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CLINICAL COURSE AND TREATMENT FEATURES OF ORAL LEPTOTRICHOSIS

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The oral microflora is highly diverse and includes actinomycetes, fungi, protozoa, spirochetes, rickettsia and viruses. Among them, Candida albicans has the highest pathogenicity, particularly associated with causing mycoses. Leptotrichia, similar to the fungi residing in the oral cavity, shares morphological characteristics, cell wall structure and antigenic properties. Morphologically, cell wall structure and antigenic composition are considered part of the opportunistic flora of the oral cavity and obligate anaerobes. In this regard, some authors hypothesize that abundant growth of Leptotrichia does not necessarily indicate pathology. Others consider eptotrichosis as a disease akin to opportunistic mycoses. However, there is a third perspective, where some authors classify leptotrichosis as an HIV-associated disease. Such divergence in opinions prompts a critical evaluation and leads to conclusions about the necessity of treating leptotrichosis. Moreover, in recent years, the number of individuals diagnosed with leptotrichosis has significantly increased. Therefore, leptotrichosis appears to be a distinct response of the oral mucosa to Leptotrichia infection, the activation and proliferation of which occur under specific conditions. The treatment was carried out according to the commonly accepted protocol, supplemented with the use of the drug to expedite the recovery process. The diagnosis was established based on clinical, anamnestic and laboratory study methods. The illness is chronic, with the possibility of observation over many months and years. Treatment is prolonged and requires persistence. The treatment plan may undergo changes. Clinical and laboratory indices serve as criteria for recovery.

Key words: candidiasis, leptotrichosis, treatment, oral mucosa.

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ОСОБЛИВОСТІ КЛІНІЧНОГО ПЕРЕБІГУ І ЛІКУВАННЯ ЛЕПТОТРИХОЗУ ПОРОЖНИНИ РОТА

Мікрофлора порожнини рота дуже різноманітна і вміщує актиноміцети, гриби, найпростіші, спірохети, рікетсії, віруси. Найбільш високу патогенність, що викликають мікози, мають Candida albicans. Лептотрихії, як і гриби, що наявні в порожнині рота, за морфологічними даними, будовою клітинної стінки, антигенною структурою — ϵ частиною умовнопатогенної флори порожнини рота, облігатними анаеробами. У зв'язку з цим, одні автори висловлюють думку, що рясно вегетуючі лептотріхії не свідчать про патологію. Інші, мають протилежну думку, вважаючи, що лептотрихоз ϵ захворюванням, наближеним до опортуністичних мікозів. Але існує і третя думка — деякі автори класифікують лептотрихоз як ВІЛ-асоційованих захворювань. Така розбіжність думок спонукає оцінювати їх критично та робити висновки про необхідність лікування лептотрихозу. Також, в останні роки, кількість хворих із діагнозом «Лептотрихоз», значно збільшилась. Таким чином, лептотрихоз — це своєрідна реакція слизової оболонки на лептотрихозну інфекцію, активація і розмноження якої проходить при наявності певних умов. Лікування проводилося за загальноприйнятою схемою та з використанням препарату для прискорення строків лікування. Діагноз встановлювали на основі клініко-анамнестичних та лабораторних методів дослідження. Захворювання довготривале. Його можливо спостерігати протягом багатьох місяців і років. Лікування триває довго, вимагає наполегливості. Схема лікування може змінюватись. Критерієм одужання ϵ клініко-лабораторні показники.

Ключові слова: кандидоз, лептотрихоз, лікування, слизова оболонка порожнини рота.

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The issue of fungal infections affecting the oral mucosa is currently relevant due to the overall health of the population, influenced by numerous somatic diseases, economic factors and the uncontrolled and irrational use of antibiotics, cytostatics, immunosuppressants and hormonal medications. Their actions can lead to the suppression of saprophytic microflora and the development of dysbiosis in the oral cavity.

An important aspect of this issue is the local factors, including the state of oral hygiene, lack of sanitation, periodontal tissue pathology, mucous membrane diseases (leukoplakia 82 %, erythematous lichen planus up to 76 %), diabetes mellitus up to 67 %, salivary gland pathology, dysfunctional removable and non-removable prosthetic constructions, especially in the elderly (around 60 %). However, there are cases where the disease occurs despite complete oral sanitation and the presence of somatic pathology (7 %), such as gastrointestinal diseases, diabetes mellitus, neurological disorders, etc.

