# SUBACUTE SCLEROSING PANENCEPHALITIS: EPIDEMIOLOGY, CLINICAL PRESENTATION AND DIAGNOSIS

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***Abstract****. Subacute sclerosing panencephalitis (SSPE) is a rare but devastating neurological disorder caused by persistent measles virus infection. This review provides a comprehensive overview of SSPE, focusing on its epidemiology, clinical presentation, and diagnostic challenges. Primarily affecting children and young adults, SSPE presents with diverse and often atypical symptoms, making diagnosis difficult. This review synthesizes recent research to highlight the importance of a thorough clinical evaluation, incorporating detailed history, physical examination, neuroimaging, electroencephalography (EEG), and cerebrospinal fluid (CSF) analysis, to ensure timely and accurate diagnosis. Early recognition and intervention are crucial to improve outcomes for individuals affected by this debilitating disease.*

***Keywords****: subacute sclerosing panencephalitis, SSPE, measles, neurological complications, diagnosis, atypical presentation.*

## INDRODUCTION

Subacute Sclerosing Panencephalitis (SSPE) is a rare but devastating disease of the central nervous system, often occurring in children. It is caused by persistent measles virus infection and can present with atypical symptoms such as recurrent febrile seizures[1]. The disease can progress rapidly, particularly in cases of co-infection with HIV[2]. The incidence of SSPE has been linked to a reduction in measles vaccination, highlighting the importance of vaccination in preventing this disease[3]. A measles outbreak in South Africa led to a cluster of SSPE cases, underscoring the need for vigilance in screening for the disease, especially in children who were infants during the outbreak[4]. About the epidemiology of SSPE: Age Distribution: SSPE primarily affects children, with typical onset between 10 and 14 years old[5,6]. However, adult-onset SSPE is rare and may present with atypical features[7,8]. Atypical Presentations: Atypical presentations of SSPE have been reported, including cases with initial symptoms such as visual loss, seizures, and neuropsychiatric symptoms[5,9,10]. These atypical presentations can complicate accurate diagnosis and highlight the need for a high degree of suspicion[9]. Mortality and Vaccination: The decline in SSPE mortality reflects that of measles, and it is suggested that autochthonous SSPE will disappear in the United States assuming high measles vaccination rates are maintained[11]. SSPE presents diagnostic challenges due to its varied and atypical clinical manifestations.

Clinical Presentation: SSPE can manifest with diverse symptoms such as necrotizing retinitis, myoclonic jerks, altered sensorium, loss of bowel and bladder control, and focal myoclonus[12–15]. Diagnostic Difficulties: Diagnosing SSPE can be challenging, especially in developed countries, leading to delays in accurate identification[13,16–18]. Diagnostic Tools: A thorough clinical evaluation, including vaccination history, physical examination, electroencephalogram (EEG), and cerebrospinal fluid (CSF) analysis, is crucial for making a diagnosis[13,14,17,18]. Imaging Findings: Neuroimaging abnormalities, such as bilateral

putaminal and corpus callosum involvement, can be atypical and may initially mimic metabolic disorders, complicating the diagnostic process[19,20]. Age of Onset: SSPE typically occurs in childhood and young adults, but adult-onset cases have been reported, presenting as rapidly progressive dementia and focal myoclonus[14,15]. Electrophysiological Features: Myoclonus in SSPE may involve the cortex and cortico-subcortical structures at earlier stages, progressing to more caudal structures as the disease advances[21].

**METHODS**

A comprehensive literature search was conducted using the PubMed, MEDLINE, Embase, Cochrane Library, and Google Scholar databases (19.05.2024). The following keywords and their combinations were used to identify relevant articles: "Subacute sclerosing panencephalitis," "SSPE," "measles inclusion body encephalitis," "measles," "neurological complications," and "virus."

