29	26.1*	0	0
Predominance of colorless nasal discharge	E	54	87.1[a]	12	29.3*	94	84.7*	22	62.9
	IE	8	12.9*	11	26.8	82	73.9*	15	42.9
Postnasal drip	E	33	53.2	35	85.4*	31	27.9	11	31.4
	IE	23	37.1*	28	68.3**	32	28.8*	0	0
Subfebrile temperature	E	9	14.5*	34	82.9*[a]	8	7.2**	11	31.4
	IE	23	37.1*[a]	22	53.7*	25	22.5*[a]	3	8.6
Ear fullness	E	34	54.8[a]	32	78*	43	38.7*	19	54.3
	IE	25	40.3	29	70.7*	35	31.5**	5	14.3
Ear pain	E	26	41.9[a]	19	46.3[a]	37	33.3[a]	15	42.9
	IE	1	1.6	8	19.5*	4	3.6	0	0

Note: *Statistically significant difference relative to the control group (CG). Conclusion made at the significance level of 0.05. **Statistically significant difference relative to the control group (CG). Conclusion made at the significance level of 0.01. [a]Statistically significant difference between disease periods. Conclusion made at the significance level of 0.05. DP – disease period; E – during exacerbation; IE – inter-exacerbation period.

At the stage of endoscopic ENT examination, the triad of signs typical of AVRS, corresponding to the first three rows of Table 2, was identified with very high probability in MG I patients. At the same time, nasal mucosal edema during exacerbation was also significantly frequent in MG III, being observed in 85 of 111 children (76.6 %).

Mucopurulent discharge in the middle and/or upper nasal meatus was most characteristic of MG II during exacerbation and was the only group in which it significantly persisted in the inter-exacerbation period, in 9 patients (22 %), indicating concomitant bacterial rhinosinusitis. Mucopurulent discharge in the common nasal meatus, reflecting bacterial burden without sinus involvement, was also most typical of MG II in both periods: 35 (85.4 %) during exacerbation and 33 (80.5 %) between exacerbations.

Abnormal coloration of the pharyngeal tonsil was found in all main groups in both disease periods: in MG I, 47 (75.8 %) and 38 (61.3 %); in MG II, 36 (87.8 %) and 32 (78 %); and in MG III, 92 (82.9 %) in both periods, with $p<0.01$ versus CG during the inter-exacerbation period.

Mucopurulent deposits on the pharyngeal tonsil had significant relevance in MG II patients (CNP+PTH) in both phases of the disease, namely 41 (100 %) and 40 (97.6 %), whereas, despite a significant difference relative to the control group, they did not have a leading role in MG III patients (CNP+AR) in the inter-exacerbation period. In contrast, in MG I patients (CNP), they were detected in 51 (82.3 %) patients during the inter-exacerbation period, with a significant decrease in their presence to 23 (37.1 %) during exacerbation ($p<0.05$). This may be related to pronounced tonsillar edema during

the respective period, as well as to the predominance of respiratory virus in the upper respiratory tract mucosa during AVRS.

Signs of acute otitis media (AOM), including hyperemia, thickening and/or bulging of the tympanic membrane, and exudate behind it, were significantly more frequent on examination during exacerbation in MG I (CNP) and MG II (CNP+PTH) patients, namely 36 (58.1 %) and 22 (53.7 %), respectively. Moreover, in children without PTH they were observed even more often than in those with PTH, confirming that the size and condition of the lymphoid tissue are different characteristics.

Table 2

Quantitative characteristics of symptoms during endoscopic visualization in all groups of patients with CNP during different disease periods

Videoendoscopic findings	DP	MG I, n=62		MG II, n=41		MG III, n=111		CG, n=35	
		abs.	%	abs.	%	abs.	%	abs.	%
Hyperemic nasal mucosa	E	60	96.8*	13	31.7*	45	40.5	22	62.9
	IE	2	3.2[a]	2	4.9	4	3.6[a]	2	5.7[a]
Edema of the nasal mucosa	E	59	95.2**	11	26.8	85	76.6*	16	45.7
	IE	3	4.8[a]	5	12.2	93	83.8	3	8.6[a]
Petechiae on the mucosa of the upper respiratory tract	E	55	88.7**	0	0	37	33.3	19	54.3
	IE	0	0[a]	0	0	1	0.9[a]	0	0[a]
Mucopurulent discharge in the upper and/or middle nasal meatus	E	22	35.5	25	61*	44	39.6	10	28.6
	IE	4	6.5	9	22*[a]	3	2.7	0	0[a]
Mucopurulent discharge in the common nasal meatus	E	32	51.6	35	85.4*	33	29.7*	26	74.3
	IE	34	54.8*	33	80.5**	7	6.3	1	2.9
Abnormal coloration of the pharyngeal tonsil	E	47	75.8*	36	87.8*	92	82.9*	14	40
	IE	38	61.3**	32	78**	92	82.9**	1	2.9
Edema of the pharyngeal tonsil, smoothing of its surface	E	53	85.5*	38	92.7*	103	92.8*	12	34.3
	IE	31	50[a]	27	65.9	85	76.6	5	14.3
Mucopurulent deposits on the pharyngeal tonsil	E	23	37.1	41	100**	36	32.4	11	31.4
	IE	51	82.3**[a]	40	97.6**	35	31.5*	0	0
Grade 3 adenoid vegetations	E	0	0	36	87.8*	31	28	9	25.7
	IE	0	0	36	87.8*	25	22.5	9	25.7
Signs of acute otitis media (AOM)	E	36	58.1*	22	53.7*	33	29.7	12	34.3
	IE	2	3.2[a]	7	17.1*[a]	1	0.9[a]	0	0
Transudate behind the tympanic membrane without signs of inflammation	E	11	17.7	26	63.4*	55	49.5*	8	22.9
	IE	15	24.2*	24	58.5*	32	28.8*	2	5.7
Enlarged cervical lymph nodes	E	41	66.1**	36	87.8**	33	29.7*	4	11.4
	IE	41	66.1**	31	75.6**	18	16.2*	2	5.7