Currently, oral candidiasis is found in a third of HIV-infected individuals and in 90 % of AIDS patients, as well as in patients with the past medical history of COVID-19 [1, 6].

Normally, the human body contain hundreds of different types of microorganisms. Among them, bacteria and viruses dominate, while simpler organisms are represented by a much smaller variety of species. In a healthy body, the permanent microflora serves as a biological barrier that impedes the proliferation of pathogenic microorganisms entering from the external environment. It also plays a role in self-cleansing of the oral cavity and acts as a constant stimulator of local immunity. Persistent changes in the composition and properties of the microflora, caused by a decrease in the body's reactivity, resistance of the mucous membrane of the oral cavity, as well as certain therapeutic interventions (radiation therapy, the use of antibiotics, immunosuppressants, etc.), can lead to the development of various oral cavity diseases. The causative agents of these diseases may include both pathogenic microorganisms entering from the outside and opportunistic representatives of the constant microflora of the oral cavity.

The oral microflora is diverse and includes actinomycetes, fungi, protozoa, spirochetes, rickettsiae and viruses. It is important to note that a significant portion of the microorganisms in the oral cavity of adults consists of anaerobic species [2, 3].

According to literature data and our own clinical observations, Candida albicans is reported to have the highest pathogenicity among fungi, accounting for up to 80 % of the total pathology [13, 14].

Literature sources predominantly provide information on the clinical manifestations, diagnosis and treatment of diseases caused by this type of pathogen [12, 13].

However, similar clinical symptoms are observed in other fungal stomatitis cases, which can only be studied through laboratory tests during internal syndrome-specific differential diagnostics. These fungal stomatitis cases are categorized as non-Candida groups.

Generally, publications report that fungal infections are classified as mycoses, yeast infections, yeast-like infections, and specifically, fungal infections in a separate group known as non-Candida [11].

The largest group of bacteria consistently present in the oral cavity consists of cocci, constituting 85–90 % of all types (including streptococci and staphylococci), as well as actinomycetes. Rod-shaped lactobacilli also exist in certain quantities in a healthy oral cavity. Similar to streptococci, they are producers of lactic acid [4, 5].

Leptotrichia belong to the lactic acid bacteria and are the causative agents of homofermentative lactic acid fermentation; they are strict anaerobes. They have the appearance of long threads of varying thickness with pointed or swollen ends. These threads are segmented, forming dense tangles. They do not form spores, have a rod-like appearance, and belong to the Fusobacterium family.

Morphologically, Leptotrichia, like the fungi, residing in the oral cavity, on their cell wall structure and antigenic structure are part of the conditionally pathogenic flora of the oral cavity and are obligate anaerobes [8, 9].

In this regard, some authors hypothesize that abundant growth of Leptotrichia does not indicate pathology. Others consider Leptotrichosis as a disease similar to opportunistic mycoses. However, there is also a third opinion, when some authors classify leptotrichosis as HIV-associated diseases [6, 7]. Such divergence of opinions encourages a critical evaluation and conclusions about the necessity of treating leptotrichosis [10, 15]. Moreover, in recent years, the number of patients diagnosed with leptotrichosis has significantly increased. Thus, leptotrichosis represents a distinctive response of the oral cavity to leptotrichosis infection, the activation, and proliferation of which occur under certain conditions.

The purpose of the study was to establish the manifestations of lephtotrichosis in the oral cavity, and its symptoms: burning sensation in various areas of the oral mucosa, sometimes loss of taste sensations, the presence of a coating on the tongue, sometimes with pigmentation in various shades of gray, may be associated with candidal lesions of the oral mucosa or red flat lichen.

Materials and methods. The study involved patients who sought care at the Municipal Enterprise "Poltava Regional Center of Dentistry – Dental Clinic" of Poltava Regional Council, the Department of Postgraduate Education of Dentists at Poltava State Medical University (PSMU), Poltava. Additionally, patients with various somatic pathologies, accompanied by changes in the oral cavity, were referred from the Department No. 3 of Internal Medicine with Phthisiology at PSMU.

