

## CLINICAL AND NEUROLOGICAL SIGNS OF SUBACUTE SCLEROSING PANENCEPHALITIS IN CHILDREN

<https://doi.org/10.5281/zenodo.18464285>

**Ishanhodzhayeva G.T.**

*Tashkent State Medical University*

Subacute sclerosing panencephalitis (SSPE) is a rare, progressive, degenerative disease of the central nervous system caused by persistent measles infection. The disease is classified as a slow-moving viral infection. The virus sometimes enters the brain during a measles infection. The measles virus can cause immediate symptoms of brain infection (encephalitis) or remain in the brain for a long time without causing problems. SSPE occurs due to reactivation of the measles virus.

SSPE occurs with varying rates worldwide, which is related to the level and availability of medical care, with immunization being the main factor reducing the incidence. In developed countries, it is considered a rare disease, with an incidence of 1 in 1,000,000 children. According to statistics, in the United States, the disease previously occurred at a rate of approximately 7-300 in 1,000,000 people who had measles virus infection, and in 1 person in a million people who received the measles vaccine. However, doctors believe that people who developed SSPE after vaccination likely had a mild, undiagnosed case of measles before vaccination, and that the measles, not the vaccine, caused the SSPE. SSPE is characterized by a history of primary measles infection at an early age (before 2 years), followed by the development of progressive neurological disorders after a 6-8-year latency period. Children infected with measles as infants have a higher risk of developing SSPE than those infected at age 5 and older. Widespread immunization has reduced the incidence of SSPE in developed countries by more than 90%. Available epidemiological data, along with viral genotyping results, do not indicate that the vaccine-induced measles virus can cause SSPE.

Autoimmune mechanisms, as well as acquired or congenital immune system defects, play a role in the pathogenesis of the disease. The underlying cause is the persistence and reproduction of the measles virus in brain cells after the disease, due to impaired immunological mechanisms. Viral reproduction in the central nervous system is accompanied by activation of autoimmune processes, leading to damage and death of neurons. The brain exhibits encephalitis with the presence of glial nodules ("nodular panencephalitis") and demyelination in the subcortical structures (leukoencephalitis). Changes are localized primarily in the gray and

white matter of the cerebral hemispheres, brainstem, and cerebellum. Microscopic examination reveals perivascular lymphomonocytic infiltration, neuronal damage and degenerative changes, and glial proliferation. The PSPE clinic identifies four stages of disease development, each characterized by specific clinical manifestations, distinguishing it from other diseases and facilitating early diagnosis, helping to track the progressive course of the disease.

The challenges of treating SSPE stem from the fact that there is currently no specific therapy capable of completely curing the disease. Antiviral drugs such as isoprinosine can slow disease progression, but their effectiveness is limited, especially in the later stages. Immunomodulatory agents such as interferon-alpha or intravenous immunoglobulins are used to enhance the immune response and suppress viral activity, but they also do not always lead to significant improvement in the patient's condition.

Proper patient care and prevention of infectious complications are of great importance. Etiotropic treatment with antiviral agents (ribavirin, inosine) is carried out. Pranobex and interferon preparations have been used, but they are ineffective. Anticonvulsants effective against myoclonus (diazepam, valproic acid derivatives) are prescribed for symptomatic therapy. Muscle relaxants (tolperisone, baclofen) are used to relieve spastic hypertonicity. Respiratory failure in the final stages of the disease is an indication for mechanical ventilation. Careful care and symptomatic treatment can prolong the patient's life for a short period of time.

**The aim** of our study was to investigate the clinical and neurological manifestations of PSPE in children.

**Materials and methods.** We examined 14 patients admitted to the pediatric neurology department of the multidisciplinary clinic of Tashkent State Medical University. The age of the children ranged from 3 to 7 years, with an average age of 5.2 years. Of these, 9 were boys (64%) and 5 were girls (36%). To verify the diagnosis, we used the serological indirect ELISA test for the detection of specific measles antibodies (Anti - Measles). Virus Serum IgG (normal range: 0-0.12 IU/ ml) was measured. All patients also underwent brain MRI and EEG. Patients were monitored at the onset of clinical manifestations and during follow-up. A thorough medical history, neurological examination, and neuropsychological evaluation were performed.

**Study results.** Analysis of the anamnestic data revealed that all patients examined had a history of measles before the age of 2. The variety and severity of focal neurological symptoms increased with the duration of the illness before treatment.

In the patients we examined, behavioral changes such as untidiness, stubbornness, aggressiveness, and irritability were prevalent in 87% (12 patients) of the disease manifestations. A detailed interview revealed cognitive impairment in all patients, including inattention, forgetfulness, sleep disturbances, and speech disorders.

