



CLINICAL AND LABORATORY CHARACTERISTICS OF PNEUMOCOCCAL MENINGITIS IN ADULTS

Vahidova Adolat Mamatkulovna

Oripova Pokiza Olimovna

Jalalova Feruza Abdusalomovna

Bobokandova Mekhriniso Fazliddinovna

Shomurodovna Gulistan Togaimurodovna

Department of Microbiology, Virology and Immunology

Samarkand State Medical Institute

Samarkand, Republic of Uzbekistan

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Abstract:

The analysis of the incidence of pneumococcal meningitis was carried out in the period from 2008-2018 according to the data of a retrospective analysis of the case histories of patients who were hospitalized in the regional clinical infectious diseases hospital in the city of Samarkand. The clinical picture of the examined patients with pneumococcal meningitis was characterized by an acute onset of the disease with a pronounced intoxication syndrome. Among the examined patients with pneumococcal meningitis by the bacteriological method, *S. Pneumonia* was confirmed in 12.4% of the total. In pneumococcal meningitis, such residual effects are often detected in adults: sensorineural hearing loss (16.4%), hypertensive syndrome (38%), cerebrovascular accident (45.6%). At the present stage, the diagnosis of pneumococcal meningitis requires the use of a complex of methods, including not only microscopic, bacteriological and serological examination (latex agglutination), but also PCR detection of pathogenic microorganisms in the cerebrospinal fluid, the diagnostic value of which is more than 80%. Neuroprotective therapy (osmotic diuretics, anticonvulsants, nootropics) can improve the outcome of pneumococcal meningitis and appears to be a promising treatment option. Adults, existing risk factors for the development of pneumococcal meningitis (elderly and immunocompromised persons) are shown specific prophylaxis of pneumococcal infection (vaccination).

Keywords: Adults, vaccination, third generation cephalosporins, PCR, complications, bacteriological analysis.

INTRODUCTION.

After the introduction of vaccination against meningococcal, pneumococcal and hemophilus infections, the incidence of bacterial purulent meningitis has decreased somewhat. In the world, one of the leading places in the etiological structure of bacterial meningitis is *S. pneumoniae* and is second only to meningococci (52.2%). The highest incidence of pneumococcal meningitis (PM) is registered in the age group from 45 to 64 years. After the introduction of vaccination against pneumococcal infection in children, the incidence of pneumococcal infection increased among adults. Lethality in pneumococcal meningitis reaches 30%. In the age structure of fatalities, the main proportion falls in the age group older than 45 years, of which 29% are 45-64 years; 30% are older than 65 years. Pneumococcal meningitis is not prone to epidemic spread and, as a rule, affects people with weakened immune. defense against the background of existing pneumococcal. infection (sinusitis, otitis media, pneumonia, etc.). To verify the diagnosis in pneumococcal meningitis, clinical features of the disease are taken into account, indicating the need to use. express diagnostic methods from the first days of the disease (latex agglutination and PCR). According to the literature, latex-agglutination reaction can give false-positive and false-negative results in some cases, therefore it is justified to use this method together with high-sensitivity tests (PCR) and bacteriological methods. Such approach to the diagnosis of the disease can increase the probability of detecting the infection by 20% or more. In recent years, detection of pneumococcal infection in patients has increased from 11.5% to 55.2%, which is associated with improved diagnosis of pneumococcal infection. Analysis of pneumococcal meningitis morbidity in the adult population of Samarkand has not been carried out so far. A more detailed study of clinical and laboratory characteristics of pneumococcal meningitis in adults at the present stage is of practical

PURPOSE OF THE STUDY:

Study of clinical and laboratory characteristics of pneumococcal infection in adults in Samarkand region for the last 10 years.

MATERIALS AND METHODS OF THE STUDY:

The material for the study were the patients who applied to the regional clinical infectious hospital of Samarkand city for the last 10 years. anamnestic, clinical and laboratory.

RESULTS OF THE STUDY AND DISCUSSION:

Analysis of PM morbidity was carried out in the period from 2008-2018 according to the data of retrospective analysis of the medical records of patients who were hospitalized in the regional infectious clinical hospital of Samarkand city.

