



Bilateral Ptosis, Zosteriform Rash and Flaccid Bladder in a 10-Year-old boy

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Abstract

We present a case report of a 10-year-old completely immunized boy presenting with a 2-week history of bilateral eyelid drooping, fatigue followed by bladder and bowel paralysis. This was followed by the appearance of a vesicular painful and itchy rash which directed further diagnosis and treatment as it was consistent with a varicella reactivation rash. This case is a very important addition to the current body of literature on varicella-related neurological complications. It outlines that varicella reactivation can present in completely vaccinated, immunocompetent young children as a neurological syndrome affecting the autonomic nervous system primarily and the rash can occur a few weeks later after presentation of the neurological symptoms.

Keywords

varicella zoster virus (VZV), vaccination, neurological syndrome, immunocompetent, bilateral ptosis, case report

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Introduction

Varicella zoster virus (VZV) is a pathogenic and ubiquitous human alpha herpes virus which causes varicella (chickenpox), usually in children. It may become latent in the peripheral autonomic, sensory, and cranial nerve ganglionic neurons along the entire human neuroaxis.¹

Varicella is usually an uncomplicated exanthema with a pruritic vesicular rash; however, it can result in serious illness in children who are immunocompromised.² The most frequent neurological complication of varicella is encephalitis and acute cerebellar ataxia due to a post-infectious meningoencephalitis that is typical of VZV.³

Decades later, the virus may reactivate either spontaneously or after a number of triggering factors to cause herpes zoster (shingles). The most frequent and important complication of VZV reactivation is postherpetic neuralgia; however, activation of VZV may also cause vasculitis, encephalitis, segmental motor weakness and myelopathy, cranial neuropathies, Guillain-Barré syndrome, enteric features, and zoster sine herpette (ZSH).

Although rare, zoster has occurred in healthy children or young adults. Presumably, such infection is the result of a transient decrease in cell mediated immunity to VZV, perhaps caused by another viral infection.

Individuals who have received live attenuated varicella vaccines may still develop varicella after an exposure to the virus (either a person with varicella or one with zoster). Vaccinees who nevertheless develop varicella usually have mild cases with fewer vesicles and complications.²

This case study discusses a rare presentation of neurological manifestations of reactivation of varicella zoster virus presenting as bilateral ptosis associated with a complete paralysis of bladder and bowel function in a fully vaccinated child.

Case Study

A 10-year-old boy with a history of Attention Deficit Hyperactivity Disorder (ADHD) presented with a 2-week history of bilateral eyelid drooping, (Figure 1) intermittent double vision and fatigue. The eyelid droop was acute in

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Figure 1. Bilateral ptosis at the time of presentation to the neurology clinic.

onset. The double vision was transient and had resolved when the patient was evaluated in neurology. The patient also complained of an intermittent burning/itching sensation to the left forearm. He had mild changes in appetite, but no changes to urine or stool output, initially. The patient was afebrile and did not have any recent history of fever, diarrhea, abdominal pain, or head trauma. The patient's mother reported that the patient had a mild upper respiratory infection 1-week prior to the onset of the symptoms. There were no recent changes to his home medication namely Methylphenidate.

In the Emergency Department (ED), the neurological examination revealed reactive pupils and normal extraocular movements; however the patient had bilateral ptosis. The rest of the cranial nerves were normal. Strength, tone and reflexes were normal and sensory examination was normal. No rash was evident. His weight was 30 kg.

Initial investigation included CT of the head and MRI of the brain with and without contrast that were normal. Cerebrospinal fluid (CSF) studies including Enterovirus Polymerase Chain Reaction (PCR), Oligoclonal bands, Myelin basic protein and routine CSF analysis were obtained. Serum acetylcholine binding antibodies and anti-muscle specific kinase (MuSK) IgG antibodies were also drawn. An ice pack test was performed at bedside which was negative.

The patient was treated as ocular myasthenia gravis due to isolated bilateral ptosis and was sent home with pyridostigmine 30 mg every 6 hours, prednisone 15 mg every other day and famotidine.

The patient returned two days after discharge with complaints of eye pain following outpatient ocular dilation for ophthalmology examination and bilateral lower extremity pain. He received 3 doses of prednisone at 15 mg prior to his admission. He complained of persistent burning and itching of his left forearm, persistent bilateral ptosis and fatigue. Since he did not respond to the pyridostigmine and steroids, acetylcholine receptor antibodies were negative, and he was now having prominent sensory symptoms, Guillain-Barre Syndrome variant such as Miller Fischer

was considered in the differential diagnosis and he was admitted for treatment with intravenous immunoglobulins (IVIG).