**Table 1**

**Manifestation of clinical manifestations of PSPE in children**

No.	Clinical manifestations	boys	girls	total
1	Personality change	4	-	4
2	Behavioral deviation	6	4	10
3	Growing defects in the Navy	9	3	12
4	Hyperkinesis	2	-	2
5	Disorders of autonomic regulation	6	2	8
6	Sleep disorders	5	2	7

When symptoms were mild, the parents of all the children examined did not seek medical attention, attributing these behavioral changes to age-related childhood behaviors. As symptoms worsened, the parents of four children sought medical attention, where they were diagnosed with ADHD or MMD. The parents of the remaining four children did not seek medical attention. The patients we examined were hospitalized when symptoms of the second stage of the disease appeared. Only one child was diagnosed with severe symptoms in the first stage during an outpatient visit and was hospitalized.

Brain MRI scans of all patients revealed foci of hyperintensity in the white matter of the brain using T2-weighted sequences and FLAIR modes. These changes were indicative of inflammation and demyelination. In five patients, these foci covered large areas of the brain. Seven patients showed cortical atrophy, particularly in the frontal lobes.

EEG examination revealed epileptiform activity with periodic complexes of high-amplitude bursts alternating with periods of low-amplitude activity in 6 patients (43%). Eight patients (57%) showed minimal EEG changes in the form of organic-type disorganization.

**Conclusions.** Diagnosis can be challenging in the early stages of the disease. SSPE itself is extremely difficult to diagnose, so laboratory testing to confirm any clinical case is essential for early diagnosis and timely, adequate treatment to alleviate the disease.

## REFERENCES:

1. Ишанходжаева Г.Т., Кодирова З.М. Подострый склерозирующий панэнцефалит у детей: проявления когнитивных нарушений // Научный журнал «Медицинские науки и биология». 2024, Том 3. Стр. 108-113
2. Ишанходжаева Г.Т., Қодирова З.М. Болаларда ўткирости склеротик панэнцефалит: бирламчи клиник-неврологик намоёндалари // International journal of scientific researchers (IJSR) indexing, 2024, Volume 5, Issue 1, стр. 867-869
3. Сатторов, С. Анализ нейровизуальных изменений при подостром склерозирующем панэнцефалите: исследование динамики МРТ и ЭЭГ // Наука и инновация. 2024, 2(30), 65–68. <https://inlibrary.uz/index.php/scin/article/view/46231>
4. Скрипченко Н.В., Иванова Г.П., Скрипченко Е.Ю., Мурина Е.А. Панэнцефалиты у детей в современных условиях: клиничко-этиологические и МРТ-аспекты // Журн. невро. и псих. им. Корсакова. 2019;119 (6): 20-31
5. Шакарян А.К., Демкина А.М., Зверева Н.Н., Ртищев А.Ю. Подострый склерозирующий панэнцефалит: актуальная угроза. Российский вестник перинатологии и педиатрии. 2023;68(4):613. <https://doi.org/10.21508/1027-4065-2023-68-4-6-XX>
6. **Ishanhojaeva G.T., Kodirova Z.M.** Subacute sclerosing panencephalitis in children: cognitive impairment // Journal of Modern Educational Achievements, 2024, Volume 10, Issue 10, P. 233-238
7. Krumova S., Andonova I., Stefanova R., Nenkova G., Genova-Kalou P. Measles Virus and Subacute Sclerosing Panencephalitis. Clin Lab, 2022, Sep 1;68(9), doi:10.7754/Clin.Lab.2021.211147.
8. Garg R.K., Mahadevan A., Malhotra H.S., Rizvi I., Kumar N., Uniyal R. Subacute sclerosing panencephalitis. Rev. Med. Virol. 2019;29:e2058. doi: 10.1002/rmv.2058
9. Hashimoto K., Hosoya M., Hosoya M. Advances in Antiviral Therapy for Subacute Sclerosing Panencephalitis. Molecules. 2021;26:427. doi: 10.3390/molecules26020427
10. Hosoya M., Mori S., Tomoda A., Mori K., Sawaishi Y., Kimura H., Shigeta S., Suzuki H. Pharmacokinetics and effects of ribavirin following intraventricular administration for treatment of subacute sclerosing

panencephalitis. *Antimicrob. Agents Chemother.* 2004;**48**:4631–4635.  
doi: 10.1128/AAC.48.12.4631-4635.2004

11. Mathieu C., Bovier F.T., Ferren M., Lieberman N.A.P., Predella C., Lalande A., Peddu V., Lin M.J., Addetia A., Patel A., et al. Molecular Features of the Measles Virus Viral Fusion Complex That Favor Infection and Spread in the Brain. *MBio.* 2021;**12**:e00799-21. doi: 10.1128/mBio.00799-21

12. Mekki M., Eley B., Hardie D., Wilmshurst J.M. Subacute sclerosing panencephalitis: Clinical phenotype, epidemiology, and preventive interventions. *Dev. Med. Child Neurol.* 2019;**61**:1139–1144. doi: 10.1111/dmcn.14166

13. Sibel P. Y., Veysi D., Candan G. at all. Immune alterations in subacute sclerosing panencephalitis reflect an incompetent response to eliminate the measles virus. PLoS One. 2021; 16(1): e0245077. 2021 Jan 7. doi: 10.1371/journal.pone.0245077, PMCID: PMC7790413, PMID: 33411786