According to the data of the processed inpatient records with bacterial purulent meningitis, meningococcal meningitis was detected in 59% of patients, pneumococcal meningitis in 26% of patients, hemophilic meningitis in 6% of patients and purulent meningitis of unspecified etiology in 9% of patients.

Over 19 years old accounted for 19.6% of the total number of hospitalized patients. The analysis of age structure determined 19 - 25 years (7.8%), 25 - 30 years (26.9%), 30 - 40 years (19.7%), and older 40 years (45.6%). According to the analysis, we determined that PM occurs frequently in people of working age (69.1%). Which is consistent with the data of other researchers. During our study there were no gender differences among patients with pneumococcal meningitis (women - 44.3%, men - 55.7%). The place of residence of patients was also analyzed and the predominance of patients from Samarkand region (87.3%) was established.

In this regard, we analyzed the distribution of sickness rate by districts of Samarkand region. At the same time we found that in those districts where people are engaged in farming, cattle breeding, trade in the open space the diseases of pneumococcal aetiology are more frequent.

Analysis of seasonality, in adults showed that seasonality was not characteristic. They mostly had diseases in the form of sporadic cases. Older patients associated their disease with hypothermia (56%).

The study of the working conditions of older patients is of no small importance in the diagnosis of PM: wage workers (15.3%), unemployed (26.4%), retired (18.7%), disabled (12.2%), university students (9.6%), college students (15.2%), office staff (2.6%). Hired workers and the unemployed work outside, in unfavorable conditions. Professions associated with cold working conditions are more susceptible to morbidity with PM.

The analysis of fluctuations in the annual dynamics of morbidity revealed that the incidence of PM over the past 10 years had a wave-like character, with a downward trend since 2015. The decrease in the number of patients since 2015 seems to be associated with the introduction of vaccination in the National calendar of active immunization of the population. But there has been a steady increase among adults with a confirmed diagnosis of Pneumococcal meningitis. This shows that adult morbidity is not trending downward. Therefore, it is necessary to introduce the pneumococcal vaccine into the national vaccination calendar in adults aged 18 to 49 years and 50 years and older in order to prevent the incidence of pneumococcal meningitis. The anamnesis of 70.3% of patients revealed diseases that were the primary focus of pneumococcal infection. Thus, pneumonia was detected in 27.7% of patients, sepsis - in 3.7%, otitis media - in 11.2%, sinusitis - in 9.2% of patients. The number of patients with unfavorable life history (craniocerebral injuries, multiple respiratory diseases, previous meningitis) was 18.5%. In 66.5% of patients with pneumococcal meningitis, concomitant pathology in the form of: chronic bronchitis (22.3% of cases), pneumonia (7.8% of cases), cardiovascular pathology (2.7% of cases), nervous system diseases (5.3% of cases), allergic diseases (6.7% of cases), diabetes (4, 9% of cases), viral hepatitis (28.9% of cases), chronic tonsillitis (13.4% of cases), rheumatoid arthritis (1.2% of cases), acute suppurative otitis media (1.2% of cases), ARI (12.1% of cases), herpes infection (2.5% of cases). The severity of the disease in many cases depended on the primary focus of pneumococcal infection. It means that organization of clinical examination in primary care in order to detect patients with primary foci of pneumococcal infection and severe concomitant diseases prevents widespread forms of PM. According to severity, 85.7% of patients had the severe form, and 14.3% of patients had the moderately severe form. The mild form was not detected in the patients we examined.