Inclusion criteria encompassed studies focusing on SSPE in children, including case reports, case series, clinical trials, reviews, and epidemiological studies published in English and Russian between 2015 and 2024. Articles discussing the epidemiology, clinical presentation, and diagnosis of SSPE in pediatric populations were prioritized. Studies exclusively addressing treatment, prognosis, or other aspects not directly related to the core themes of this review were excluded.

The initial search yielded 211 of articles(Figure 1.0). After removing duplicates and screening titles and abstracts, 181 of studies were assessed for full-text eligibility. Finally, 49 articles met the inclusion criteria and were included in this review. Data extracted from the selected studies included information on prevalence, incidence, risk factors, clinical features, diagnostic modalities, and challenges in diagnosing SSPE in children.

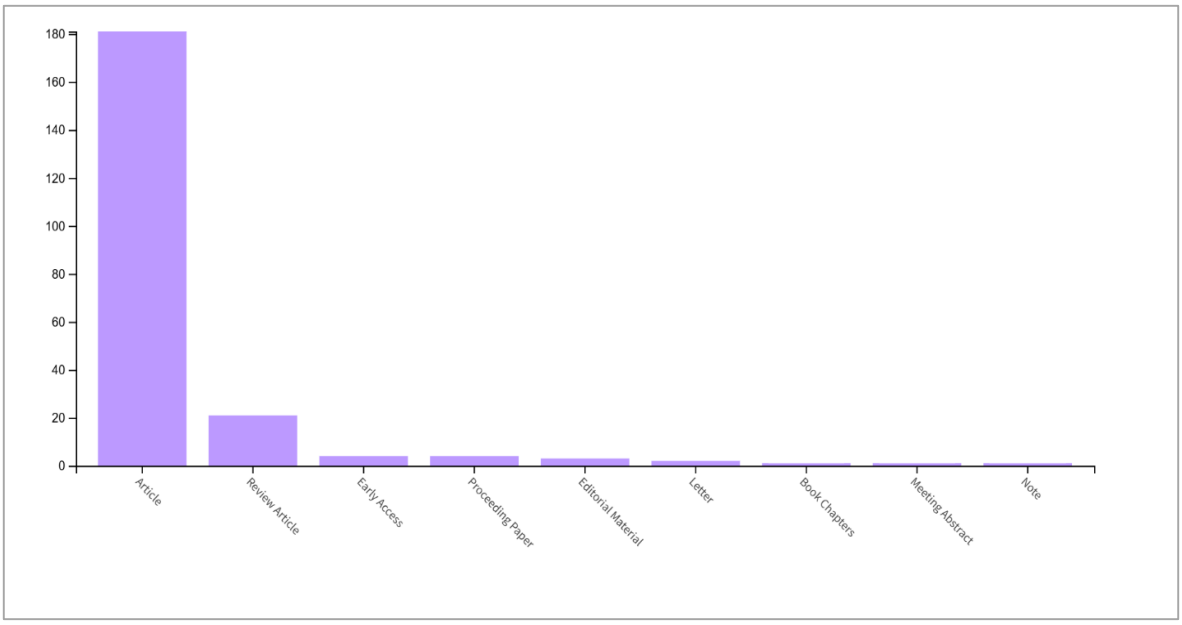


***Figure 1. Types of documents.***

Results and discussion.

Virology

Measles Virus Mutation: The measles virus strains involved in SSPE differ from typical wild-type measles viruses. They harbor significant mutations, particularly within the genes encoding the matrix (M), fusion (F), and hemagglutinin (H) viral proteins[22,23]. These mutations are believed to critically disrupt the production of infectious virus particles.

Viral Persistence: The mutated measles virus in SSPE establishes a persistent infection within the brain. The exact mechanisms of viral persistence remain an area of active research. However, factors like defective viral assembly and evasion of the host immune response likely play a significant role[24].

The Hyperfusogenic F Protein: The mutations in the F protein are of particular interest. These mutations can induce a hyperfusogenic state in the virus, enabling extensive cell-to-cell fusion[23]. This leads to the formation of giant multinucleated cells (syncytia), a hallmark of SSPE pathology.

