

# Neurological Complications of Primary Varicella Zoster Virus Infection in Children- Case Reports

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**Abstract:** *Introduction:* VZV is a human neurotropic alpha herpes virus, and humans are the only reservoir. Infection can involve any part of the nervous system. The incidence of neurological manifestations associated with VZV is 1-3 per 10,000 cases.

The clinical manifestations of varicella-zoster virus (VZV) infections of the central nervous system (CNS) include aseptic meningitis, encephalitis, cerebral infarction associated with granulomatous vasculitis, myelitis, and multiple cranial neuropathies.

The aim of this study, by reporting a series of 5 cases of chickenpox hospitalized in the Clinical Infectious Diseases Hospital from Constanta, is to demonstrate some of the neurological complications of varicella zoster virus infection in children, highlighting the importance in early recognition and prompt initiation of specific treatment.

*Case reports:* Two cases of acute post-infectious cerebellitis in children aged 7 and 9 years were hospitalized in our clinic.

The clinical picture presented by the 2 patients consisted of fever, headache, altered consciousness with coordination and gait disorders.

Other two cases of acute transverse myelitis, a 12-year-old boy, with onset in a febrile state at 9 days post varicella, initially with left knee pain associated with hypo-hyperaesthesia-like tenderness disorders, subsequently decreased lower limb muscle strength and bladder sphincter disorders. In the case of the second patient, the onset was on day 12 of evolution, with gait and balance disorders, with acute urine retention.

A fifth case, a 2-year-old child, hospitalized for altered consciousness with drowsiness, listlessness, photophobia and fever with suspicion of encephalitis.

Neither of the children didn't receive acyclovir from the onset of the rash.

*Conclusion;* Clinicians should be aware of the neurologic complications of VZV infection, because early recognition and initiation of acyclovir therapy is necessary for these disorders.

**Keywords:** Chickenpox, Neurological, Complications, Acyclovir, Corticosteroids.

## INTRODUCTION

VZV is a human neurotropic alpha herpes virus, and humans are the only reservoir. Infection can involve any part of the nervous system. The incidence of neurological manifestations associated with VZV is 1-3 per 10,000 cases. Both primary VZV infection (chickenpox) and VZV reactivation can cause various neurological manifestation, but usually neurological manifestations following primary VZV infection are uncommon (0.01-0.03%) [1].

Cerebellar ataxia and encephalitis are seen frequently; while transverse myelitis, aseptic meningitis, Guillian-Barré syndrome, rarely can be observed [1].

In the Clinical Infectious Diseases Hospital from Constanta, prior to the onset of the covid 19 pandemic, between 2016-2020 153 cases of chickenpox in children were hospitalized, neither of them presenting neurological complications. Between 2020-2023, 43 cases were hospitalized, of these 5 cases presenting with neurological complications, such as cerebellitis, transverse myelitis and meningoencephalitis.

The aim of this study, by reporting a series of 5 cases of chickenpox, is to demonstrate some of the neurological complications of varicella zoster virus infection in children, highlighting the importance in early recognition and prompt initiation of specific treatment. The cases discussed were admitted and managed by the infectious diseases specialists, in the department of children of the Clinical Infectious Diseases Hospital from Constanta, Romania, also the patients benefited from evaluation by a pediatrician neurologist specialist.

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### Case Reports 1 and 2 - Acute Cerebellitis

First we describe 2 cases of acute post-infectious cerebellitis in children aged 7 and 9 years old hospitalized in our clinic. Neither received antiviral treatment at home with Aciclovyr.

The clinical picture presented by the 2 patients consisted of fever, headache, altered consciousness with coordination and gait disorders.

In the case of the 9-year-old patient the onset of neurological symptoms was 10 days after the appearance of the varicella rash, and in the case of the 7-year-old patient the onset was after 7 days.

Cytological and biochemical examination of CSF at the time of diagnosis revealed clear, hypertensive CSF with negative Pandy reaction, 5 elements/mmc, with normal levels of proteins, chlor and glucose, with no possibility at that moment to test for the specific antibodies for VZV, or for AND of VZV in the CSF.