Patients were hospitalized with the following diagnoses: "ARI" (47.3%), "Chronic tonsillitis" (13.1%), "Meningococcal infection" (7.8%), "UCI. Bronchopneumonia" (12.3%), "Purulent meningitis" (19.5%). The vast majority of patients (74%) were admitted on the 2nd or 3rd day after the disease on the intensive care unit where the treatment lasted on average 7.2 ± 1.76 days (duration of stay in the hospital). Terms of patients hospitalization depended on clinical form of preceding focal pneumococcal infection. More often (25.3% of cases) the severe course of the disease occurred in patients with comorbidities (2.4%), and they had high mortality rates. Subarachnoid hemorrhage on the 2nd day, 4th day, 5th day, 6th day, 8th day and 9th day of hospitalization was detected in 11.1% of hospitalized patients, which resulted in lethal outcome. In this regard, from the first days of the disease the patients were in the intensive care unit. Sensorineural hearing loss (16.4%), hypertensive syndrome (38%), and cerebral circulation disorders (45.6%) were observed in the patients as residual effects

In patients with undetected primary focus of the disease, no serious complications and consequences were registered (29.7%). Neurological complications were the main cause of death in adults, especially in young patients. The current problem of late pre-hospital diagnosis and, accordingly, late admission of patients to an infectious hospital is probably associated with a more gradual onset of the disease, which is reflected in the severity of patients on admission and requires the vigilance of practitioners.

According to the results of our studies, the clinical picture of the patients was characterized by an acute onset of the disease with a pronounced intoxication syndrome. The patients complained of weakness (98.0%), drowsiness (24.2%), dizziness (59.5%), headache and pain in the eyeballs in everyone. In 19.0% of cases there were catarrhal phenomena in the form of dry or wet cough, serous nasal discharge. In 9.5% of the patients, the occurrence of a fine-point hemorrhagic rash on the skin of the torso and extremities was registered. According to the analysis of the clinical course of the disease, the patients had meningeal syndrome in 100% of cases, general cerebral syndrome in 94% and general infectious syndrome in 96% of cases. Rapid development of meningeal syndrome was noted in 91.2% of patients. 47% of patients complained of headache, describing it as intense, raspy, without specific localization and intensifying with movement, against the background of various sound and light stimuli. At the height of the headache, 14.2% of the patients noted the appearance of sudden vomiting, not related to food intake, not bringing relief, differing in intensity in different patients. In all patients from meningeal syndromes stiffness of occipital muscles was registered, Kernig's symptom was positive in 78.8% of patients, and Brudzinski's symptom (upper, middle or lower) was determined in 58.3% of patients. In 52.6% of patients, the meningeal syndrome was regarded as moderate, with "flickering" meningeal signs, and in 46.67% of patients it was weakly pronounced (neck stiffness of the occipital muscles was doubtful, other symptoms were inconstant). In 49.5% of patients, stiffness of the occipital muscles was pronounced, in the form of a plank-like condition. In general infectious syndrome we found an increase in body temperature of varying severity, pale skin, loss of appetite, lethargy, pale skin, weakness in all patients. Fever up to 38.5 C was observed in 36.8% of patients, and up to 39.5 C - in 40.7% of patients. Temperature elevation to hyperpyretic numbers was most often registered in patients with a complicated course - 22.5% of patients.

