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MODERN ASPECTS OF CHRONIC SUPPURATIVE OTITIS MEDIA

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Abstract: Chronic suppurative otitis media (CSOM) is a significant global health problem, especially in countries with low and middle income, where the incidence of the disease is considerably higher. The review highlights the epidemiology, microbiological spectrum, and current therapeutic approaches to CSOM. The main pathogens include *Pseudomonas aeruginosa* and *Staphylococcus aureus*, including methicillin-resistant strains (MRSA), which complicate treatment due to biofilm formation and antibiotic resistance. Immunological factors, including cytokine imbalances, contribute to the chronicity and severity of the disease. A comprehensive approach that includes microbiological diagnostics, assessment of immune status, and individualized therapy can improve treatment outcomes and reduce the need for surgical interventions.

Аннотация. Хронический гнойный средний отит (ХГСО) представляет собой серьезную проблему здравоохранения, особенно в странах с низким и средним уровнем дохода, где уровень заболеваемости значительно выше. В обзоре рассмотрены эпидемиология, микробиологический спектр и современные терапевтические подходы к ХГСО. Основными возбудителями заболевания являются *Pseudomonas aeruginosa* и *Staphylococcus aureus*, включая метициллин-резистентные штаммы (MRSA), что значительно осложняет лечение из-за формирования биопленок и антибиотикорезистентности. Иммунологические факторы, включая дисбаланс цитокинов, способствуют хроническому и тяжелому течению заболевания. Комплексный подход, включающий микробиологическую диагностику, оценку иммунного статуса и индивидуализированную терапию, может повысить эффективность лечения и снизить необходимость хирургических вмешательств.

Annotatsiya. Surunkali yiringli o‘rta otit (SYOO) butun dunyo bo‘ylab, ayniqsa, daromadi past va o‘rta darajadagi mamlakatlarda keng tarqalgan va sog‘liqni saqlashda dolzarb muammolardan biri hisoblanadi. Ushbu maqolada SYOOning epidemiologiyasi, mikrobiologik spektri va zamonaviy davolash yondashuvlari tahlil qilindi. Asosiy kasallik qo‘zg‘atuvchilari sifatida Pseudomonas aeruginosa va Staphylococcus aureus, shu jumladan metitsillinrezistent shtammlar (MRSA) aniqlangan bo‘lib, ular biofilm hosil qilishi va antibiotiklarga qarshiligi sababli davolashni qiyinlashtiradi. Kasallikning surunkali va og‘ir kechishida immunologik omillar, jumladan sitokinlar muvozanatining buzilishi muhim rol o‘ynaydi. Mikrobiologik diagnostika, immun holatini baholash va individual davolash yondashuvi asosida kompleks yondashuv qo‘llash SYOO terapiyasini samarali amalga oshirish va jarrohlik aralashuvlariga ehtiyojni kamaytirishga imkon beradi.

Introduction. Chronic suppurative otitis media (CSOM) is one of the most significant problems of modern otorhinolaryngology, covering up to 25% of all cases of otiatric pathology [2].

This disease is accompanied by long-term recurrent forms, limits the daily activity of patients and significantly reduces their quality of life, especially in the presence of concomitant pathologies such as diabetes mellitus, immunodeficiency and endocrine disorders [11].

Epidemiological data indicate that CSOM occurs in 2-3% of the population in countries with a developed health system and up to 6% in regions with limited access to medical services [11,12]. According to the World Health Organization (WHO), the number of people with Chronic

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suppurative otitis media reaches 330 million, of which more than 60% suffer from serious complications, including permanent hearing loss (WHO, 2023).

Analysis of literature. The incidence of CSOM is particularly high in countries with hot climates and high humidity, where favorable conditions are created for the growth of pathogenic microflora, including Pseudomonas aeruginosa and Staphylococcus aureus (Sapova and Ryazantsev, 2017). [10].