During this admission, the patient developed mild ataxia and severe constipation. Anal manometry showed significantly decreased sensation suggesting a neuronal process. Simultaneously, he developed urinary retention with a complete loss of bladder sensation requiring intermittent catheterization. Physical examination showed a loss of anal wink, but did not reveal any loss of deep tendon reflexes. The strength in upper and lower extremities continued to be normal, reflexes were normal and there was no evidence of sensory loss. He now developed a pruritic rash on his left extensor elbow that spread to upper back and anterior chest over a course of a week. The rash initially was excoriated in appearance, but later became papular/vesicular in characteristic. He was started on gabapentin for bilateral leg pain.

Extensive evaluation throughout both admissions, including CT imaging of head, MRI of brain and total spine, MRI of lumbar spine (twice) and chest X-ray were normal. CSF studies were normal aside from 2+ oligoclonal bands. Antibody testing including MuSK, Ganglioside (GQ1B), anti-low density lipoprotein receptor-related protein antibodies (LRP4), extractable nuclear antigen 7 (ENA7), aquaporin 4 (neuromyelitis optica), myelin oligodendrocyte glycoprotein (MOG) and paraneoplastic antibodies were negative. A mitochondrial gene panel was inconclusive. Electromyography (EMG) and nerve conduction velocity (NCV) studies were performed twice identifying decreased amplitude over the bilateral facial nerves and absence of F waves from the bilateral peroneal nerves.

Rheumatology and infectious disease were consulted due to the rash (Figure 2). The rash was consistent with reactivation of varicella in the C8-T1 and C5-C6 dermatomes. The differential was reactivation of vaccine varicella causing a shingles like picture and subsequent demyelinating polyneuropathy predominantly affecting the Mueller muscles in the eyes and the bladder and distal bowel autonomic innervation.

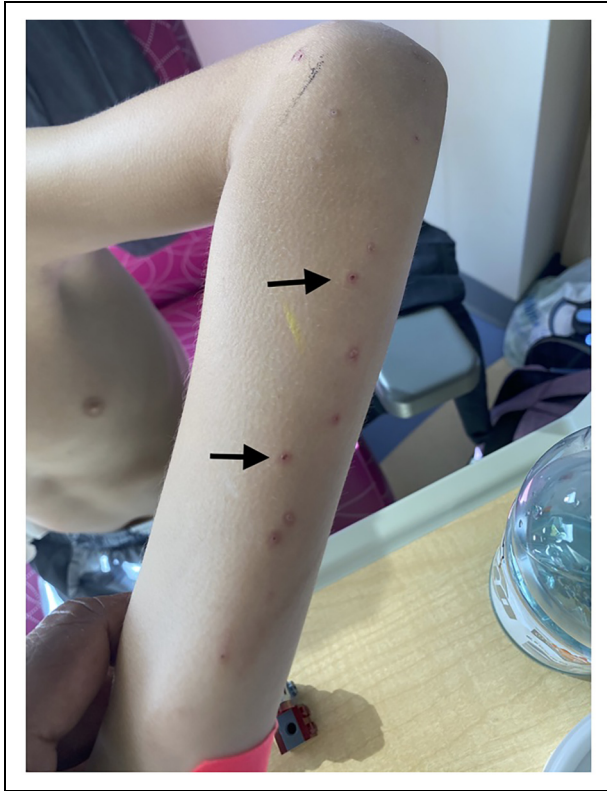


Figure 2. Zosteriform rash on the left forearm (black arrows).

The patient was started on intravenous acyclovir and a Zoster IgM was obtained. Ptosis completely resolved by the fourth day of acyclovir treatment with improvement in fatigue and ataxia. (Figure 3) However, the urinary retention and constipation persisted. Given the absent F waves and presence of oligoclonal bands that are often a marker of acute demyelinating illness in younger children⁴ as well as persistence of complete bladder and distal bowel paralysis, he received 3 cycles of plasmapheresis as immunotherapy.

Prior to discharge, his ptosis had fully resolved, ambulation was back to baseline and urinary retention and constipation had improved. During follow up at 4-months, he had regained partial sensation in his bladder and did not require urinary catheterization to urinate. Bowel sensation has also improved and he was able to defecate with some assistance of a laxative. Gabapentin was stopped as pain in his legs had resolved completely.

