CASE REPORT

Recurrent herpes zoster related myelitis in an immunocompetent child


Abstract

Cases of varicella-zoster virus (VZV) myelitis have been reported in immunocompromised adults, but we report the rare occurrence of recurrent VZV myelitis in an immunocompetent child who initially developed myelitis with paraparesis after a right-sided T11-L1 distribution herpes zoster or shingles. Recurrent cervico-dorsal myelitis caused by VZV, five-and-a-half months later, was verified by the presence of new-onset clinical symptoms and signs, extensive spinal cord lesion on MRI and evidence of anti-VZV IgM antibodies in the serum.

Introduction

Herpes zoster is more common in the elderly and myelitis or myelopathy is a rare complication that usually develops in the immunocompromised host. We report a rare case of recurrent HZ related myelitis in an immuno-competent child.

Case history

An 11-year-old girl, reported to us with a one-and-a-half months history of weakness in all the four limbs with decreased sensation below the clavicles. Her history revealed that seven months prior to admission, she had developed a vesicular eruption over the T11 to L1 dermatomes on the right side of the body. The eruptions subsided within ten days of onset but were followed 4 days later by the development of an acute onset asymmetric paraparesis (R > L) along with sensory loss below the umbilicus (T11 level) and retention of urine for which she was catheterised. The illness evolved over 10 days and then remained static for the next two weeks. This was followed by a complete recovery over the next one month, without any specific treatment. Subsequently she remained asymptomatic and ambulatory for the next 2 months. Around 5 months after the onset of the initial problem she underwent surgery for right-sided nephrolithiasis under general anaesthesia, without any complications. One month post-surgery she developed an acute onset quadriplegiasis (lower limbs > upper limbs) which evolved over 7 days and was accompanied by decreased sensation below the clavicles (T2 level) but without any bladder or bowel involvement. There was no history of a preceding skin rash during this recurrent episode. The upper limb weakness started improving within a week and recovered significantly over the next 15 days, but the lower limb weakness persisted without much improvement over the next one month. Besides a history of chicken pox at 4 years of age, the past history was insignificant.

On examination at the time of presentation, her vitals were maintained. General examination was unremarkable except for the presence of hyperpigmented, healed scar marks on the skin over the T11 to L1 dermatomes on the right side (Fig. 1). There was no bony tenderness or

Fig. 1: Hyperpigmented, healed scar marks on the skin over the T11 to L1 dermatomes on the right side.

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deformity of the spine. On examination, higher mental functions and cranial nerves were intact. Tone was normal in the upper but increased in both the lower limbs. Power was grade IV/V in both the upper limbs, and grade II/V in both the lower limbs. All DTRs were brisk and plantars were bilaterally extensor, with retained abdominal reflexes. She had a 50% loss of sensation for touch and pain below the T2 spinal level, with bilateral impaired vibration and joint position sense.

Laboratory data revealed normal complete blood count, blood biochemistry, and connective tissue profile. Her HIV status was negative. X-ray chest, cervical and dorsal spine were normal. MRI of the cervico-dorsal spine revealed a hyperintense intramedullary signal involving the cord from C6 to D8 level on T2-weighted images and a post-gadolinium enhancement of the cord at the mid-dorsal level suggestive of myelitis (Fig. 2). CSF examination was essentially normal (no cells; protein - 46 mg%; sugar - 71 mg%). ELISA test for varicella-zoster IgM antibodies was negative in the CSF but positive in the serum, suggestive of a recent exposure to the virus. CSF-PCR for VZV-DNA was not done due to financial constraints.

A diagnosis of recurrent herpes zoster related myelitis was made. She was treated with oral acyclovir, 400 mg five times daily for 14 days and also given IV methylprednisolone pulse therapy in a dose of 500 mg/day for 5 days followed by tapering doses of oral steroids over a period of one month, with a significant recovery of 50% at one month post-treatment follow-up.

