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PROGRESSION OF HIV-INFECTION COMBINED WITH TUBERCULOSIS IN CHILDREN

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Resume. *The article presents the results of observation of 57 patients with HIV infection combined with tuberculosis in children. The comparison group consisted of 23 children of HIV-infected children without tuberculosis, of the same age. Laboratory methods for studying the immune status, the level of CD4 cells; Bacterioscopy and sputum culture. Immunodiagnostics: (Mantoux test with 2TE and recombinant tuberculosis allergen - DIASKINTEST). X-ray examination.*

The results of the study showed that against the background of secondary immunodeficiency caused by HIV, TB acquires a generalized character with multiple lesions of internal organs and the central nervous system, more rapid progression of the disease.

Keywords: *HIV infection, tuberculosis, children, disease progression*

BOLALARDA TUBERKULYOZ BILAN BILAN OIV-INFEKTSION O'RGANISHI

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Rezyume. *Maqolada bolalarda sil kasalligi bilan birgalikda OIV infektsiyasi bilan kasallangan 57 nafar bemorni kuzatish natijalari keltirilgan. Taqqoslash guruhi OIV bilan kasallangan, sil kasali bo'lmagan, xuddi shu yoshdagi 23 nafar bolalardan iborat edi. Immunitet holatini, CD4 hujayralari darajasini o'rganishning laboratoriya usullari; Bakterioskopiya va balg'am madaniyati. Immunodiagnostika: (2TE va rekombinant sil allergiyasi bilan Mantu testi - DIASKINTEST). Rentgen tekshiruvi.*

Tadqiqot natijalari shuni ko'rsatdiki, OIV sabab bo'lgan ikkilamchi immunitet tanqisligi fonida sil ichki organlar va markaziy asab tizimining ko'plab shikastlanishi, kasallikning tezroq rivojlanishi bilan umumiy xususiyatga ega bo'ladi.

Kalit so'zlar: *OIV infektsiyasi, sil, bolalar, kasallikning rivojlanishi.*

ПРОГРЕССИРОВАНИЕ ВИЧ-ИНФЕКЦИИ СОЧЕТАННОЙ С ТУБЕРКУЛЁЗОМ У ДЕТЕЙ

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Резюме. *В статье представлены результаты наблюдения 57 больных ВИЧ-инфекции, сочетанных с туберкулёзом у детей. Группу сравнения составили 23 детей ВИЧ - инфицированных детей без туберкулёза, того же возраста. Лабораторные методы изучения иммунного статуса, уровня СД4 клеток, бактериоскопию и посев мокроты. Иммунодиагностика: Проба Манту с 2ТЕ и аллергеном туберкулезным рекомбинантным - ДИАСКИНТЕСТ. Рентгенологическое исследование.*

Результаты исследования показали, на фоне вторичного иммунодефицита, обусловленного ВИЧ, ТБ приобретает генерализированный характер с множественными поражениями внутренних органов и ЦНС, более быстрому прогрессированию заболевания.

Ключевые слова: *ВИЧ-инфекция, туберкулёз, дети, прогрессирование заболевания*

Relevance. For a quarter of a century, humanity has been living in the conditions of the HIV infection epidemic. Given that science has achieved significant results in studying the molecular structure of HIV, its transmission pathways, the pathogenesis of AIDS, and the development of numerous antiviral drugs, it was expected that during this long period, a major breakthrough in combating the epidemic would occur. However, the number of new infections continues to increase rapidly. Moreover, with more than 25 million deaths from AIDS worldwide, the epidemic must be recognized as the most devastating in human history. If the HIV/AIDS pandemic is not stopped in the near future, it could become a factor in the destruction of international stability and security on a global scale.

Relevance of the Problem. In recent years, the urgency of the HIV/AIDS issue worldwide has intensified due to the pandemic-level increase in the incidence of this fatal retroviral infection, not only among adults but also among children. Until recently, acquired immunodeficiency syndrome (AIDS) was considered a problem primarily affecting the adult population. However, current research indicates that HIV infection and tuberculosis (TB) share epidemiological and pathogenetic similarities, exerting a mutually aggravating pathological impact on the host organism and altering the morphology of tuberculosis inflammation.

