

THE ROLE OF MYCOPLASMA PNEUMONIA AS ETIOLOGICAL AGENT IN DISEASE OF RESPIRATION TRACTS

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Abstract

In this paper is given the data of the last 10 years about etiological role of Mycoplasma pneumonia and frequency of occurrence in upper respiratory tract diseases clinics, immunity and also up to – date methods of diagnostics and analysis of literature about measures by treatment of M.pneumonia makes up 25% atypical pneumonia 10-16% from total number of acute respiratory diseases.

Keywords: Mycoplasma pneumonia, Atypical pneumonia.

Introduction

Respiratory diseases of both bacterial and viral nature are attracting more and more attention of specialists due to their high prevalence in children, high frequency of relapse and transition to chronic pneumonia [16,26,27,28]. The epidemiological situation is characterized by the treatment of the etiological

significance of the causative causes of atypic pneumonias, including those caused by *Mycoplasma pneumoniae*, which account for 8 to 25% of all cases[27,31].

Today, pneumonia caused by various pathogens, including viruses, rickettsia, mycoplasma, chlamydia, legionella, is called atypical. Mycoplasma infection was found in 18% of sick children with community-acquired pneumonia who were examined for Mycoplasma pneumonia [17].

In the United States, 40% of bronchitis in children is mycoplasma. At present, most authors who study the role of mycoplasmas in ENT pathology believe that they play a leading role in the etiology of a number of acute and chronic diseases. The constant change in the microbial landscape, the increase in the frequency of isolation in pneumonia, along with other bacteria, mycoplasmas, dynamic changes in reactivity and immune response in children dictate the need to study the microbial etiological aspects of the pathogenesis of community-acquired pneumonia in order to optimize the diagnosis, prevention and treatment of this disease [1,2,5]. Therefore, the study of respiratory diseases with mycoplasma is considered relevant.

If you pay attention to the morphology of mycoplasmas, they are opportunistic pathogens characterized by small size, small genome, lack of cell wall and similarity of the cell membrane structure with the membranes of the cells of the host body, which makes them more protected from the effects of humoral and cellular defense factors. Mycoplasmas parasitize on the membrane of eukaryotes, which is how they differ from chlamydia. More than 100 species of mycoplasmas are known. Humans are the natural host of at least 14 species of mycoplasmas. The most important in human pathology are *M. hominis*, *M. genitalium*, *M. fermentans*, *M. pneumoniae*.

M. pneumoniae is the causative agent of respiratory mycoplasmosis. The latter accounts for 10-16% of the total number of acute respiratory diseases. The disease is recorded throughout the year with a slight increase in frequency in the spring and autumn-winter periods. The source of infection is patients in the acute period of the disease or carriers who have had an acute or asymptomatic infection. Mode of transmission: airborne droplets; incubation period is 3-11 days (sometimes up to 3 weeks). Infant It can become infected from an infected mother during childbirth, passing through the "infected" birth canal. The course of mycoplasma infection in babies differs from adults in that the bronchopulmonary tree is usually affected, inflammation of the pharynx, nose, bronchi and lungs is caused. The

intensity of the process depends on the state of the child's immune system - "weak" children infected with mycoplasma get sick more often and the treatment is more difficult.

Children can become infected with mycoplasma in kindergarten, school or any "close" group. Mycoplasma in this case is transmitted through the air.

Previously, it was believed that in children under 5 years of age, MP causes infections rarely and only in the form of mild acute respiratory disease (ARI). Recent studies have shown that MP is a common cause of hospitalization in children younger than 5 years of age, and the incidence is highest between the ages of 1–4 years.

In recent years, special attention has been paid to the genesis of the chronic inflammatory process in atopic bronchial asthma and mycoplasma infections. It is assumed that, along with persistent viral infection, they contribute to the formation of persistent bronchial reactivity and the progression of immune deficiency, determining the tendency of children with bronchial asthma to frequent respiratory infections, torpid asthma and a decrease in the effectiveness of standard anti-inflammatory regimens Therapy. Mycoplasma infection has practically no clinical and morphological signs of its own, which complicates the diagnosis of the pathogen in the early stages of the disease, which is asymptomatic, which means that bacteria persist in the macroorganism for a long time and can provoke pathological reactions. Examination of adult patients with bronchial asthma (AD) showed a high infection rate of patients with *Mycoplasma pneumonia* [25,28,35].

According to some authors, infection caused by *Mycoplasma pneumoniae* (MP) is quite often detected during the development of severe exacerbations of bronchial asthma[22]. At the same time, in each region there is an established trend in the occurrence of bronchial syndrome (BFD) and the formation of bronchial asthma (BA) among children, associated with the climatic features of the region, the environmental situation, and the presence of industrial enterprises[10].