Discussion

Varicella-zoster virus (VZV) is an exclusively human, highly neurotropic, alpha-herpes virus. Primary infection causes chickenpox, after which the virus becomes latent in cranial nerve ganglia, dorsal root ganglia, and autonomic ganglia along the entire neuraxis. Decades later, reactivation of the latent infection can result in herpes zoster (HZ) with dermatomal vesicular rash or shingles, usually restricted to one to three dermatomes or zoster sine herpete (pain without rash). Neurological complications of HZ include: dorsal root or cranial nerve ganglionitis, post-herpetic neuralgia, segmental sensory loss or zoster paresis, polyradiculoneuritis, aseptic meningitis, meningoencephalitis, ventriculitis, leukoencephalopathy, vasculopathy, necrotising angitis, and transverse myelitis or myelopathy.

Usually, primary varicella is a disease of childhood, whereas its reactivation infection, herpes zoster is encountered in the aged with declining VZV-specific cell-mediated immunity. Of all patients with zoster, more than 66% are older than 50 years; fewer than 10% are younger than 20 years, and only 5% are younger than 15 years. Varicella in infancy can predispose to zoster earlier in adulthood. Our patient however had neither and was not immunocompromised but developed recurrent zoster-related myelitis.

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Around 25 - 40% cases of transverse myelitis are caused by viral infections. Myelitis or myelopathy however, is a rare complication of HZ that usually develops in the immunocompromised host. It was first reported by Hardy in 1876, but most subsequent reports have described either single or a few cases only. The reported frequency of transverse myelitis during or after varicella infection is around 0.3 to 0.8% only. Moreover, the occurrence of recurrent myelitis is rare and more so in the immunologically normal patients, as was the case with our patient. There are only a few case reports of recurrent VZV myelopathy developing weeks to months and even years after an initial episode of myelopathy in immunocompetent adults but none in childhood. McAlpine et al and O’Donell et al reported patients with recurrent myelitis associated with encephalitis and Nakano et al reported a patient with pure recurrent myelitis.

Onset of herpes zoster myelitis is usually acute or subacute with a mean delay of 2 weeks between the initial vesicular rash and the neurological disturbance. The temporal course is variable and the disease usually evolves over 1 to 3 weeks. Neurological symptoms usually begin unilaterally, ipsilateral to the rash, but subsequently...
become bilateral. Motor manifestations usually predominate, followed by spinothalamic and posterior column sensory abnormalities or bladder dysfunction. A self-limiting, monophasic, spastic paraparesis with or without sensory features and sphincter problems usually occurs in the immunocompetent patients. An insidious, progressive, and sometimes fatal myelitis is seen mostly in immunocompromised patients. A chronic or remitting exacerbating myelopathy may also be encountered.

The diagnosis of HZ myelitis is usually not difficult when the neurological symptoms develop in temporal proximity to the rash. It is however, important to remember that VZV myelitis may develop in the absence of a skin rash also. In our case, the first attack of transverse myelitis developed within 2 weeks of the appearance of the rash but the second attack occurred after a delay of five-and-a-half months and without a recurrence of the rash. Only a few cases of recurrent VZV myelitis without a preceding skin rash have been reported in the literature so far. No diagnostic test is completely accurate for VZV myelitis. Magnetic resonance imaging (MRI) is nonspecific and usually shows longitudinal enhancing cord lesions, in proximity of the involved dermatome. In our case however, the MRI during the recurrent attack of myelitis, revealed signal changes extending several segments above the initial site of the skin rash. CSF (cerebrospinal fluid) profile usually includes a mononuclear pleocytosis with normal or elevated protein. The diagnosis is confirmed by finding VZV-specific DNA or anti-VZV IgG in cerebrospinal fluid but the virus cannot usually be isolated from the blood or CSF. Evidence of active VZV infection is supported by any of the following positive tests: anti-VZV IgM in serum or cerebrospinal fluid; anti-VZV IgG in cerebrospinal fluid; VZV DNA in blood mononuclear cells or cerebrospinal fluid. In our case, ELISA test for Varicella-Zoster IgM antibodies was negative in the CSF but positive in the serum, suggesting a recent exposure to the virus.