Pathogenesis

Immune dysregulation: Although a compromised immune response is suspected in the development of SSPE, the precise mechanisms remain under investigation. Impaired cell-mediated immunity, ineffective antibody responses, and molecular mimicry might contribute to the persistent viral infection [24,25].

Neuronal Spread: The measles virus in SSPE appears to spread transneuronally (from neuron to neuron), facilitated by the altered viral proteins[22]. This leads to a slow, progressive infection across the brain.

Inflammation and Demyelination: Persistent viral infection and the accompanying immune response trigger widespread inflammation in the brain[25]. This inflammation, along with direct viral damage, leads to the destruction of myelin sheaths that insulate nerve fibers, resulting in demyelination. Demyelination severely disrupts the transmission of nerve signals, contributing to the progressive neurological decline observed in SSPE.

If we look at the previous real cases taken by neurologists, we can see that information related to our topic:

Case Report

Sex / Age: M / 2 y.o. and 11 m.o.

Chief Complaints:

Seizures: Atonic and myoclonic (repetitive jerks)

Dysphagia (difficulty swallowing): Since 25.09.2022

Slowly progressive developmental delay

History of Present Illness:

This previously healthy male child experienced recurrent head drops and falling down starting on 10.07.2022. Prior to this, he was meeting age-appropriate developmental milestones. He has had a progressive decline in milestones since then. Repetitive, periodic myoclonic jerks at a frequency of 6-8 seconds (only while awake) were noted starting on 15.09.2022. Dysphagia began on 25.09.2022.

Past Medical History:

Birth history: GA 36-37 weeks, birth weight 2200g, delivered via Cesarean section due to preeclampsia.

Physical Examination:

Generalized central hypotonia (low muscle tone)

Pyramidal signs (suggesting involvement of the corticospinal tract)