General cerebral syndrome was manifested by regurgitation, gushing vomiting, restlessness, lethargy, convulsive syndrome. Swelling of the brain in pneumococcal meningitis develops more frequently than in other meningitides, sometimes as early as day 1-3 of the disease. In our observations in 2.3% of patients there were focal symptoms in the form of nasolabial fold smoothing, ptosis, anisocoria, gaze paresis at the initial stage of infection. Psychomotor agitation was present in 18.2% of patients, in the form of loss of consciousness, recurrent clonic convulsions. The occurrence of the above symptoms was an unfavorable prognostic sign. In 29.5% of patients there was revealed a decrease in the threshold of sensitivity to various stimuli (light), which is the result of lesion of the cells of the spinal nodes, posterior roots, receptors of cerebral membranes. Some patients with pneumococcal meningitis have deviations from the typical course. According to some researchers, sometimes patients with pneumococcal meningitis have a predominance of lymphocytes in the spinal fluid. And in our case, one patient, who was admitted with serous meningitis, after serological tests revealed pneumococcal meningitis. According to researchers, about 50% of patients with pneumococcal meningitis need intensive care in the intensive care unit. But despite this, 30-70% of them are fatal. In 85.7% of patients with pneumococcal meningitis there were signs of lesions of the nervous system, accompanied by the development of complications in the form of cerebral edema, unstable hemodynamics, impaired consciousness. All patients underwent a comprehensive clinical and laboratory examination using bacteriological diagnostic methods, and from 2012 to 2018 an immunochromatographic test for the presence of pneumococcal soluble antigen in cerebrospinal fluid (Binax NOW-Streptococcus pneumoniae Test) was performed in order to determine pneumococcal meningitis etiology. The test was performed on the first day of hospitalization in patients who had not taken antibacterial medication. For the latex agglutination reaction (LAA) (Pastorex meningitis, Bio-Rad, USA) the cerebrospinal fluid of meningitis patients was used to identify the soluble *S. pneumoniae* antigen (sensitivity 90 - 100%, specificity 100%). General blood count showed leukocytosis $11-26 \times 10^9/l$ (76.7%), elevated SLE up to 60 mm/s (57.8%). . Some patients with pneumococcal meningitis have deviations from the typical course. According to some researchers, sometimes patients with pneumococcal meningitis have a predominance of lymphocytes in the spinal fluid. And in our case, one patient, who was admitted with serous meningitis, after serological tests revealed pneumococcal meningitis. According to researchers, about 50% of patients with pneumococcal meningitis need intensive care in the intensive care unit. But despite this, 30-70% of them are fatal. In 85.7% of patients with pneumococcal meningitis there were signs of lesions of the nervous system, accompanied by the development of complications in the form of cerebral edema, unstable hemodynamics, impaired consciousness. All patients underwent a comprehensive clinical and laboratory examination using bacteriological diagnostic methods, and from 2012 to 2018 an immunochromatographic test for the presence of pneumococcal soluble antigen in cerebrospinal fluid (Binax NOW-Streptococcus pneumoniae Test) was performed in order to determine pneumococcal meningitis etiology. The test was performed on the first day of hospitalization in patients who had not taken antibacterial medication. For the latex agglutination reaction (LAA) (Pastorex meningitis, Bio-Rad, USA) the cerebrospinal fluid of meningitis patients was used to identify the soluble *S. pneumoniae* antigen (sensitivity 90 - 100%, specificity 100%). General blood count showed leukocytosis $11-26 \times 10^9/l$ (76.7%), elevated SLE up to 60 mm/s (57.8%). In our case a positive bacteriological blood culture was observed in 6.4%. According to some authors, prehospital antimicrobial therapy reduces the diagnostic accuracy of the study by 20%. This can explain the

low percentage of culture isolation.

Thus, at the present stage the diagnosis of pneumococcal meningitis requires a complex of methods, including not only microscopic, bacteriological and serological examination, but also PCR study of pathogenic microorganisms in the spinal fluid, the diagnostic value of which is over 80%.

In recent years, pneumococci resistant to benzylpenicillin have been isolated. And also, there is a tendency of increasing resistance of *S. Pneumoniae* to macrolides. In this regard, third generation cephalosporins (cefotaxime, ceftazidime, cefaperazone, ceftriaxone) are considered the drugs of choice for antimicrobial therapy in adults in the pre-hospital phase and in the hospital. According to the literature, some specialists recommend using high-dose ceftriaxone or cefotaxime for at least 10-14 days. If resistance to third generation cephalosporins is found, Vancomycin and Rifampicin are recommended. If bacteriological analysis reveals a pathogen and determines its sensitivity to antibacterial drugs, correction of antibacterial therapy is carried out. In our observations the patients successfully used a combination of two antibiotics: fluoroquinolones and III generation cephalosporins. Glucocorticosteroids and neuroprotective therapy were used as adjuvant agents. For pathogenetic and symptomatic therapy, nootropic drugs, GABA receptor agonists were used. Pathogenetic therapy (having neuroprotective, neurometabolic, neurotrophic, sedative and anticonvulsant effects) gave positive results in severe and complicated forms of pneumococcal meningitis (76.5%).