At the beginning of the study, each patient provided informed consent, signing a document that explained the purpose and methods of the study, as well as the treatment approach. Data were analyzed using descriptive statistics. The total of 114 patients aged 40 to 75 years, including 40 men and 74 women, all with somatic pathology, have been involved into study.

The treatment was carried out according to the generally accepted scheme, utilizing the drug Afta Clear (GUM) to expedite the treatment process. The diagnosis was established based on clinical-anamnestic and laboratory methods. The inclusion criteria were patients with a confirmed diagnosis of lephtotrichosis, with a complete set of clinical and laboratory examination data. This permitted the

formation of the following groups of patients: the study group and the observation group. In the first group of patients (n=69), treatment was carried out according to the treatment options proposed by us. In patients with a combination of Candida spp. and lephtotrichosis, the following measures were taken: counselling with internists; professional and individual oral hygiene; diet excluding carbohydrates and dairy products; antifungal drugs (antimycotics): either fluconazole 100 mg once a day for 10-14 days (active ingredient – fluconazole; manufacturer – Darnytsa, Ukraine) or amphotericin B (active ingredient – amphotericin B; manufacturer – Bharat Serums, India) or itraconazole (active ingredient – itraconazole; manufacturer – Ananta Medicare, Johnson & Johnson); polyvitamins (Alpha Vit – a vitamin-mineral complex; manufacturer – AT Vitamins, Ukraine) for 30 days; antihistamines for 5–7 days; sedatives due to a high level of anxiety; oral mucosa immunostimulating drugs (Lysobact: lysozyme chloride, pyridoxine hydrochloride – 10.0 mg; manufacturer Bosnalijek d.d., Bosnia and Herzegovina), Echinacea purpurea L., manufacturer - Sandoz, 20 drops three times a day for 14 days); alkaline rinses; rinsing with 1 % clotrimazole solution (active ingredient: clotrimazole; manufacturer: Medana Pharma Spol, Poland); rinsing with 1 % miramistin solution (active ingredient: miramistin; manufacturer: Darnytsa, Ukraine); solutions containing the topical nonsteroidal drug benzidamine (Tantum-Verde and others); antifungal agents for local application, including suspensions of nystatin (active ingredient: nystatin; manufacturer: LLC Farmkompaniya Zdorovya, Ukraine), 2.5 % natamycin (active ingredient: natamycin; manufacturer: Ukraine), 0.1 % amphotericin B (active ingredient: amphotericin B; manufacturer: Amphotret, India), Candid (active ingredient: clotrimazole; manufacturer: Glenmark, India), clotrimazole cream (active ingredient: clotrimazole: manufacturer: GlaxoSmithKline, Poland), miramistin ointment (active ingredient: miramistin; manufacturer: Darnytsa, Ukraine), and others. In the observation group of patients (n=45), after counselling with internists, professional and individual hygiene of the oral cavity, treatment was carried out using the drug Afta Clear (Active ingredients: hyaluronate, taurine. Manufacturer: BMG Farma Srl., Italy, Milan) to reduce the duration of treatment. Exclusion criteria for patients included: unconfirmed diagnosis of leptotrichosis by clinical and laboratory studies, the use of other remedies for treatment as they deemed necessary (selftreatment) and the presence of chronic somatic diseases at the stage of exacerbation or decompensation.

The duration of the disease ranged from 2 to 3 months to a year. Patients sought treatment from a dentist but received it inconsistently because they did not experience the desired effect from the performed treatment. Consequently, the examination and treatment plan include recommendations for patients to visit appropriate internists [12].

Objective examination was carried out according to the recommendations of the World Health Organization (WHO), taking into account the complete dental status and specifying the condition of the oral mucosa and its features: appearance, color, relief, presence of affected elements, their localization, characteristics and degree of pain. Special attention was paid to the areas of affection: cheeks, tongue, lips, etc. The presence/absence of plaque was assessed, including its quantity, color and appearance.

Results of the study and their discussion. During the study, it was found that patients mostly complained of a burning sensation in various areas of the oral mucosa, sometimes loss of taste sensations, the presence of coating on the tongue, sometimes with pigmentation in various shades of gray (51 %).