The pathogenesis of VZV myelitis is unclear. Both, direct viral invasion of the cord and an abnormal immune response to the infectious agent involving allergic and vascular mechanisms have been implicated. Demonstration of the VZV antigen in CSF cells by immunofluorescence or isolation of VZV from the CSF is a confirmative evidence for viral infection of the central nervous system but is rarely successful. Pathologic and virologic analyses of the spinal cord from fatal cases has however, revealed frank invasion of VZV in the parenchyma and, in some instances, spread of the virus to adjacent nerve roots.

Previous neuro-pathological reports of HZ myelitis have reported findings of a necrotising inflammatory myelopathy with or without associated vasculitis. Demyelination has also been reported and may be secondary to viral infection and destruction of oligodendrocytes, since Cowdry type A inclusions have been detected in these cells. Pathological involvement in HZ myelitis is usually most severe in the dorsal root entry zone and posterior horn of the spinal cord segment corresponding to the involved dermatome with a variable spread both horizontally and vertically. The major neuropathological findings in 9/13 patients with HZ myelitis in a study by Devinsky et al, included posterior horn abnormalities in all 9 patients, demyelination in 6/9 patients, and vasculitis with necrosis in 4/9 patients. The spinal cord pathology suggests four principal mechanisms of injury: direct infection and/or immune-mediated destruction of oligodendrocytes with resultant demyelination; infarction secondary to vasculitis; leptomeningitis; and infection of other components including neurons, astrocytes, and ependymal cells.

Our patient is a unique and rare case of recurrent herpes zoster related myelitis in an immunocompetent child in which the first attack of myelitis followed the occurrence of shingles within 2 weeks but the second attack of myelitis occurred not only after a long gap of five-and-a-half months of the initial attack, but also at a site much higher than the initial site, and without a recurrence of active shingles. The first attack from which the patient recovered spontaneously, appears to be related to direct viral invasion of the spinal cord at the site of infection. Whether the second attack represents a recurrent active ascending viral infection of the cord or a delayed immune-mediated hypersensitivity reaction at a site distant from the primary site of infection remains debatable.

The spectrum of clinical outcomes in VZV myelitis ranges from spontaneous recovery to ascending progression and death. Rapid progression and flaccidity below the level of lesion carry a poor prognosis.

Antiviral drugs, can prevent multiplication and spread of the virus in the CNS and prevent or attenuate the evolving myelopathy. Treatment decisions about zoster should take into account the patient’s age and immune status. In immunocompromised patients, intravenous acyclovir (5 to 10 mg/kg three times daily for 5 to 7 days) is recommended. In immunocompetent patients age 50 and older, treatment with oral antiviral drugs – acyclovir (800 mg 5 times a day), famciclovir (500 mg three times a day), or valacyclovir (1g three times a day) is recommended for 10 - 14 days. In immunocompetent patients younger than age 50, antiviral drugs are not
required, but speed healing of the rash\textsuperscript{1}. Our patient was however given a course of oral acyclovir in view of the recurrence of myelitis.

Steroids have also been used for treatment, but the benefit is unknown and double-blind, placebo-controlled studies to confirm additional efficacy are also lacking. In certain cases it may be worthwhile to explore the use of corticosteroids under antiviral coverage\textsuperscript{2}. There is a case report of recurrent HZ myelitis resistant to acyclovir, responding to methylprednisolone pulse therapy\textsuperscript{1}. We also used methylprednisolone pulse therapy and oral steroids in our patient. Human interferon alpha has also been used to treat recurrent HZ myelitis\textsuperscript{12}.

In conclusion, our case exemplifies that physicians must maintain a high index of suspicion in atypical cases of myelitis. Moreover, early diagnosis and treatment of VZV myelitis with antiviral therapy is important to arrest the evolving myelopathy and prevent its recurrence.

References