Neuroimaging investigations showed absence of morphological and signal abnormalities in the cerebral hemispheres and brainstem with normal ventricular system position and size.

Electroencephalogram (EEG) performed in one patient showed a pattern not interpretable for the actual brain pathology. During the hospitalization a pediatrician neurologist specialist observed the evolution, and concluded that the clinical appearance of the patients is in the context of the primoinfection with VZV.

The evolution of patients under antiviral treatment, intravenous acyclovir for 14 days and dexamethasone was favorable with remission of symptoms and without significant neuropsychological sequelae. A follow up after the discharge wasn't necessary, because of the complete remission of the symptoms.

### Case Reports 3 and 4 - Acute Transverse Myelitis

In the following we present 2 cases of acute transverse myelitis in 2 male patients, a 12-year-old and a 9-year-old. Their anamnesis revealed that neither of them received antiviral treatment at home. The first patient, a 12-year-old boy, with onset in afebrile state at 9 days post varicella eruption, initially with left knee pain associated with hypo-hyperaesthesia-like tenderness disorders, subsequently decreased lower limb muscle strength and bladder sphincter disorders. In the case of the

second patient, the onset was on day 12 of evolution, with gait and balance disorders, with acute urine retention. MRI cranio-cerebral with spinal cord segments were performed in both cases, with evidence of characteristic modifications - hyperintense intramedullary signal changes involving the cervico-dorsal segments of the spinal cord. CSF examination revealed moderate pleocytosis, 40 elements in the first patient and 90 elements in the second patient, with absolute lymphocytosis in both cases. The presence of the virus was demonstrated with PCR from the CSF that revealed the DNA of varicella-zoster virus. We didn't have the possibility in our laboratory to test for varicella-zoster antibodies from the CSF. Therapy consisted of intravenous Acyclovir, metylprednisolon in decreasing doses, with resolution of their neurological deficits, after 14 days of treatment with Acyclovir, and metylprednisolone was maintained in decreasing doses up till 28 days. The patients were observed by a pediatrician neurologist, who recommended the corticotherapy. The second patient, the 9 year old, was seen by the neurologist after one month from his discharge, the physical examination was normal, with a second MRI which showed resolution of the lesions.

### Case Report 5 - Encephalitis

A fifth case, a 2-year-old child, on day 8 from the onset of varicella rash with typical evolution until day 5. Hospitalized for altered consciousness with drowsiness, listlessness, photophobia and fever. Cerebrospinal fluid examination revealed 34 elements/mmc with predominantly lymphocytes with biochemistry within normal limits. A Multiplex Meningitis/Encephalitis Panel was performed which showed presence of DNA varicella-zoster virus. In this case a craniocerebral MRI was not performed, due to the impossibility of sedation and at the same time following the neurological examination it was decided that it was not necessary, the neurological examination being normal without deficits. Therapy consisted of intravenous Acyclovir for 21 days, cerebral depletives and dexamethasone with good evolution, the child being discharged after 25 days of hospitalization. The patient didn't present for his follow-up after one month from discharge, the parents informing us by phone of the child's good evolution.

### DISCUSSION

It is cited that common CNS complications of chickenpox are cerebellar ataxia and encephalitis, but also rare complications are transverse myelitis, aseptic meningitis, Guillian-Barri syndrome [2]. Complications

have usually a mild evolution, a good prognosis and very low mortality [3].

Cerebellar ataxia occurs in about 1 in 4000 varicella cases [1]. The frequent affected age for cerebellar ataxia is between nine- and six-years old children. The pathogenesis of the condition is not completely well known, it is described a direct viral invasion of the cerebellum, but also an immunological status is considered to have a role in the pathogenesis of ataxia. The replication of VZV in CNS is indicated by the presence of specific antibodies against VZV. CSF findings are usually normal, but with a mild percent of lymphocyte pleocytosis and increased content of protein may accompany the condition. The clinical presentation may include headache, vomiting, lethargy, stiffness in the neck and nystagmus. The majority of the patients improve within 1-3 weeks without any sequel [1, 5, 6].

