AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 5,October ,2025

HISTOLOGICAL CHANGES IN THE NERVOUS SYSTEM OF CHILDREN WITH ACUTE VIRAL ENCEPHALITIS

Oynurakhon Otabek qizi In'omova
Kokand University, Andijan Branch
Clinical Practice, Group 25-24

Scientific Supervisor: Lecturer of the Department of Histology, Cytology, and Embryology,
Mukhammadjonova Dilyorakhon Khusanjon qizi

Abstract: Acute viral encephalitis in children is a severe neurological disorder characterized by inflammation and injury of the central nervous system. This study investigates the histopathological changes occurring in the nervous system during the acute phase of infection. Findings reveal significant neuronal degeneration, microglial activation, astrocytic proliferation, and perivascular lymphocytic infiltration. These changes indicate a complex interplay between protective immune responses and mechanisms of secondary neuronal injury. Understanding these histological alterations is essential for prognosis, early intervention, and development of targeted therapeutic strategies to improve neurological outcomes in pediatric patients.

Keywords: Acute viral encephalitis, Pediatrics, Nervous system, Histopathology, Neuronal degeneration, Microglial activation, Astrocytic proliferation, Inflammatory infiltration

Introduction

Acute viral encephalitis is a severe inflammatory disease of the central nervous system (CNS) that predominantly affects children and often leads to significant neurological and histopathological alterations. It is caused by a wide range of neurotropic viruses such as Herpes simplex virus (HSV), Enteroviruses, Arboviruses, and Japanese encephalitis virus, which invade the brain parenchyma and induce extensive cellular damage [1]. The disease is characterized by acute onset of fever, headache, seizures, and altered consciousness, often resulting in long-term neurological sequelae in surviving patients [2].

The pathogenesis of acute viral encephalitis involves direct viral cytopathic effects and immune-mediated mechanisms, which together contribute to neuronal injury, vascular damage, and glial activation [3]. Histologically, these changes are manifested as perivascular lymphocytic infiltration, neuronal degeneration, microglial proliferation, and astrocytic hypertrophy. In severe cases, widespread necrosis of neurons, demyelination, and microglial nodules are observed, indicating extensive tissue destruction and impaired neural connectivity [4].

In children, the immature immune system and developing neural tissue increase susceptibility to viral invasion and inflammatory responses, leading to distinct histopathological patterns compared to adults [5]. The examination of histological features provides essential insights into the progression and outcome of viral encephalitis, enabling early diagnosis, appropriate treatment, and prevention of irreversible brain damage.

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5,October ,2025

Therefore, the present study aims to analyze the histological alterations in the nervous system of children diagnosed with acute viral encephalitis and to identify key pathological markers that can aid in the understanding of disease mechanisms and prognostic evaluation.

Materials and Methods

This study was conducted to investigate the histological changes occurring in the nervous system of children diagnosed with acute viral encephalitis. The research was performed in collaboration with neuropathology and pediatric infectious disease departments.

Study Design and Sample Selection

Brain tissue samples were obtained from 25 pediatric patients (ages 2–12 years) who were clinically and laboratory-confirmed to have acute viral encephalitis. The diagnosis was established based on neurological symptoms (fever, seizures, altered consciousness, and focal deficits), cerebrospinal fluid (CSF) findings, and polymerase chain reaction (PCR) detection of viral nucleic acids. Control samples were taken from 10 age-matched children who died from non-neurological causes.

Tissue Preparation and Staining Techniques

The collected brain tissues were fixed in 10% neutral buffered formalin for 48 hours, dehydrated in graded alcohol, and embedded in paraffin wax. Sections of 4–6 µm thickness were prepared and mounted on glass slides. For general histological evaluation, hematoxylin and eosin (H&E) staining was used. Additional special stains—such as Nissl staining for neuronal structure and Luxol Fast Blue for myelin integrity—were applied when necessary.

Immunohistochemistry

Immunohistochemical analysis was performed using antibodies against glial fibrillary acidic protein (GFAP) to identify astrocytes, CD68 to mark activated microglia, and viral antigen markers specific for herpes simplex virus and enteroviruses. Visualization was achieved through a horseradish peroxidase (HRP) detection system with diaminobenzidine (DAB) as the chromogen. Counterstaining was done with hematoxylin.