Note: *Statistically significant difference relative to the control group (CG). Conclusion made at the significance level of 0.05. **Statistically significant difference relative to the control group (CG). Conclusion made at the significance level of 0.01. [a]Statistically significant difference between disease periods. Conclusion made at the significance level of 0.05. DP – disease period; E – during exacerbation; IE – inter-exacerbation period.

Transudate behind the tympanic membrane without signs of inflammation occurred significantly more often relative to the control group in patients of all main groups during both disease periods, except for MG I, in which AOM predominated specifically during exacerbation.

Enlarged cervical lymph nodes were observed in all main groups during both disease periods, but in MG I (CNP) and MG II (CNP+PTH) this difference was highly significant ($p<0.01$), whereas in MG III (CNP+AR) it was significant at $p<0.05$, which, in our opinion, is related to the lesser contribution of the infectious factor to the chronicity of nasopharyngitis in patients with atopy.

Pathological colonization levels ("++++" and "+++") were characteristic of all main study groups: MG I – 32 (51.6 %) and 42 (67.7 %), MG II – 38 (92.7 %) and 24 (58.5 %), MG III – 42 (37.8 %) and 54 (48.6 %) during exacerbation and without exacerbation, respectively, in contrast to the CG, whose representatives demonstrated complete stabilization of the quantitative characteristics of the microbiota during the inter-exacerbation period.

The state of colonization of the nasopharyngeal mucosa in all groups of the examined children during the inter-exacerbation period according to nasocytogram assessment is presented in Fig. 2.

Microbiological examination of nasopharyngeal secretions in children with CNP revealed both quantitative and qualitative alterations in the microbiocenosis during exacerbation and in the inter-exacerbation period. In MG I, during the first 3 days of exacerbation, moderate colonization by opportunistic microorganisms was observed: pyogenic streptococcus 3.22±1.4 CFU/mL, epidermal staphylococcus 4.54±1.2 CFU/mL, and Staphylococcus aureus 4.41±0.68 CFU/mL, together with symbiotic flora, including S. viridans 2.53±0.78

CFU/mL and S. salivarius 3.13±1.03 CFU/mL, as well as Candida 2.75±0.56 CFU/mL. After AVRS, colonization by Pneumococcus pneumoniae, Haemophilus influenzae, Klebsiella pneumoniae, and Staphylococcus aureus increased, whereas S. epidermidis increased insignificantly. S. viridans and S. salivarius decreased in the inter-exacerbation period, with complete disappearance of S. viridans. Recovery of symbiotic flora was insignificant for Lactobacillus spp. but significant for Bifidobacterium spp.

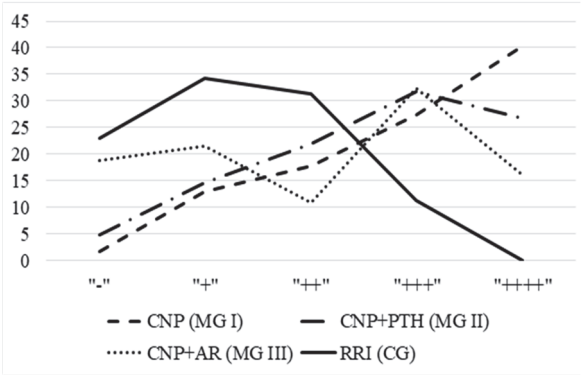

Fig. 2. Quantitative assessment of nasal mucosal colonization in the study groups during the inter-exacerbation period.

In MG II, exacerbation was characterized by marked microbial imbalance with excessive colonization by pyogenic streptococcus 6.64±0.23 CFU/mL, epidermal staphylococcus 5.12±0.09 CFU/mL, Staphylococcus aureus 5.41±0.15 CFU/mL, Pneumococcus pneumoniae 4.03±0.15 CFU/mL, Haemophilus influenzae 3.86±0.23 CFU/mL, Pseudomonas aeruginosa 4.24±0.22 CFU/mL, and Candida 2.67±0.45 CFU/mL. After exacerbation, Streptococcus pyogenes, Haemophilus influenzae, and Pseudomonas aeruginosa decreased significantly, whereas Staphylococcus aureus, S. epidermidis, and Pneumococcus pneumoniae decreased without significance. Symbiotic flora was almost absent during exacerbation; after it, restoration was significant for S. viridans and S. salivarius, but not for Lactobacillus spp. and Bifidobacterium spp.