In our study, the 2 cases with cerebellitis were children with age between 7 and 9 years old with clinical picture of fever, headache, altered consciousness with coordination and gait disorders. The onset of neurological symptoms was between 7 and 10 days after the appearance of the varicella rash. The examination of CSF revealed clear, hypertensive CSF with negative Pandy reaction, 5 elements/mm<sup>3</sup>, with normal levels of proteins, chlor and glucose, with normal neuro-imaging. The patients had a good evolution, the period of hospitalization was about 14 days.

The frequency of transverse myelitis during or after varicella infection is 0.3% [9]. The symptoms are typically bilateral sensory deficit at a given level, paraparesis, quadriparesis, motor weakness and abnormal bladder and rectal function. The pathogenesis of VZV myelitis has been thought as a result of direct viral invasion, because of findings of VZV particles in glial cells, and the virus was isolated from the spinal cord of patients [10]. Demonstration of the VZV antigen in CSF cells by immunofluorescence or isolation of VZV from the CSF is a confirmative evidence for viral central nervous system infection but it is rarely successful [11]. In the cases of our patients with acute transverse myelitis, the clinical appearance was mainly represented by ataxia and sphincter disorders. The CSF revealed a mononuclear pleocytosis, the presence of the virus was demonstrated with PCR from the CSF that revealed the DNA of varicella-zoster virus. The neuro-imaging revealed in the case of the patients with acute myelitis hyperintense intramedullary signal changes involving

the cervico-dorsal segments of the spinal cord, but also visible lesions in the brainstem-bulbar, in the case of the 12 years old patient.

The most serious CNS complications of varicella, encephalitis, has an incidence of 1-2 episodes per 10,000 varicella cases, with the highest incidence in adults and infants [1]. The role of active varicella-zoster virus (VZV) replications in the pathogenesis of chicken pox encephalitis is not yet defined. However, a significant role may play a possible direct viral cytopathology, also a post-infectious demyelination may be reported.

After a week from the exanthema appearance, fever, headache, vomiting, and change in general condition and convulsions may be present. The CSF findings pressure is increased with a mild to moderate degree of lymphocytosis, a slight degree of increased protein content and normal level of glucose. Mortality is approximately 5-10% while the ratio of convulsion between long-term sequels is 10-20% [1, 2, 4]. Our 2-year-old patient, had the neurological onset with high fever in the 8 day of the evolution of varicella. The diagnosis was sustained based on the examination of the CSF with the identification of the virus by PCR method. A CT scan was also effected with no modifications of edema.

Regarding the treatment, there are no established treatment regimens for the neurological complication of VZV infection. In this cases as soon as the diagnosis is considered, the antiviral therapy with intravenous acyclovir should be initiated according to some researchers [7].

The prognosis of meningitis is good, encephalitis and myelitis often result in sequelae, and a delay in the initiation of acyclovir treatment leads to a possible poor prognosis [8].

There is no evidence showing the therapeutic effect of adjunctive corticosteroid use, being known that the use of corticosteroids in immunosuppressive doses are contraindicated due to the risk of superinfections. However, it is cited the corticosteroids suppress the inflammatory response accompanied by cytotoxicity due to the host immune response to viral infection, and in cases of encephalitis/vasculitis, myelitis, and cranial polyneuropathy, the adjunctive administration of dexamethasone or steroid pulse therapy with acyclovir is recommended [8]. All our patients benefited from treatment with intravenous acyclovir, the dosage being

20 mg/kgc every 8 hours for 14 to 21 days, also corticosteroids, mainly dexamethasone 0,5mg/kgc and methylprednisolone in 0,5-1 mg/kgc, for 7 days in the case of cerebellitis and encephalitis, and 14 to 28 days in the case of myelitis.

## CONCLUSION

In the neurological complication of varicella zoster virus although considered rare, we see that in a short period of time compared to previous years, they can be noticed and is very important to be rapid recognised and treated by specialists.

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