Table 1

The impact of the oral cavity state on the quality of life

No.	Sections	Situation	Score
1.	Functional Limitations	Impaired pronunciation	3 %
		Deteriorated sense of taste	5 %
2.	Physical Pain	Burning pain in the mouth	10 %
		Discomfort during eating	20 %
3.	Psychological Discomfort	Feelings of shyness	-
		Feeling tense	26 %
4.	Physical Disturbances	Dissatisfaction with diet	4 %
		Forced interruptions during meals	2 %
6.	Psychological Disturbances	Difficulty relaxing	22 %
		Feeling somewhat embarrassed	-
7.	Social Disturbances	Irritation from people or situations	3 %
		Difficulties in performing regular activities	-
8.	Physical Defects	Life is generally less satisfying	7 %
		Overall impossible function	-
	Total		100 %

Noteworthy, the patients are concerned about the unusual appearance of the tongue, which they immediately associate with oncological diseases. To confirm or refute such assumptions, they search for

information on the internet. Only microscopic and bacteriological examinations can confirm or refute a probable diagnosis and reassure the patient regarding oncology. This prompted us to carry out a survey on "The Impact of the Oral Cavity State on Quality of Life".

The conducted survey on the "Impact of the Oral Cavity State on the Quality of Life" showed that 26 % of patients experienced psychological discomfort, feeling tension due to the illness; 22 % reported psychological disturbances, finding it difficult to relax; 20 % experienced physical disturbances, facing discomfort during eating; and 10 % felt a burning pain in the mouth. Functional limitations in pronunciation were observed in 3 %, and a deterioration in the sense of taste was reported by 5 % of patients. Social disturbances (annoyance from people or situations) were noted by 3 %, and 7 % of patients mentioned physical defects that made life less satisfying and forced them to interrupt meals -2 % (Table 1).

Our study revealed that in lephtotrichosis, the coating covers individual areas of the oral mucosa. It adheres tightly to the surrounding tissues and is difficult to remove, exposing a swollen, bleeding surface. No inflammatory phenomena are observed. The oral mucosa appears normal. There is no fever (Figs. 1 and 2).



Fig.1. The 43-year-old male patient M. The diagnosis: Leptotrichosis glossitis.



Fig 2. The 45-year-old male patient D. The diagnosis: Leptotrichosis glossitis.

Leptotrichia are found not on the surface of the coating but in the keratinized squamous epithelium. The appearance of the affected surface is unusual – dense, spiky, sharp-ended growths, gray or yellowish-gray in color.

Women are more often affected than men, with a ratio of 65 % to 35 %, respectively. The course of the disease is chronic, characterized by a prolonged, asymptomatic course; sometimes, patients complain of a foreign body sensation at the base of the tongue or in the throat. It is classified by severity as mild, moderate or severe, with the hyperplastic form being more common. Culturing is considered a pathognomonic diagnostic method.

Microscopic examination indicates the presence of rods with one or two pointed ends. They are short and may be arranged in pairs. Young cells are typically gram-positive. In mature cells, long intertwining threads are formed, along which granules are arranged. Leptotrichia grow well on Brucella agar, forming convex, smooth colonies with serrated edges. Not every laboratory can achieve their growth in nutrient media. The characteristics of Leptotrichia are revealed through laboratory study. They thrive in anaerobic conditions with a carbon dioxide content of 5-10 %, on Brucella agar or agar with a suspension of heart and blood muscle. The optimum growth is achieved at a temperature of 37°C. Our choice of alkaline solutions for treating lephtotrichosis is motivated by the fact that lephtotrichia belong to the lactic acid bacteria family and act as initiators of homofermentative lactic acid fermentation.

Based on the findings of our clinical studies, we have come to the conclusion that despite the oftenasymptomatic course of leptotrichosis, it is not a physiological but a pathological process. If the process were physiological, there would be keratinization of the oral mucosa and thread-like papillae. In a long-

Table 2

term process, pronounced hyperkeratosis is observed. Moreover, a physiological process should occur throughout a person's life, rather than only under certain conditions, as in patients with leptotrichosis. According to our data, foci of lesions can sometimes induce an inflammatory reaction in the affected tissue. The success of the therapy we performed supports the conclusion that treating a physiological process would have been futile.