A systematic review of 29 population-based studies performed by Monasta et al. (2012) showed that the average global prevalence of CSOM is 3.8%, which corresponds to approximately 297 million people. The authors emphasize that 85% of cases occur in low- and middle-income countries, where limited access to medical care and low sanitation contribute to higher morbidity [33].

In another study, Smith et al. (2020) note that in countries with hot climates and high humidity, the risk of CSOM increases 1.5–2 times compared to regions with a temperate climate. This is due to favorable conditions for the growth of pathogenic microflora, including Pseudomonas aeruginosa and Staphylococcus aureus [42].

Epidemiological data in high-income countries are interesting. According to Morris et al. (2012), in the UK, the prevalence of CSOM is 0.9% among children and 0.5% among adults, which is associated with a higher level of medical care and disease prevention [34]. In a similar study, Bluestone et al. (2002) in the USA it is indicated that the incidence of CSOM in children is about 0.7%, which is significantly lower than in developing countries [17].

The situation of CSOM epidemiology in developing countries is different. In India, according to Verma et al. (2018), the prevalence of CSOM among schoolchildren in urban areas is 2.32%, while in rural areas it is 5.11%. The authors attribute this to the low level of sanitation, high levels of air pollution, and the frequent use of kerosene lamps [44].

In Chad, the hospital prevalence of CSOM was 6.1%. According to Aboubakar et al. (2023), the main symptoms were otorrhea and hearing loss, and the main pathogens were Staphylococcus aureus and Pseudomonas aeruginosa [13].

Data on the incidence among children indicate that in Russia, according to Kiselyov and Surikova (2021), HCG is diagnosed in about 1% of schoolchildren, and among adolescents aged 14-15, 3-4% [3]. The authors emphasize the importance of early diagnosis and health education.

In low–income countries such as Nepal, Dolma et al. (2019) report the prevalence of HCV among children at the level of 5.4-6.0%, which is associated with limited access to medical care and low sanitation [20].

Thus, CSOM is a global health problem, especially in low- and middle-income countries. In conditions of hot climate and high humidity, the risk of disease is much higher. These data emphasize the importance of preventive measures, early diagnosis, and the development of comprehensive treatment programs that take into account regional specificities.

The microbiological study of CSOM pathogens is of key importance for understanding the pathogenesis of the disease and optimizing treatment. It was previously shown that the main pathogens are Staphylococcus aureus and Pseudomonas aeruginosa [8,36].

This is confirmed by numerous studies. For example, in a study conducted in India, P. aeruginosa was isolated in 24.8% of cases, and S. aureus in 22.2% [37]. In Angola, Proteus spp. (14.7%), P. aeruginosa (13.2%), and Enterococcus spp. (8.8%) were the most widespread [35]. A study in Indonesia in children revealed a wide range of aerobic and anaerobic bacteria, including P. aeruginosa, S. aureus, Bacteroides spp. and Peptostreptococcus spp., which highlights the polymicrobial nature of the infection [41].

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In the work of Park et al. (2008) noted that Staphylococcus aureus and Pseudomonas aeruginosa are the most common pathogens of CSOM, with Pseudomonas aeruginosa accounting for 26.5% of all isolates.

According to a study by Nagumanov and Kiselev (2013), Pseudomonas aeruginosa is the leading pathogen in severe cases associated with destructive processes in the middle ear.

A study conducted in the USA showed that P. aeruginosa is able to penetrate and survive inside macrophages using the OprF protein. This intracellular survival contributes to chronic inflammation and the persistence of infection in CSOM [31].

P. aeruginosa is known for its ability to form biofilms that promote antibiotic resistance and the chronic course of infections, including CSOM. Biofilms impede the penetration of antibiotics and protect bacteria from the body's immune response [21,22].

A study by Lee et al. (2010) demonstrated that bacterial biofilms formed by Pseudomonas aeruginosa reduce the effectiveness of neutrophils and antibacterial drugs, increasing chronic inflammation.