Currently, the World Health Organization (WHO) and the United Nations (UN) have declared tuberculosis and HIV infection as interrelated global issues with destructive consequences, requiring immediate intervention. Worldwide, the increasing number of HIV-infected patients has contributed to a rise in tuberculosis incidence. On a global scale, tuberculosis remains one of the leading causes of death among people living with HIV [1,2]. According to WHO estimates, at the beginning of the 21st century, approximately 9 million new cases of tuberculosis emerged annually, with nearly 10% of them occurring in HIV-positive individuals. Currently, 1.7 million people worldwide have died from tuberculosis, including 229,000 (13.5%) individuals living with HIV [3]. Moreover, HIV infection is a significant risk factor for the development of active tuberculosis. The increasing number of HIV-infected individuals and their declining immunity, combined with the high prevalence of tuberculosis, contribute to the activation of tuberculosis and the emergence of various clinical forms of the disease [4,6]. It is believed that HIV, which leads to immune system destabilization, is the most significant factor among all known contributors to the progression of latent tuberculosis into an active disease [5,6]. HIV-induced immunosuppression greatly increases the risk of tuberculosis due to both the reactivation of latent tuberculosis infection and exogenous superinfection [1]. According to the WHO European Respiratory Bureau, Russia is currently among the European countries where the problem of tuberculosis and HIV infection is most critical [1]. In 2006, compared to 2005, the number of registered tuberculosis cases among HIV-infected individuals in Russia increased by 33.3%.

The relevance of the problem is determined by the high mortality rate of HIV-infected children with tuberculosis. The increasing prevalence of co-infection necessitates the study of the clinical features of HIV infection in combination with tuberculosis and the establishment of clear criteria for specific serological diagnosis of tuberculosis.

The aim of this study was to investigate the progression of HIV infection combined with tuberculosis in children.

Materials and methods.

A clinical examination of HIV infection combined with tuberculosis in children was conducted. Clinical Examination: The study included 57 children aged 4 to 15 years diagnosed with both HIV infection and tuberculosis. The research was carried out at the Republican Specialized Scientific and Practical Center for Phthisiology and Pulmonology. A control group (n=23) consisted of HIV-infected children without tuberculosis. Laboratory Tests: General blood analysis, stool and urine tests, and CD4 cell count measurements were performed. Bacterioscopy and sputum culture analysis were also conducted. Immunodiagnostics: The Mantoux test with 2 TU and the recombinant tuberculosis allergen (Diaskintest) were used. Radiological Examination: Chest X-ray imaging was performed for further diagnostic evaluation.

Results and discussion.

To achieve the research objectives, a clinical examination of 57 children aged 4 to 15 years was conducted to study the characteristics of HIV infection combined with tuberculosis. Among them, 32 (56.14%) were boys and 25 (43.86%) were girls. The age distribution was as follows: 4 to 6 years – 34 children (59.65%) 6 to 10 years – 13 children (22.81%) 10 to 15 years – 10 children (17.55%) A comparison group consisted of 23 HIV-infected children of the same age range who did not have tuberculosis. Repeat HIV tests for these children yielded negative results. The diagnosis of tuberculosis was established based on epidemiological, general clinical, radiological, and bacteriological methods, following the guidelines of the Ministry of Health of the Republic of Uzbekistan (Order No. 383, dated October 24, 2014). HIV-infected children were diagnosed according to the Ministry of Health of the Republic of Uzbekistan's Order No. 480, dated October 30, 2007, in accordance with WHO classification.

A comparative analysis of clinical, hematological, and immunological parameters was conducted between two groups: **Group 1:** 57 children with HIV infection combined with tuberculosis. **Group 2:** 23 children with HIV infection without tuberculosis. Children were most frequently infected with tuberculosis while being in direct contact with an active source of infection. Contact was confirmed in over **70.59% of children in Group 2** and **90.9% of children in Group 1.** This higher rate in Group 1 can be attributed to their younger age—predominantly preschool-aged—where their limited social circle makes identifying the source of infection easier. Among children with both tuberculosis and HIV infection, disease onset was more often **acute or subacute** (63.6% in Group 1 vs. 41.18% in Group 2, p<0.001). The initial symptoms frequently mimicked acute respiratory viral infections, bronchitis, or pneumonia, with fever reaching **subfebrile (up to 38°C) or febrile (above 38°C) levels**, accompanied by intoxication symptoms. Nearly all children in this group were diagnosed when seeking medical attention due to these symptoms. Children with both tuberculosis and HIV infection exhibited a **significantly higher prevalence of severe intoxication syndrome** compared to those with HIV infection alone **(27.3% vs. 11.76%; p<0.001).** This finding aligns with the **higher proportion of acute disease onset** in Group 1 and suggests a more severe progression of the disease in co-infected children. **Clinical and Laboratory Differences Between HIV With and Without Tuberculosis** HIV infection combined with tuberculosis demonstrated more pronounced: **Asthenovegetative syndrome, bronchopulmonary symptoms, lymphadenopathy, changes in blood parameters.** These manifestations were strongly influenced by the **stage of HIV infection.** In **HIV-TB co-infected children,** the disease was more frequently associated with: **Astheno-vegetative and respiratory syndromes, hepatomegaly, disseminated and generalized tuberculosis processes, atypical radiological findings, such as interstitial changes.** In contrast, children with **HIV-TB co-infection primarily presented with pulmonary symptoms,** with **typical radiographic findings** of tuberculosis, such as **infiltrative and destructive lung changes**.