Microscopic Examination and Quantitative Analysis

The stained sections were examined using a light microscope under magnifications of ×100, ×400, and ×1000. Histological changes were evaluated in the cerebral cortex, basal ganglia, cerebellum, and brainstem. Quantitative measurements were taken for:

- Neuronal degeneration (expressed as percentage of damaged neurons per microscopic field)
- Perivascular lymphocytic infiltration (graded as mild, moderate, or severe)
- Microglial nodules and astrocytic proliferation (counted per high-power field)

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5,October ,2025

All observations were recorded and analyzed statistically to identify correlations between viral type and histological damage severity.

Data Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 26.0. Descriptive statistics were calculated for all histological variables. Comparisons between groups (viral type and severity level) were made using Student's t-test and ANOVA. A p-value < 0.05 was considered statistically significant.

Results

The histological analysis of the nervous system in children with acute viral encephalitis revealed significant structural and cellular alterations, which varied depending on the viral etiology and severity of inflammation. The most prominent changes were observed in the cerebral cortex, basal ganglia, cerebellum, and brainstem.

Microscopic examination showed widespread neuronal degeneration, characterized by cytoplasmic shrinkage, nuclear pyknosis, and eosinophilic neuronal necrosis. Perivascular lymphocytic infiltrations were seen in most cases, indicating an active inflammatory process around the small blood vessels. Glial proliferation, particularly astrocytosis and microglial activation, was evident in affected brain regions. In severe cases, microglial nodules were observed, representing focal accumulations of activated microglia surrounding necrotic neurons.

In the cerebral cortex, diffuse neuronal loss and reactive gliosis were prominent, especially in cases associated with herpes simplex virus (HSV) infection. In contrast, enteroviral infections showed relatively milder neuronal damage but more pronounced perivascular edema and microglial nodules. Cerebellar tissues displayed Purkinje cell degeneration and vacuolization in the molecular layer, while brainstem sections exhibited neuronophagia and vascular congestion.

Quantitative evaluation demonstrated a significant difference in neuronal degeneration and glial proliferation between viral types ($p < 0.05$). The mean percentage of damaged neurons in HSV-related encephalitis reached 48.6%, compared to 32.4% in enteroviral cases. Similarly, the degree of astrocytic proliferation was higher in HSV infections.

The summarized histological findings are presented in **Table 1**, which shows the comparative patterns of neuronal and glial changes in different types of viral encephalitis.

Table 1. Histological Changes in the Nervous System of Children with Acute Viral Encephalitis

Histological Parameter	HSV Encephalitis (n = 12)	Enteroviral Encephalitis (n = 13)	Control Group (n = 10)
Neuronal degeneration (%)	48.6 ± 5.3	32.4 ± 4.1	4.2 ± 1.1

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5,October ,2025

Histological Parameter	HSV Encephalitis (n = 12)	Enteroviral Encephalitis (n = 13)	Control Group (n = 10)
Perivascular lymphocytic infiltration (grade)	Severe	Moderate	None
Microglial activation (nodules/HPF)	7.8 ± 1.2	5.3 ± 0.9	0.6 ± 0.2
Astrocytic proliferation (GFAP-positive cells)	56.7 ± 6.8	39.5 ± 5.4	8.1 ± 2.1
Myelin damage (Luxol Fast Blue, score 0–3)	2.6 ± 0.5	1.9 ± 0.4	0.2 ± 0.1

HPF – high-power field; values are mean ± SD.

Overall, the histopathological evaluation demonstrated that HSV-induced encephalitis in children causes more severe neuronal damage and glial activation than enteroviral encephalitis. The intensity of inflammation, neuronal necrosis, and gliosis was closely correlated with the duration of the disease and the severity of clinical symptoms such as seizures and loss of consciousness. These findings suggest that early antiviral therapy and neuroprotective interventions could play an essential role in minimizing irreversible neuronal loss and improving neurological outcomes.

Discussion

The present study investigated the histological changes in the nervous system of children affected by acute viral encephalitis. Our findings demonstrated pronounced neuronal degeneration, perivascular infiltration by inflammatory cells, microglial activation, and astrocytic proliferation. These histopathological alterations are consistent with the acute inflammatory response induced by viral infection, highlighting the vulnerability of the pediatric central nervous system to viral neurotropic agents.

Neuronal degeneration, as observed in this study, can lead to irreversible functional deficits, particularly in areas such as the hippocampus and cerebral cortex, which are critical for cognitive and memory functions. The observed microglial activation reflects the innate immune response of the brain attempting to contain viral replication and clear apoptotic debris. However, excessive microglial activity may exacerbate neurotoxicity and contribute to secondary neuronal injury, as previously described in studies of pediatric viral encephalitis [1,2].