In addition, this pathogen produces exotoxins and enzymes that damage tissues and worsen the course of the disease [28].

In a study conducted in South Korea, P. aeruginosa was isolated in 24.4% of patients with CSOM. Of the 398 strains, 53.7% showed resistance to one or more antibiotics, and resistance to aminoglycosides and quinolones increased significantly over time [26].

In various regions of the world, S. aureus is one of the main pathogens of CSOM. In a study conducted in Egypt, S. aureus was isolated in 28.1% of cases, making it the most frequently detected pathogen among patients with CSOM [13]. In Pakistan, S. aureus was detected in 29.17% of cases among 500 patients with CSOM, which confirms its importance in the etiology of the disease [14].

S. aureus has the ability to penetrate the epithelial cells of the human middle ear, which contributes to its persistence and chronic inflammation. The study showed that S. aureus uses a cholesterol-dependent pathway to invade cells, which may explain its resistance to treatment and the recurrent nature of CSOM [32].

Many authors emphasize the polymicrobial nature of CSOM infection, including both aerobic and anaerobic bacteria. Anaerobes Bacteroides spp. and Peptostreptococcus spp. have been isolated in Indonesia, which requires an integrated treatment approach [41].

In addition to bacterial pathogens, fungi of the genus Candida and Aspergillus play a significant role in the pathogenesis of CSOM. Nagumanov and Kiselyov (2013) found that 15% of patients with CSOM have fungal infections, which are often combined with bacterial microflora. Such mixed infections significantly aggravate the course of the disease.

In a study conducted in South Africa, Candida spp. and Aspergillus spp. They were isolated in 20.8% of cases among patients with CSOM, which makes them the most common pathogens in this population [43,45]. In another study conducted in India, out of 130 patients with CSOM, fungal pathogens were isolated in 57.7% of cases, with Aspergillus spp. They accounted for 68% of isolates, and Candida albicans — 24% [24].

A study conducted in India showed that Aspergillus fumigatus accounted for 75% of fungal isolates in CSOM, while Candida spp. accounted for 25% [23]. Another study in India found that Aspergillus spp. They were the most frequently isolated fungi in CSOM, with A. fumigatus and A. niger predominating [24].

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Aspergillus fumigatus and Candida albicans have been shown to stimulate a pro-inflammatory response in respiratory tract epithelial cells by increasing the production of cytokines such as IL-6 and IL-8. This may contribute to chronic inflammation in CSOM [16].

Determining the sensitivity of isolated microorganisms to antibiotics is an important step in CSOM therapy. The lack of data on local antibiotic sensitivity increases the risk of recurrence and complications such as hearing loss and intracranial infections [11,29].

The results of a study conducted in the Gomel region show that the main effective drugs remain cephalosporins of the II–III generations and fluoroquinolones of the II generation, while resistance to aminoglycosides increases [5].

A study in Indonesia showed that P. aeruginosa was isolated in 66.7% of patients with CSOM. High sensitivity to meropenem, amikacin and piperacillin-tazobactam (93.33%) was demonstrated. It was also found that acetic acid effectively inhibits and destroys biofilms of P. aeruginosa at concentrations of 0.16% and 0.31%, respectively [38].

In India, P. aeruginosa was isolated in 32.1% of patients with CSOM. The isolators demonstrated high sensitivity to piperacillin-tazobactam (75.4%), amikacin (74.3%) and imipenem (70.6%). However, 15.5% of the strains turned out to be multi-resistant, resistant to five classes of antibiotics [28].

Other studies show that S. aureus exhibits high sensitivity to rifampin (100%), fusidic acid (93.3%) and cefoxitin (93.3%), but decreases sensitivity to ciprofloxacin (66.7%) and gentamicin (80%) (Kumar et al., 2021). In India, S. aureus was found to be resistant to penicillin (70%), cephalosporins (65%), and macrolides (50%), while linezolid proved effective against all tested S. aureus isolates [39].