Discussion

This case is a very important addition to the current body of literature on varicella-related neurological complications. It outlines that varicella reactivation can present in completely vaccinated, immunocompetent young children as a neurological syndrome affecting the autonomic nervous system primarily and the rash can occur a few weeks later after presentation of the neurological symptoms.

The presentation of this case was baffling due to the late appearance of a rash with initial presentation of isolated bilateral

ptosis followed by gradual emergence of bladder and bowel retention indicating sacral parasympathetic involvement, but without motor involvement and without loss of deep tendon reflexes.

Bilateral acquired ptosis can be caused by neurogenic, myogenic, traumatic, aponeurotic and mechanical causes. Here, the differential included myogenic and neurogenic causes including myasthenia gravis, myotonic dystrophy, oculopharyngeal muscular dystrophy, GBS variant such as Miller Fisher syndrome, and rare neuro-metabolic disorders such as chronic progressive external ophthalmoplegia.⁵

In our patient, there was no involvement of the third nerve innervated extra ocular muscles, therefore the ptosis was related to weakness of the Muller muscles. This was confirmed by a detailed examination by a pediatric ophthalmologist. Mueller muscles (also called superior tarsal muscles) are innervated by post ganglionic fibers originating from the superior cervical ganglion. Fibers from the superior cervical ganglion can also carry varicella-zoster virus to the meninges to cause meningitis. Thus, the same virus pathway from the superior cervical ganglion may lead to both meningitis and/or ptosis.

Neurological problems like meningitis have been described in immunocompetent children related to varicella zoster reactivation after the child had chicken pox or had received immunization.⁶ Immunity to varicella-zoster virus may be waning sufficiently in some twice-immunized adolescents to make them vulnerable to varicella vaccine virus reactivation and subsequent meningitis.⁷ However, at this time, there is no consensus as to the explanation for cases of varicella vaccine meningitis in immunized and immunocompetent children.⁸

The appearance of rash almost 10 days after the neurological manifestations was another interesting feature in this case delaying the diagnosis. The child had received 2 doses of varicella vaccination at 1 and 5 years of age. We could not find any records of the site of vaccination.

The absence of rash has been reported in 24% of children presenting with varicella zoster reactivation related meningitis⁹ and has been reported in immunocompetent adults presenting with varicella related meningitis.¹⁰

Once the rash appeared, the clinical concern for a varicella zoster infection became stronger. Zoster IgM antibody was negative. However, the clinical features and the dermatomal distribution of the rash pointed towards this being consistent with a herpes zoster reactivation rash. Furthermore, the rapid response to acyclovir confirmed the diagnosis.

VZV reactivation is usually manifest by a painful dermatomal distribution vesicular eruption on an erythematous base, as well as unpleasant sensations (dysesthesias) produced by touch (allodynia). Rash and pain usually develop within a few days of each other, although pain can precede rash by weeks to months as in the case of our patient (preherpetic neuralgia).¹¹

It was originally thought that zoster in vaccinees mainly involved the vaccinated area of the skin. However, vaccinees who have received live attenuated varicella vaccine containing the Oka vaccine(vOka) strain of VZV may develop vOka-associated zoster in locations far from the vaccination site.¹²



Figure 3. Bilateral ptosis completely resolved by the fourth day of Acyclovir treatment.

This patient also experienced urinary retention and constipation with decreased sensation on anal manometry. Varicella induced bladder dysfunction in our case was caused by neuritis caused by sacral para-sympathetic involvement. Most cases reporting urinary dysfunction related to VZV are associated with a rash in the lumbosacral distribution^{13,14} unlike our case leading us to consider varicella induced immune mediated polyneuritis as a possible pathophysiology behind the presentation.

We feel that this is a unique case report of a 10-year-old immunocompetent vaccinated child presenting with serious neurological problems related to VZV vaccine reactivation. Varicella Zoster virus should be considered as a cause of unexplained neurological symptoms in the pediatric age group.

Author Contributions

The authors confirm contribution to the paper as follows: S.A and G.K conceived the study idea and design; S.A completed data collection; S.A and G.K performed analysis and interpretation of results; All authors contributed to the draft of the manuscript preparation and approved the final version of the manuscript.


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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

Trial Registration

Not applicable, because this article does not contain any clinical trials.

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