Astrocytic proliferation, also noted in our results, likely represents a reactive gliosis aimed at maintaining the integrity of the blood-brain barrier and providing metabolic support to stressed neurons. While gliosis is initially protective, persistent or excessive astrocytic activation can contribute to scar formation and interfere with normal neuronal network reconstruction [3].

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5,October ,2025

Moreover, perivascular lymphocytic infiltration indicates an adaptive immune response, which, while necessary for viral clearance, may induce additional tissue damage through cytokine-mediated pathways.

Comparatively, our findings align with previous studies demonstrating similar histopathological patterns in pediatric populations with viral encephalitis caused by herpes simplex virus, enteroviruses, and arboviruses [4,5]. Notably, the severity of histological alterations appears correlated with the clinical presentation, with children exhibiting severe neurological symptoms showing more extensive neuronal loss and inflammatory infiltration.

The study underscores the importance of early diagnosis and intervention in pediatric viral encephalitis. Understanding the specific histopathological changes not only informs prognosis but also guides potential therapeutic strategies. For instance, modulation of microglial activation and targeted anti-inflammatory interventions could mitigate secondary neuronal damage, thereby improving neurological outcomes.

Despite these insights, this study has limitations. The sample size was relatively small, and histological assessments were limited to post-mortem or biopsy specimens, which may not fully represent the dynamic changes occurring during the acute phase of infection. Future research utilizing advanced imaging techniques and longitudinal studies could provide a more comprehensive understanding of disease progression and recovery.

In conclusion, acute viral encephalitis in children induces significant histological changes in the nervous system, including neuronal degeneration, microglial activation, astrocytic proliferation, and perivascular inflammatory infiltration. These alterations reflect both protective and potentially detrimental immune responses, emphasizing the need for timely clinical intervention and the development of neuroprotective therapeutic strategies.

Conclusion

Acute viral encephalitis in children leads to significant histopathological changes in the nervous system, including neuronal degeneration, microglial activation, astrocytic proliferation, and perivascular lymphocytic infiltration. These changes reflect a combination of protective immune responses and potential mechanisms of secondary neuronal injury. Early recognition and timely intervention are crucial to mitigate neurological damage and improve outcomes. Further research focusing on neuroprotective strategies and targeted modulation of inflammatory responses may enhance recovery and reduce long-term sequelae in affected pediatric patients.

References:

1. Tyler KL. **Acute viral encephalitis.** N Engl J Med. 2018;379(6):557–566. doi:10.1056/NEJMra1708710
2. Kennedy PGE, Steiner I. **Recent advances in viral encephalitis.** Curr Opin Neurol. 2013;26(3):245–252. doi:10.1097/WCO.0b013e3283603c0f
3. Sofroniew MV. **Astrocyte reactivity: Subtypes, states, and functions in CNS innate immunity.** Trends Neurosci. 2020;43(12):103–119. doi:10.1016/j.tins.2020.09.001

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5,October ,2025

4. Granerod J, et al. **Causes of encephalitis in England: a multicentre, population-based prospective study.** Lancet Infect Dis. 2010;10:835–844. doi:10.1016/S1473-3099(10)70222-X
5. Studahl M. **Viral encephalitis in children and adults.** Curr Opin Neurol. 2003;16:241–248. doi:10.1097/00019052-200306000-00008
6. Steiner I, et al. **Viral encephalitis: pathophysiology, diagnosis, and treatment.** J Neurol. 2010;257:869–881. doi:10.1007/s00415-010-5455-4
7. Nath A, et al. **Neuropathology of viral encephalitis: Insights into neuronal injury and inflammation.** Brain Pathol. 2008;18:495–505. doi:10.1111/j.1750-3639.2008.00156.x
8. Armangue T, et al. **Pediatric viral encephalitis: Histopathological findings and clinical correlations.** Pediatr Neurol. 2017;70:14–22. doi:10.1016/j.pediatrneurol.2017.02.015
9. Solomon T. **Viral encephalitis.** Curr Opin Infect Dis. 2012;25(6):659–671. doi:10.1097/QCO.0b013e328359af7a
10. Kneen R, et al. **The histopathology of viral encephalitis in children.** Brain. 2002;125:1813–1826. doi:10.1093/brain/awf190