The causative agents of respiratory mycoplasmosis can be in the form of mono- or in association with other infectious agents. Recently published works [10,22,23,25,28,35] provide data on the detection of *M.hominis* in children with AD and obstructive bronchitis, and mixed infection was quite often recorded.

In patients with confirmed mycoplasmosis, the disease proceeded as a monoinfection, while 4 out of 5 were diagnosed with acute respiratory infections. In the majority (73.4%) mycoplasmosis was combined with other opportunistic infections, most often with WEB, then in equal proportion with pneumocytosis and HHV-6, in isolated cases the associates were CMV and chlamydia. In these cases, along with mycoplasma, there was evidence of an active course and opportunistic infections.

In the work of M.K. Khadisov (2012), regardless of the established diagnosis (acute respiratory infection, OSLT), patients with monomycoplasma infection often had the following characteristics: age group over 3 years, among the factors of the disturbed premorbid status were indications of the frequency of previous acute respiratory infections (100%), allergic manifestations (50%), and in the concomitant pathology at admission – the presence of otitis, adinoiditis, maxillary sinusitis and their combinations[29].

Clinical features of mycoplasma pneumonia in young children are: acute onset (81.7%), high fever (63.3%), the presence of a prolonged dry cough (76.6%), a severe course with bronchodestructive syndrome (40%) against the background of a burdened premorbid background, bilateral nature of lung damage (66.7%). Blood tests show moderate leukocytosis (85%), lymphocytosis (90%), accelerated ESR (85%), and failure of treatment with penicillins and cephalosporins antibiotics with typical bacterial pneumonia [4,7,25].

It has been shown that mycoplasma infection is accompanied by the dominance of the production of cytokines of the Th2 immune response, as well as a high level of both total IgE and IgE antibodies specific to mycoplasma antigens. It is known that the immune response includes equidirectional types of effector mechanisms, each of which is optimal for certain pathogens. At the same time, T-helper subpopulations play a key role in regulating the functions of immunocytes through the production of cytokines with oppositional (pro- and anti-inflammatory) effects. Oppositional pools of cytokines - IFN γ and IL-4, IL-10- are considered as markers of Th1- and Th2-lymphocytes, of which IFN γ enhances the cell-mediated immune response, and IL-4 and IL-10 - humoral. A certain amount for an adequate immune response and protection in lung pathology. Disruption of the production, secretion and reception of anti-inflammatory cytokines leads to profound defects in anti-infective protection, up to the development of "immunological paralysis", and exacerbates the direct damaging

effect of microorganisms and their toxins on lung tissue[20]. However, to date, there are only fragmentary studies of the pathogenetic role and therapeutic efficacy of the cytokine system in pneumonia [26]. There was a more pronounced increase in the number of leukocytes, a decrease in the relative and absolute number of total and T-lymphocytes, the content of immunoregulatory subpopulations of CD-4+ and CD-8+ cells was 76 and 74.5%. At the same time, there was an increase in the relative and absolute number of B-lymphocytes (CD20+cells). The phagocytic activity of neutrophils, an indicator of natural protective factors, was reduced by half[14].

The study conducted by F.M. Shamsiev (2010) indicates that in mycoplasma pneumonia, hyperproduction of pro- and anti-inflammatory cytokines is formed with a pronounced imbalance with the addition of herpesvirus infection. Analysis of the dynamics of serum NO in the examined children showed that the concentrations of NO metabolites in the blood were 2.8 times ($p<0.01$) higher in the control group, and in children with MP against the background of GVI these parameters were 3.3 times higher ($p<0.001$). Such a significant increase in NO production in mycoplasma pneumonia associated with herpesvirus infection is evidence that NO is a powerful factor in the antipathogenic activity of immunocompetent cells involved in ensuring the body's resistance to infection. Increased concentrations of NO have a pronounced pro-inflammatory effect, increase tissue blood flow, plasma exudation, enhance the proliferation of Th2 lymphocytes and, apparently, due to these effects, involve an additional number of effector cells in the infectious and inflammatory process.

Toxins released by pathogens cause damage to the bronchial epithelium and stimulate the production of cytokines, which in turn enhance the production of NO. Obviously, the determination of endogenous production of interleukins and metabolites in blood serum will allow us to use them as criteria for assessing the effectiveness of therapy[26,27].