CONCLUSIONS:

1. Pneumococcal meningitis in adults often reveals residual phenomena as sensorineural hearing loss (16.4%), hypertensive syndrome (38%), and cerebral circulatory disorders (45.6%).
2. At the present stage the diagnostics of pneumococcal meningitis requires a complex of methods, including not only microscopic, bacteriological and serological examination, but also PCR-testing of pathogenic microorganisms in the spinal fluid, the diagnostic value of which is over 80%.
3. Neuroprotective therapy is effective in improving the outcome of pneumococcal meningitis and is a promising treatment (osmotic diuretics, anticonvulsants, nootropics).
4. Adults with risk factors for pneumococcal meningitis (the elderly and immunodeficient) are indicated for specific pneumococcal prophylaxis (vaccination).

LITERATURE:

1. Rabbimova N.T., Yarmukhamedova N.A., Rustamova Sh.A., Oripova P.O. (2020) "Clinical and epidemiological aspects of pneumococcal meningitis in adults" *Problems of Biology and Medicine* № 5 (122). C.178-183.
2. Yarmukhamedova N.A., Rustamova Sh.A., Karamatullaeva Z.E., Oripova P.O. "Samarkand viloyatida pneumococcal meningitis clinical and laboratory kechish xususiyatlari" *Problems of Biology and Medicine* № 1 (107). Samarkand 2019, P. 134-138.
3. Kamalova Malika, Islamov Shavkat. MORPHOLOGICAL FEATURES OF ISCHEMIC AND HEMORRHAGIC BRAIN STROKES. *JCR*. 2020; 7(19): 7906-7910. doi:10.31838/jcr.07.19.898
4. Yarmukhammedova N.A., Mustaeva G.B., Rustamova Sh.A., Oripova P.O. "Clinical and epidemiological aspects of pneumococcal meningitis in children (on the example of Samarkand region" *Problems of Biology and Medicine* No. 2 (109). Samarkand 2019, P. 166-170.
5. Martynova G.P., Kutishcheva I.A., Bogvilene Ya. A., Solovieva I.A., Kuznetsova N.F., Alyieva L.P. "Actuality of vaccination against pneumococcal infection for children in Krasnoyarsk". *Epidemiologia i Vaccinoprofilactica. [Epidemiology and Vaccinal Prevention]*. 2015; 14 (2): 60 -65.
6. Ilkhomovna, K. M., Eriyigitovich, I. S., & Kadyrovich, K. N. (2020). Morphological Features Of Microvascular Tissue Of The Brain At Hemorrhagic Stroke. *The American Journal of Medical Sciences and Pharmaceutical Research*, 2(10), 53-59. <https://doi.org/10.37547/TAJMSPR/Volume02Issue10-08>
7. S Ziyadullaev, O Elmatov, N Raximov, F Raufov //Cytogenetic and immunological alterations of recurrent bladder cancer. *European Journal of Molecular & Clinical Medicine* ISSN 2515-8260 Volume 7, Issue 2, 2020
8. National association of specialists in healthcare associated infections. The current situation of pneumococcal infections in the world and in the Russian Federation. Available on: <http://nasci.ru>(in Russian).
9. Pneumococcal Diseases in Adults after Vaccinations in Children, Japan, 2010-2013. *Emerging Infectious Diseases*. 2015; 11: 1956-1965.
10. Shomurodov. K.E. Features of cytokine balance in gingival fluid at odontogenicphlegmon of maxillofacial area. // *Doctor-aspirant* 2010.-42 Vol.-No.5.1.-P.187-192;
11. Tillyashaykhov M. N., Rakhimov N. M. Khasanov Sh. T., Features of Clinical Manifestation of the bladder cancer in young people// *Doctor Bulletin*. - Samarkand, 2019. - №2. - P. 108-113
12. Ilkhomovna, K. M., Eriyigitovich, I. S., & Kadyrovich, K. N. (2020). Morphological Features Of Microvascular Tissue Of The Brain At Hemorrhagic Stroke. *The American Journal of Medical Sciences and Pharmaceutical Research*, 2(10), 53-59. <https://doi.org/10.37547/TAJMSPR/Volume02Issue10-08>
13. Weisfelt M, van de Beek D, Spanjaard L, Reitsma JB, de Gans J. Clinical features, complications, and outcome in adults with pneumococcal meningitis: a prospective case series. *The Lancet Neurology*. 2006; 2: 104-105.