In MG III, microbial shifts were less pronounced and included pyogenic streptococcus 3.26±0.08 CFU/mL, epidermal staphylococcus 2.42±0.12 CFU/mL, Staphylococcus aureus 2.36±0.07 CFU/mL, Klebsiella pneumoniae 3.12±0.7 CFU/mL, and Haemophilus influenzae 3.56±0.25 CFU/mL, without Candida association. After exacerbation, Haemophilus influenzae, Klebsiella pneumoniae, Staphylococcus aureus, S. epidermidis, and Streptococcus pyogenes decreased significantly. Unlike MG II, symbiotic flora, including lactobacilli, bifidobacteria, and salivary streptococci, was preserved during exacerbation and increased later without significant difference.

The significance of the bacterial factor during the intervals between exacerbations, which may ensure chronicity of nasopharyngitis in the studied patients, was assessed according to the degree of nasopharyngeal dysbiosis (Fig. 3).

MG III (CNP+AR) differed from the CG by substantial changes in the microbiome: 68 representatives of this group (61.3 % of cases) had grade 2 dysbiosis, and none had normoflora in the nasopharyngeal zone. In MG I, 54 (87.1 %) patients had signs of grade 2 dysbiosis, while only 5 (8.1 %) and 3 (4.8 %) had grade 1 and grade 3 dysbiosis, respectively, which also indicates substantial microbiome changes in these patients relative to the CG.

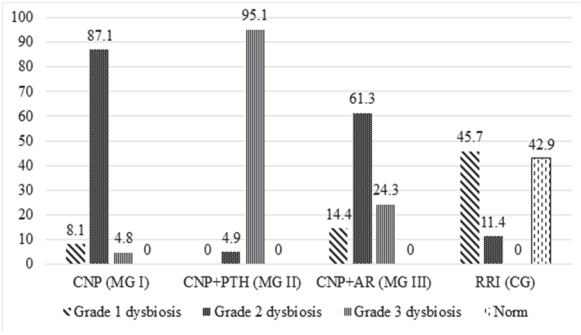

Fig. 3. Distribution of degrees of nasopharyngeal dysbiosis during the inter-exacerbation period of CNP among the study groups.

The marked predominance of grade 3 dysbiosis in children with chronic nasopharyngitis associated with pharyngeal tonsil hypertrophy (MG II) indicates the most severe disturbance of the nasopharyngeal microbial ecosystem in this group. This may be explained by mechanical obstruction of the choanae and nasopharynx by hypertrophic lymphoid tissue, impaired mucus drainage, secretion retention, and subsequent persistence of bacterial colonization. These findings are consistent with published data showing that adenoidal hypertrophy contributes to chronic upper airway inflammation and microbial imbalance [1, 9], and is associated with recurrent and chronic infectious processes due to impaired local defense and altered nasopharyngeal aeration [2, 3]. The very high rate of grade 3 dysbiosis in MG II (95.1 %) supports the view that pharyngeal tonsil hypertrophy is not merely an anatomical feature, but an active pathogenetic factor in the chronicity of nasopharyngitis. A further contributing mechanism may be Epstein–Barr virus persistence, which is associated with changes in lymphoid tissue and local immune regulation, thereby facilitating microbial persistence and dysbiotic transformation [4, 11]. Thus, grade 3 dysbiosis in MG II appears to result from combined anatomical obstruction, persistent bacterial colonization, and immune dysregulation.

Limitations. The study was limited by the single-center design and by the fact that the groups

were formed only from children whose parents could confidently characterize the course of the disease and whose descriptions were confirmed by medical documentation.

Conclusions

1. It was shown that patients with CNP, depending on associated conditions of the nasopharyngeal zone, can be divided into three different variants of disease course. Data from retrospective analysis of documentation, questionnaires, analysis of complaints and symptoms during endoscopic examination both during exacerbations and between them, as well as cytological and microbiological data, reliably indicate differences in the causes of exacerbations and chronicity of CNP in children with PTH, AR, and in children without PTH and without AR.

2. Thus, patients with isolated CNP (MG I) have frequent AVRS as a trigger factor for exacerbations followed by prolonged activation of opportunistic and pathogenic bacterial flora; patients with CNP associated with PTH have a bacterial factor during both disease periods; and patients with CNP associated with AR have allergic and viral factors (frequent AVRS) during exacerbations and bacterial and allergic factors during the inter-exacerbation period.

3. The possibility of studying the effectiveness of modulation of nasopharyngeal immune defense with a differentiated approach for each CNP variant becomes realistic after assessment of immune status and immunological interpretation with consideration of comorbid factors of the nasopharyngeal zone and requires further investigation.

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