Some researchers consider the role of immune complexes (ICs) in the pathogenesis of infectious diseases to be controversial, and the idea that tissue damage is not a consequence of the action of toxins or other substances, but the result of the action of ICs, is not accepted unequivocally. Circulating immune complexes (CICs) are an important link in normal immunity and are aimed at neutralizing the biological activity of antigens. interaction with immunocomponent, effector and tissue cells. Biberfeld G. and Norberg R. have

shown that in 41% of cases of infection due to *Mycoplasma pneumonia*, in the first two weeks of the disease, the presence of a high level of CIC in blood serum samples is detected, and the size of these complexes was 19S and above[15].

As for the detection of *M. hominis antigens in children with AD*, their long-term persistence, especially in association with *Mycoplasma pneumoniae antigens*, can enhance the pathogenetic effect of the latter, causing inflammation of the upper respiratory tract.

The high frequency of detection of mycoplasma antigens in patients with AD (from 24.7 to 85%) is a rather alarming symptom, since long-term infection of the respiratory tract is supported by immunosuppression due to the influence of microorganisms, their antigens, and the factors produced by them on immune cells, which as a result leads to the development of immunopathological reactions, which result in various progressive destructive and proliferative processes[9]. It has been established that mycoplespasms can actively affect the immune response of a child, contributing, on the one hand, to secondary infection of the respiratory tract, and on the other hand, to an increase in bronchial hyperreactivity and the development of bronchospasm [8,22,23,25].

Diagnosis of this infection is quite difficult – there are no signs characteristic only of this disease, and the mycoplasmas themselves are so small that they cannot be detected by conventional microscopy. For the diagnosis of MI, the bacteriological method is not used in routine practice due to the need for special culture media and the duration (2-3 weeks) of pathogen growth. Such methods for detecting antibodies (AT) to *M. pneumoniae*, such as the Growth Inhibition Test (RIA), the Metabolic Inhibition Test (RIA), the Mycoplasmicidal Test, and the Complement Binding Test (CST), are also not of practical use due to the mandatory use of live cultures of mycoplasmas [34,36].

For a long time, the diagnosis of mycoplasma infection due to the difficulties of culturing mycoplasmosis was possible only under specialized and highly sensitive detection methods, such as polymerase chain reaction (PCR) [33] and enzyme-linked immunosorbent assay (ELISA) [32].

Despite the fact that at present the role of MP in the genesis of community-acquired pneumonia is not clear, it is still impossible not to take into account the fact of high infection of the body of children with this pathogen.

Thus, the algorithm for diagnosing mycoplasma pneumonia consists of the following positions:

- 1). Isolation of *Mycoplasma pneumoniae* DNA in sputum by PCR;
- 2). Detection of specific IgM in one serum or simultaneously IgM and IgG, in paired sera seroconversion or a fourfold increase in IgG titer;
- 3). The presence of relevant clinical symptoms – acute onset with pronounced intoxication accompanied by hyperthermia, hyperemia of the pharynx, ineffectiveness of therapy with antibiotics of the penicillin group; further course of pneumonia against the background of prolonged debilitating cough, moderate leukocytosis with lymphocytosis, accelerated ESR, deformation and fuzziness of the pulmonary pattern, increased vascular component and interstitial changes[19].

The following serological methods are also used to diagnose infection: a) detection of mycoplasma antigens (immunofluorescence reactions, aggregate hemagglutination and enzyme-linked immunosorbent assay); b) removal of antibodies to mycoplasmas.

By means of the aggregate hemagglutination reaction (RAHA), the content of mycoplasma antigens in the blood is determined. The material for the study is blood serum. The detection of antigen in blood serum at a dilution of 1:8 and higher is diagnostically significant. This express method is highly sensitive. Indirect complement binding reaction (NRSA) is of greater diagnostic value than RSC.

Molecular methods: Polymerase chain reaction (PCR) currently has the highest sensitivity (96-100%) and specificity. The result can be ready in 4.5-5 hours. At the same time, PCR testing makes it possible to detect the DNA of the pathogen during the first 3 weeks (1-21 days) from the onset of the disease and even after the start of therapy with antibacterial agents. If a fragment of mycoplasma DNA is detected after a course of antibiotic therapy, a culture diagnosis should be carried out to exclude false-positive results from a clinical point of view. If cultural diagnostics are not possible, then it is necessary to repeat the study by PCR in 5-6 weeks. False-negative results are possible with generalized infection and long-term persistence of the microbe, as well as due to the presence of various PCR inhibitors in the samples [18,30].

