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Epidemiological and Clinical Aspects of Progressive Multifocal Leukoencephalitis

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Abstract Progressive multifocal leukoencephalitis (PML) is considered one of the most complex and unresolved problems of modern neurology. This disease, as a severe demyelinating process of the central nervous system, occupies an important place in pediatric neurology practice. According to official data, in Uzbekistan, PML in the structure of neurodegenerative diseases in children is characterized by high mortality rates in children with compromised immune status.

Keywords Progressive multifocal leukoencephalitis, JC virus, Demyelinating diseases, Pediatric neurology, Immunodeficiency, Neurodegeneration, Central nervous system, Oligodendrocytes, Myelin destruction

1. Introduction

Although progressive multifocal leukoencephalitis occurs more frequently in adults, it can also occur in the pediatric population under certain clinical conditions (primary/secondary immunodeficiencies, post-transplantation immunosuppression, HIV infection, immunomodulators used in some autoimmune conditions) [1]. In children, PML course is often manifested by subacute, polyfocal neurological deficits, and rapid accurate diagnosis and maximum elimination of immunosuppressive factors determine treatment effectiveness. Significant work has been done in this field over recent decades. Numerous dissertations have been defended. Monographs and manuals have been published. It should be emphasized that the noted works are mainly devoted to various aspects of PML in JC virus reactivation and immunodeficiency states [2].

The problems of early diagnosis and treatment of PML in children, namely the assessment of clinical-instrumental parameters in the initial stages of the disease, were extensively studied in the 1980s by M.I. Petrova and I.A. Skorometsky. Subsequently, a number of studies have been conducted in this direction [3].

The first information about PML in children dates back to the middle of the 20th century. In 1958, American neurologists Åström, Mancall, and Richardson first generalized 3 cases they observed and existing data in the scientific literature, introducing the term "progressive multifocal leukoencephalitis" into science. In neurological literature, changes associated with PML have been designated by the term "demyelinating encephalopathy." In particular, it is proposed to call the condition associated with JC virus (John Cunningham virus) reactivation "progressive poliovirus encephalopathy" based on the commonality of the above-mentioned aspects. This opinion is based on similar etiology, common pathogenesis, neuroimaging changes, and neuropathological signs being of the same type [4].

Progressive multifocal leukoencephalitis (PML) has always been among the urgent problems of neurology and pediatrics sciences and practice. In particular, severe health disorders and disability-causing conditions in children due to demyelinating processes developed under the influence of JC virus (John Cunningham virus) occupy an important place in neurological practice. According to official data, in Uzbekistan, cases of this type of disease occupy a position after neurodegenerative diseases in the structure of childhood disability [5].

Significant work has been done in this field over recent decades. Numerous dissertations have been defended. Monographs and manuals have been published. It should be emphasized that the noted works are mainly devoted to various aspects of developed PML. Major works on PML problems, namely early detection and treatment issues of the disease in initial stages, were conducted in the 1980s by M.I. Fedorov and I.A. Kontsevich. Subsequently, a number of studies have been conducted in this direction. The first information about PML dates back to the middle of the 20th century. In 1958, German neurologist K. Richardson first generalized 17 cases he observed and existing data in the scientific literature, emphasizing the presence of cognitive impairments in progressive demyelination as reliable evidence [6].

In neurological literature, changes associated with progressive demyelinating disease have been designated by the term "postinfectious encephalopathy." In particular, it is proposed to call the condition developed under JC virus influence "progressive leukoencephalopathy" based on the

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commonality of the above-mentioned aspects. This opinion is based on similar etiology, common pathogenesis, neuroimaging changes (status neuroimaging), and the same type of central nervous system damage symptomatology [7].

Usually, PML proceeds with multiorgan insufficiency with changes such as mixed or metabolic acidosis, hyperglycemia, hypercreatinemia, inflammatory reactions. In these conditions, rhabdomyolysis, acute kidney injury, and immune system changes, particularly immunodeficiency syndrome, may also develop. At the same time, some researchers do not agree with generalizing conditions with different etiology, pathogenesis, and clinical-morphological signs under one term [8].

Indeed, scientific studies devoted to PML cases are mainly related to immunocompromised patients. At the same time, it is fair to acknowledge that PML cases developed in immunocompetent children do not fall into this category. In particular, PML developed after COVID-19 infection proceeds much more severely compared to immunocompetent children, and various neurological diseases are observed in them for a long time in the postinfectious period [9].

The extent and degree of health impairment in post-PML conditions is linked by all researchers to the duration of the disease. Some believe that even after 6-12 months of progression, it is possible to bring the patient to a state of stabilization. In general, in such conditions, the extent of damage and prognosis for the patient is organically linked not only to the duration of the disease but also to the location and spread of demyelination, the mechanism of cellular damage (rapid, slow, focal, etc.), and the health status of the person caring for the child [10].

Usually, PML proceeds with multiorgan insufficiency with changes such as autoimmune reactions, cytokine imbalance, neuroimmune dysfunction. In these conditions, myelin destruction, oligodendrocyte necrosis, and neuronal damage, particularly axonopathy, may also develop. At the same time, some researchers do not agree with generalizing demyelinating diseases with different etiology, pathogenesis, and clinical-morphological signs under one term. Indeed, scientific studies devoted to PML are mainly related to HIV infection in older age groups, cases in transplantology and oncohematology practice [11]. At the same time, it is fair to acknowledge that idiopathic forms of PML in children, post-oncological conditions, and immunodeficiency states do not fall into this category. In particular, the risk of PML development after the use of immunosuppressive drugs such as natalizumab and rituximab in children is quite high, and neurological deficits persist for a long time in them. The extent and degree of health impairment in post-PML conditions is linked by all researchers to the clinical stage of the disease and immune status. Some believe that even after a demyelinating process lasting 6-12 months, it is possible to return the child to life [12].

Modern concepts about the clinical course and prognosis of PML in children are mainly based on studies related to immunodeficiency diseases. However, idiopathic PML cases encountered in pediatric practice, mainly forms developing against the background of familial immunodeficiency syndromes, require special attention. In general, the course and prognosis of PML in children is organically linked not only to the clinical stage of the disease but also to the characteristics of the immune system in childhood, features of neurontogenesis, incompleteness of myelination processes, and genetic determinants of the individual.

2. Conclusions

Progressive multifocal leukoencephalitis represents a significant medical and social problem in the structure of neurodegenerative diseases in children in Uzbekistan, characterized by high mortality rates among patients with immunodeficiency conditions. The disease demonstrates a tendency toward increasing incidence in the pediatric population, which requires the development of specialized preventive and diagnostic programs.The clinical course of PML in children has substantial differences from the adult population, characterized predominantly by subacute onset with the development of polyfocal neurological deficits. The disease manifests with progressive cognitive impairments, motor disorders, and behavioral changes, which requires a multidisciplinary approach to diagnosis and treatment.

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