In our practice, 75 % (85 patients) of stomatitis cases were found to be caused by Leptotrichia, in relation to the total number of fungal infections in the oral cavity. When localized at the base of the tongue, there is a sensation of a foreign body's presence. All patients had somatic pathology (Table 2).

Distribution of comorbid somatic pathology in patients involved in study

Diseases of internal organs	Number of patients with identified somatic pathology (n=114)	
and organ systems	n	%
Gastrointestinal tract	37	32.5
Cardiovascular system	28	24.5
Ear, nose, throat diseases	12	10.5
Respiratory system	13	11.4
Endocrine system	15	13.2
Nervous disorders	6	5.3
Urogenital system	3	2.6
Total	114	100

In the analysis of our clinical observations, we identified factors influencing the pathogenesis of this pathology. It turned out that such factors include a history of prolonged gastrointestinal tract diseases (67%), especially hypo- and antacid gastritis, leading to a disturbance in the oral microbial flora and the enhanced development of specific microorganisms, including Leptotrix buccalis. Additionally, vitamin deficiencies in B and C vitamins cause disruptions in the oral microbial flora, promoting the penetration of microorganisms into the mucous membrane (27%). Chronic inflammatory processes contribute to superinfection, and the inflammatory substrate and shedding cells provide a nourishing environment for the proliferation of various microorganisms, including Leptotrix.

According to our data, leptotrichosis occurred in patients who indiscriminately treated themselves with antibiotics in 43.8 % of cases (30 out of 114 patients). In 20 patients, the disease developed along with corticosteroid use (dexamethasone, prednisolone). The emergence of the disease is also observed in patients with disorders of the autonomic nervous system (6 %). In 2 % of cases, self-healing was identified after eliminating the underlying cause of the disease.

Patients in the study group (n=69) who underwent treatment with the proposed methods reported improvement within 1.5–2 months, and recovery was observed in the majority of cases after 3 months of treatment (98 %).

In the observation group of patients (n=45), which received treatment with Afta Clear after counselling with internists and professional and individual oral hygiene, improvement was observed within 2–3 weeks, and recovery occurred in the majority of cases (92 %) after one month of treatment. In 8 % of patients, recovery was observed after 1.5 months.

The findings of the study have found that the disease has various clinical manifestations. In the first case, it has an asymptomatic course (14 %). In the second case, it presents clinical symptoms: the patient/physician notices an unusual appearance of the tongue [8, 11, 12]. And, according to our data, in the third case, it is combined with candidal lesions of the oral mucosa (29 %) or red flat lichen (6 %).

Based on the findings of our clinical studies, we have come to the conclusion that despite the frequent asymptomatic course of lephtotrichosis, it is not a physiological but a pathological process. If the process were physiological, there would be keratinization of the oral mucosa and filamentous papillae. In a prolonged process, there is marked hyperkeratosis. Moreover, a physiological process should be observed in individuals throughout their entire life, rather than occurring only under certain conditions, as in patients with lephtotrichosis. According to our data, foci of lesions can sometimes induce an inflammatory reaction in the affected tissue. The success of the therapy confirms that treating a physiological process would have been futile.

The treatment methods proposed by us differ from commonly accepted approaches and have a positive effect in the treatment of both lephtotrichosis and its combination with candidiasis.

The data presented indicate that the differential diagnosis of candidal lesions of the oral mucosa and leptotrichosis does not pose difficulties as long as they do not coexist. The main differential features include a completely different appearance of pathological formations or coating, which are easily removable in candidiasis and challenging in leptotrichosis. In candidiasis, phenomena of reactive inflammation of the mucous membrane always occur, whereas in leptotrichosis, inflammation is mostly absent. In cases of leptotrichosis with a prolonged course, complaints of burning sensations may arise, similar to those in candidiasis, as well as the presence of a foreign body on the tongue, with almost always no disturbances in the general condition. Thus, stomatitis caused by Leptotrichia belongs to chronic stomatitis, with a prolonged and challenging treatment period, involving changes in treatment regimens. The criteria for recovery are clinical and laboratory indices. The use of the Afta Clear medication accelerates the healing process by one and a half to two times.

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The study has revealed that patients diagnosed with leptotrichosis experience significant changes in their psychological state, social and physiological disturbances, and certain functional limitations that need to be addressed through medical interventions and counselling with internists.

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