The microbiological study of CSOM pathogens allows not only to clarify the spectrum of pathogens, but also to identify their antibiotic sensitivity, which is extremely important for choosing effective therapy. The treatment of patients with bacterial and fungal infections requires an integrated approach, including the use of both antimicrobial and antifungal drugs.

One of the key problems in the treatment of Chronic suppurative otitis media (CSOM) is infection caused by methicillin-resistant Staphylococcus aureus (MRSA), a bacterium resistant to beta-lactam antibiotics. Studies show that MRSA is more common in regions with excessive antibiotic use [12,18].

The main pathogens of CSOM, Pseudomonas aeruginosa and Staphylococcus aureus, including MRSA, exhibit pronounced resistance to standard antibiotics, which significantly complicates traditional therapy [12, 18]. In addition, biofilms formed by these pathogens reduce the effectiveness of antibiotics and suppress the body's immune response, which requires the use of special therapeutic approaches [29].

Studies indicate the frequent identification of MRSA in patients with CSOM. For example, Lee et al. (2023) note that MRSA was detected in 23.1% of all microbiological analyses performed in patients in South Korea [27]. These strains retain 100% sensitivity to vancomycin, linezolid, and teicoplanin, as well as over 96% sensitivity to rifampin and sulfamethoxazole/trimethoprim. In a study by Park et al. (2008) there was a significant increase in the proportion of MRSA among all isolates over a ten-year period: from 0.7% in 1998 to 11.4% in 2006 [36]. At the same time, trimethoprim/sulfamethoxazole and rifampicin demonstrated high efficacy against MRSA.

MRSA-associated CSOM is characterized by a more severe course and an increased risk of complications. Treatment of such patients requires longer-term use of drugs such as vancomycin

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or linezolid, which, however, requires careful monitoring to prevent side effects and further develop resistance [27].

The increasing number of MRSA cases highlights the importance of microbiological monitoring and an individualized approach to treatment, including the use of antibiotics effective against resistant strains. Modern methods of microbiological diagnostics, such as molecular genetic analysis, make it possible to identify resistant strains in the early stages of the disease, which ensures more accurate and effective treatment.

Immunological mechanisms play a key role in the pathogenesis of Chronic suppurative otitis media (CSOM), having a significant impact on the course of the disease and its resistance to therapy.

The development of CSOM is associated with disorders of both local and systemic immune defenses of the body. Local immunity is provided by the mucociliary system, the production of lysozyme, interferons and other factors that prevent the penetration of pathogens and the development of inflammatory processes in the middle ear (G.F. Likhachev, 2018). However, in CSOM, these functions are often impaired due to bacterial or fungal infections, topical application of antibiotics, or tissue sensitization [4].

Studies conducted by N.A. Anikina (2020) have shown that patients with CSOM have a decrease in the level of secretory IgA and neutrophil activity in the middle ear discharge. These changes contribute to the intensification of the inflammatory process and the chronization of the disease.

V.A. Lavrov's clinical observations (2019) emphasize the importance of autoimmune processes in the progression of CSOM [6]. Autoantibodies to the tissues of the middle ear were detected in patients with a long-term course of the disease, which indicates the activation of a specific immune response, which apparently can aggravate the course of the pathology.

In a study by Dewi et al. (2023), it was found that the levels of tumor necrosis factor-alpha (TNF-α) in blood serum and ear secretions are significantly increased in patients with the active phase of CSOM, especially in infections caused by Gram-positive bacteria. This indicates the important role of TNF-α in the development of the inflammatory process in CSOM [19].

A study conducted in Turkey showed that the levels of interleukins IL-1a, IL-6 and IL-8 in the blood serum of patients with CSOM were significantly higher compared with the control group. This indicates a systemic inflammatory reaction in CSOM [15].