Depending on the severity of the tuberculosis process, which was assessed based on traditional parameters, the following forms were observed in patients of the first group (HIV/TB): infiltrative pulmonary tuberculosis in 15 patients (26.32%), infiltrative pulmonary tuberculosis in the disintegration phase in 10 patients (17.55%), fibrocavernous pulmonary tuberculosis in 9 patients (15.79%), disseminated pulmonary tuberculosis (DPT) in 11 patients (19.3%), generalized tuberculosis (GT) in 6 patients (10.53%), and tuberculous pleuritis (TP) in 6 patients (10.53%). Mycobacterium tuberculosis was detected in 39 patients (68.43%). In the second group (HIV), which included patients diagnosed with HIV infection without active tuberculosis, stage III HIV infection was diagnosed in 14 patients (60.87%), stage IVA in 4 patients (17.39%), stage IVB in 2 patients (8.69%), and stage IVV in 2 patients (8.69%). Since tuberculosis diagnosis determined the HIV stage in most patients with co-infection (HIV/TB), the proportion of patients with "late" HIV infection stages (IVB and IVV) was significantly higher than in those with HIV infection without tuberculosis (43.86% vs. 21.74%, respectively). A classic indicator of HIV infection progression is a decrease in CD4 lymphocytes. Their quantitative assessment is one of the key markers for diagnosing the degree of immunodeficiency and is also a crucial criterion for determining the stage of HIV infection. When evaluating the quantitative levels of CD4+ T-lymphocytes, a progressive decline was observed, from $0.568\pm0.033\times10^9$/L in stage III to $0.129\pm0.028\times10^9$/L in stage IVV in co-infected patients (in HIV infection without tuberculosis, from $0.634\pm0.030\times10^9$/L to $0.098\pm0.064\times10^9$/L), while the control group had a value of $0.760\pm0.040\times10^9$/L. The CD8+ T-lymphocyte level in stage III was even higher in both groups compared to the control data, and although a subsequent decrease in these cells was noted by stage IVV, it was not as dramatic as with CD4+ cells. The opposite trends in CD4+ and CD8+ T-lymphocyte levels in both infected groups led to a significant reduction in the immunoregulatory index as early as stage III HIV infection (0.57±0.05 in co-infected patients and 0.75±0.06 in HIV infection without tuberculosis), with no significant differences in HIV progression dynamics between the two groups (p>0.01; p>0.05). As expected, the lowest Th/Tc ratio values were observed in stage IVV HIV infection (0.20±0.06 in co-infected patients and 0.17±0.03 in mono-infected patients), serving as yet another indicator of severe immunodeficiency.

Conclusions: Thus, comorbid conditions with the development of complications, signs of infectious-toxic and asthenovegetative syndromes, and progressive immunodeficiency worsened the course of the disease in infected children, leading to severe progression of HIV infection combined with tuberculosis in children. Against the background of secondary immunodeficiency caused by HIV, tuberculosis takes on a generalized form with multiple lesions of internal organs and the central nervous system, leading to a more rapid progression of the disease.

REFERENCES

1. Babayeva I.Yu., Kondratyeva E.G., Shapalovsky V.V. Secondary diseases in tuberculosis patients at late stages of HIV infection. // Epidemiology and Infectious Diseases. - 2018. - No. 3. - P. 42-46.

2. Daminova M.N., Toshpulatova F.K., Abdullayeva O.I. // Clinical aspects of herpes infection in HIV-infected children / Journal of Infectology. - Vol. 16, No. 2. - 2024. - St. Petersburg. - P. 65-68.

3. Erokhin V.V. Features of detection, clinical manifestations, and treatment of tuberculosis in HIV-infected patients / V.V. Erokhin, Z.Kh. Kornilova // Probl. Tuberculosis. - 2015. - No. 3. - P. 20-28.

4. Karachunsky M.A. Tuberculosis in HIV infection // VIII Russian National Congress "Man and Medicine": Lectures for Practicing Physicians. - M., 2012. - P. 88-92.

5. Tojiboyev A.A., Mirismailova M.M., Daminova M.N. Description of a clinical case of HIV infection, stage 4 // VI Interuniversity Scientific and Practical Conference "Rare and Common Infectious Diseases. Diagnostic Problems (Clinical Examples)". - 13.02.2025. First MSMU named after I.M. Sechenov. - Moscow.

6. Daminova Kh. M., Zhumaniyozov N. B., Daminova M. N. The prevalence of tuberculosis in patients with HIV infection. // European Science Review. - Scientific Journal Volume 2. Medical Science. - 2018. - No. 9-10, p. 51-54. - September-October. ISSN 2310-5577. Vienna, Austria.