Repetitive myoclonic jerks every 6-8 seconds

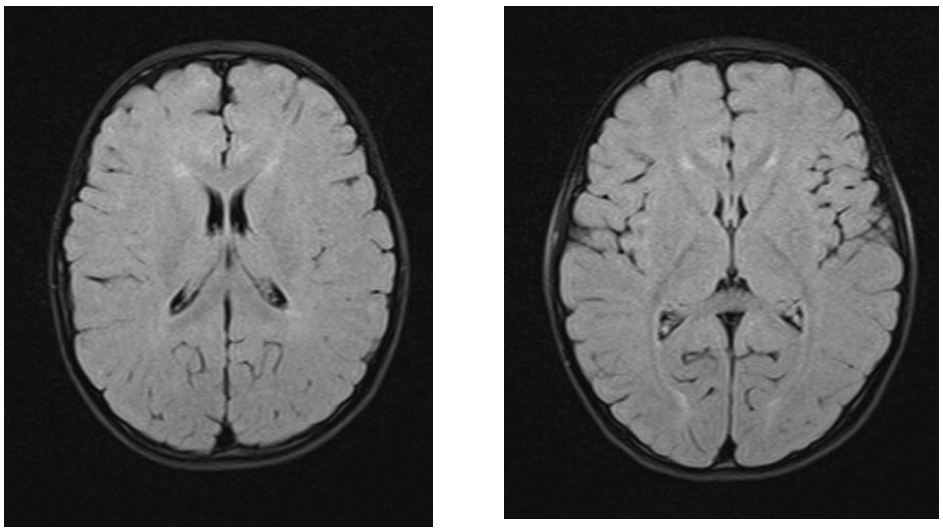

*Figure 2. MRI Brain 2022/09/11*

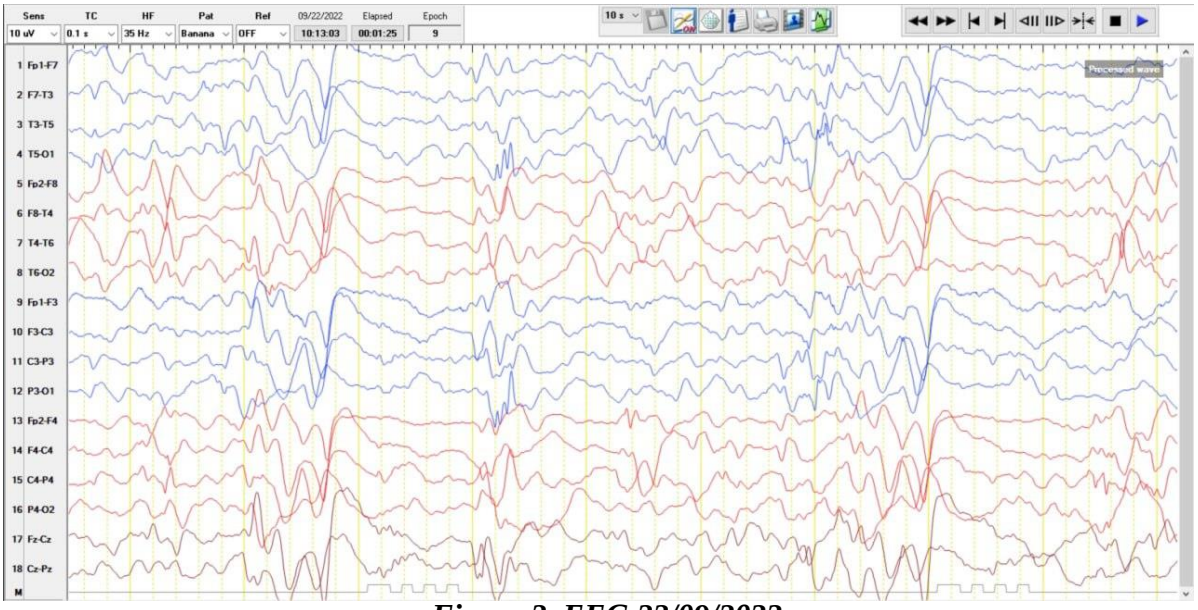


*Figure 3. EEG 22/09/2022*

| Barcode | Test ID | Test nm | Result Text | Result Unit | Reff Low Value | Reff High Value |
|---|---|---|---|---|---|---|
| 134983 | 505 | IgA | 0.43 | g/L | 0.2 | 1 |
| 134983 | 506 | IgG | 10.51 ▲ | g/L | 3.17 | 9.94 |
| 134983 | 507 | IgM | 0.64 | g/L | 0.19 | 1.46 |
| 134983 | 1083 | ?Anti-Measles Virus IgG | >5000 | U/ml | | |
| 134983 | 1084 | ?Anti-Measles Virus IgM | 3.3 | U/ml | | |

*Figure 4. Lab 22/09/2022*

It is clear that this case requires a multidisciplinary approach involving neurologists, geneticists, and infectious disease specialists. A thorough evaluation, including detailed history, physical examination, neuroimaging, EEG, and CSF analysis, is essential to establish a definitive diagnosis and guide appropriate management. Early diagnosis and intervention are crucial to optimize outcomes for this child.

## CONCLUSION

Subacute sclerosing panencephalitis (SSPE) is a devastating neurological disease with significant diagnostic challenges due to its diverse clinical manifestations and atypical presentations. While primarily affecting children, it can also occur in adults, underscoring the need for heightened awareness across all age groups. The presented case highlights the importance of a

thorough clinical evaluation, incorporating detailed history, physical examination, neuroimaging, EEG, and CSF analysis, to establish an accurate diagnosis. Early detection is crucial as SSPE is often associated with poor outcomes. A high index of suspicion, particularly in cases with unexplained neurological decline, myoclonus, and a history of measles infection or incomplete vaccination, can aid in timely diagnosis and potentially lead to early intervention strategies.

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