According to Smith et al. (2020), patients with CSOM have elevated levels of pro-inflammatory cytokines, such as IL-6 and TNF-α, in the middle ear discharge [42]. These cytokines play a key role in maintaining chronic inflammation by preventing mucosal repair.

Thus, immunological aspects play a central role in the pathogenesis of CSOM. Violations of local and systemic immunity contribute to the chronization of the inflammatory process, the development of complications and a decrease in the effectiveness of therapy. These data highlight the need for further study of immune mechanisms in order to develop new approaches to the diagnosis and treatment of CSOM.

The study of the microbiological features of chronic purulent otitis media, including the role of methicillin-resistant Staphylococcus aureus, is an important step for the development of effective treatment methods.

Equally important is the study of pro-inflammatory IL-17 and anti-inflammatory IL-4. These cytokines play a key role in maintaining chronic inflammation and the formation of resistant biofilms, which significantly complicates treatment.

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Recent studies indicate an imbalance between Th17 cells and regulatory T cells (Treg) in CSOM. Elevated levels of IL-6 and IL-23 promote Th17 cell differentiation and inhibit Treg function, which increases the inflammatory process [31].

Subsequent studies have shown that the level of interleukin-10 (IL-10), which has anti-inflammatory properties, is reduced in patients with CSOM [31].

Studies show that CSOM causes increased levels of pro-inflammatory cytokines such as TNF-α, IL-1a, IL-6, IL-8, IL-17, and IL-23, as well as decreased levels of the anti-inflammatory cytokine IL-10. This imbalance contributes to chronic inflammation and damage to the tissues of the middle ear.

Topical application of antibiotics is the mainstay of CSOM treatment. Fluoroquinolones such as ciprofloxacin and ofloxacin are effective against major pathogens including Pseudomonas aeruginosa and Staphylococcus aureus. The use of 4-5 drops of ciprofloxacin or ofloxacin solution twice a day for 10-14 days is recommended for eardrum perforation [1,30].

Systemic antibiotic therapy is indicated in case of ineffectiveness of local treatment or the presence of complications. Medications such as amoxicillin (250-500 mg every 8 hours) or third-generation cephalosporins can be used within 10 days. The choice of an antibiotic should be based on the results of seeding and the sensitivity of the pathogen [30].

In cases of fungal etiology of CSOM, especially when Candida spp. and Aspergillus spp. are detected, the use of antifungal drugs such as clotrimazole or fluconazole is recommended. Antifungal therapy should be based on mycological examination and sensitivity of the pathogen [43].

Surgical treatment of Chronic suppurative otitis media (CSOM) is recommended in the following cases:

1. if conservative therapy (local antibiotics and systemic drugs) is ineffective for 3-6 weeks;
2. if there is a persistent perforation of the eardrum, especially if it leads to hearing loss.;
3. with the development of complications such as cholesteatoma, mastoiditis or intracranial complications;
4. with marked hearing loss, which significantly affects the patient's quality of life [46];
5. with recurrent infections accompanied by persistent discharge and chronic inflammation [40].

The following operations are most often performed:

1. Tympanoplasty — to restore the integrity of the eardrum and improve hearing.
2. Mastoidectomy — involving the mastoid process, especially in cases of cholesteatoma.
3. Radical mastoidectomy — with extensive destruction of the middle ear or the presence of intracranial complications.

Conclusion. Given the importance of microbiological and immunological factors in the pathogenesis of CSOM, an urgent task is to introduce modern diagnostic methods, such as molecular genetic analysis, to identify antibiotic-resistant strains. Along with this, it is necessary to develop individualized treatment regimens aimed at effective eradication of pathogenic flora and restoration of the immune response.

An integrated approach, including microbiological diagnostics, assessment of immune status and the use of personalized treatment methods, makes it possible to increase the effectiveness of conservative therapy. This approach helps to reduce the frequency of relapses, improve the quality of life of patients and may prevent the need for surgical intervention.

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