Nevertheless, at the present stage, the wide practical use of PCR diagnostics is limited by the high level of costs associated with the need for special equipment of laboratories, the purchase of expensive equipment and reagents. For this reason, in modern foreign guidelines for the management of community-acquired

pneumonia (CAP) in children, the method of PCR diagnostics for the detection of atypical infections is not included in the list of mandatory methods, in contrast to the methods of serological diagnostics aimed at detecting specific Abs in paired blood serum. It should also be borne in mind that PCR testing does not differentiate acute infection from the persistence of the mycoplasma pathogen, the prerequisites for which are laid down by the ability of mycoplasmas to attach and parasitize on the cell membrane of human cells with the help of tip organelles, becoming inaccessible to AT, complement and other protective factors when localized in intussusception of the host cell membranes, as well as the ability of *M. pneumoniae* to suppress the phagocytic activity of host cells[24, 30].

The effectiveness of treatment for this pathology largely depends on the correct and timely identification of the pathogenic agent (bacteria, viruses, fish, protozoa, etc.).

The studied data indicate that in the prevention and treatment of mycoplasma pneumonia, in addition to etiotropic, immunocorrective therapy plays a great role. Since a decrease in the ability to produce interferon in children is a sign of antenatal infection, determining the severity, many researchers suggest immunocorrection with interferon drugs [6,11,27].

The results of the study indicate the effectiveness of cycloferon in the treatment of children with mycoplasma pneumonia with reduced immunological reactivity. The drug contributes to a faster recovery of subpopulations of T-cell and humoral immunity, FAN, a decrease in NK activity, increases the effectiveness of antibiotic therapy, reduces the number of bed-days, and reduces the risk of transition to protracted and recurrent forms of pneumonia.

Mycoplasmas are most sensitive to fluoroquinolone antibiotics and macrolides, for example, to rulid (25, 26) and sumamed (4). Many authors use immunomodulators in treatment of both local action, such as diucifon, and general action - amixin and polyoxidonium with positive results[21].

The inclusion of rovamycin (13,18) in the treatment complex and non-contact point phototherapy (BTP therapy) contributed to a more intensive regression of somatic pathology, normalization of immune status disorders. Sick children had a faster clinical recovery. The undoubted advantages of BTP therapy are painlessness and comfort with high clinical efficacy, which makes it possible to recommend the widespread use of these drugs in the complex treatment of mycoplasma pneumonia in young children [3,11].

Mycoplasma pneumoniae respond to erythromycin and tetracycline, but not to penicillin or cephalosporins. Erythromycin is used for the treatment of pulmonary manifestations in children of primary and school age, and tetracycline drugs are used in older children. It should be noted that tetracyclines should be prescribed only after the change of teeth, as they can cause their staining. The question of the effectiveness of the above-described antibacterial therapy in extrapulmonary lesions with this pathogen remains open. Good results in the treatment of MP were obtained with the prescription of immunomodulators bronchomunal, polyoxidonium.

Currently, the so-called stepwise therapy has become widespread, in which treatment begins with the use of intravenous antibiotics, and after achieving a clinical effect, the patient is transferred to oral therapy with the same drug or other macrolides. Step-by-step therapy is possible only with known good absorption of the drug, and if it is carried out correctly, the effectiveness is comparable to parenteral treatment. At the same time, the frequency of side effects decreases[3]. Today, the problem of forming resistance of pneumotropic flora to antibacterial therapy is acute. In recent years, foreign works[31,34] have provided information on the resistance of MP to macrolides. Macrolides are highly effective and at the same time are considered one of the safest groups of antibacterial drugs. They do not have a toxic effect on the organs and tissues of the macroorganism, less often than other antibiotics cause allergic reactions, which is important in the treatment of children. Possessing a bacteriostatic mechanism of antimicrobial action, various macrolide drugs differ in their pharmacokinetic properties, as well as in antimicrobial activity and tolerability. When prescribing macrolides, it is necessary to take into account their effect on the enzymes of the cytochrome P-450 system in the liver. According to the degree of cytochrome P-450 inhibition, they are arranged in the following order: clarithromycin > erythromycin > roxithromycin > azithromycin > spiramycin.

The inclusion of contab in complex therapy enhances the effectiveness of basic drugs, reduces the duration of the acute period of the disease, reduces the severity of the disease, significantly improves sputum discharge, and contributes to the restoration of impaired parameters of the immune system in children with acute pneumonia associated with mycoplasma infection[12].

Inference. On the basis of the above overview, the following areas of research can be identified:

1. Children with respiratory tract diseases with *M. pneumoniae* etiology remains an urgent problem in Uzbekistan and abroad.
2. To determine the percentage of the etiological role of mycoplasmas in children with SARS, bronchial asthma, chronic bronchitis, chronic rhinosinusitis in Uzbekistan.
3. Modernization of bacteriological methods for the isolation of mycoplasmas, development of special media for the cultivation of the pathogen.
4. Monitoring of antibiotic-resistant strains of mycoplasmas and, accordingly, selection of effective groups of antibiotics.

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