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Case report

Two cases of viral meningitis – an unusual etiology

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1. Introduction

Meningitis is always a challenge for the physicians both to diagnose and treat. Their presentation may range from a benign, self-limiting disease to a severe medical emergency. Aseptic meningitis is the most common form of meningitis with an annual incidence of 11 per 100,000 cases. The proportion of cases caused by virus is found to be increasing as compared with bacterial meningitis.[1] Viral meningitis is usually self-limiting with a good prognosis. We, in this article, describe two case reports of viral meningitis with an unusual presentation and course of hospitalization.

2. Case report

A 71-year-old female presented to us in altered sensorium. Her son gave a history of fever, since 1 day, high grade and sudden onset, associated with chills, not accompanied by rashes. He also told us that the patient had stopped recognizing her relatives all of the sudden and that she started behaving in an abnormal way. She was a diabetic, hypertensive, hypothyroid patient with coronary artery disease. She had undergone coronary artery bypass grafting 5 years back and is on regular medications for all the aforementioned illnesses. On examination, the patient was conscious, drowsy but arousable; not oriented to time, place or person; febrile; tachycardic and normotensive with SpO_2 of 98% on room air. Her blood sugar was normal. Her central nervous system (CNS) examination showed no signs of meningism or any other focal neurological deficit, and her plantars were bilateral flexors. Her respiratory, cardiac and per abdominal examinations were normal. Her haematological and biochemical profiles were normal. The patient was started on intravenous ceftriaxone empirically. Magnetic resonance imaging (MRI) brain showed old lacunar infracts in the frontal lobe and parietal lobe, with no evidence of meningeal thickening, enhancement or basal cistern enhancement/ventriculitis or any parenchymal lesion. On the second day of admission, the patient developed vesicular eruptions behind her left auricle with a sudden-onset lower motor neuron–type facial palsy (Fig. 1). Lumbar puncture was performed, and cerebrospinal fluid (CSF) analysis showed 630 cells (98% lymphocytes) and a positive Varicella zoster virus (VZV) polymerase chain reaction. Viral copies were found to be 61,74,000 copies/ml. The patient was started on intravenous acyclovir at a dose of 10 mg/kg thrice daily and oral prednisolone (30 mg daily). She was also investigated for retrovirus disease which was negative. The patient improved sensorium wise with the aforementioned therapy; however, her facial weakness persisted. The patient denied any past history or contact history of chicken pox. Lumbar puncture was repeated after 2 weeks which showed a decrease in viral load. Acyclovir was continued till 21 days, and steroids were tapered off gradually.

The second patient is a 52-year-old female who presented to us with headache, severe, bilateral and not associated with aura, vomiting or double vision. The patient also gave a history of fever, low grade, since one week, on and off, with no diurnal variation and not associated with chills or rashes. She was diagnosed to have hypertension 2 months back and was started on oral antihypertensives. On examination, the patient was conscious, oriented, afebrile and normotensive with normal pulse rate and oxygen saturation. CNS examination revealed no focal neurological deficit or signs of meningism. Other system examinations were normal. Computed tomography head and MRI brain were performed before hospital admission, which were reported to be normal. Initial investigations after hospital admission showed normal haematological and biochemical parameters. Lumbar puncture was performed in view of severe headache not responding to analgesics. Routine CSF analysis showed 855 cells (80% lymphocytes), normal glucose (130.7 mg/dl) and protein (47 mg/dl). Rapid Biofire was used later on to identify the organism which came out to be positive for VZV. The patient was started on intravenous acyclovir 10 mg/kg thrice daily. The patient improved clinically, and her headache subsided. Retrogradely, the patient was enquired for past

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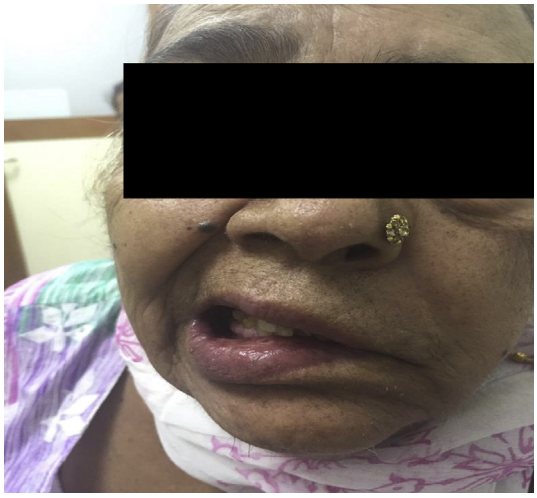

Fig. 1. Facial palsy of patient 1.

history or recent contact history of chicken pox, which the patient denied.

3. Discussion

VZV belongs to the herpes virus family that is known to cause human infections worldwide. There are two clinically distinct forms.

1. Primary infection, which results in a generalized vesicular rash.
2. Endogenous reactivation known as herpes zoster/shingles, which results in a localized rash.

The primary infection is generally self-limiting and is common in children. However, when occurring in adults, few complications are much more common than others. Neurological complications of this virus may be a part of the primary infection or a part of reactivation (Fig. 2).

3.1. Varicella zoster

Neurological complications of varicella infection itself are so rare that incidence is almost 1–3 per 10,000 cases.[2] This may be an effect of direct viral infection or an immune-mediated demyelination. As depicted in Fig. 1, acute cerebellar ataxia and encephalitis are the commonly seen complications.

Cerebellar ataxia is reported in about 1 of 4000 patients with VZV infection. Symptoms occur simultaneously with the rash, although sometimes they may precede or succeed it. They are known to occur as long as 2 weeks after the infection.[2] Nystagmus occurs in approximately 25% of cases, while other associated features included headache, vomiting and neck rigidity. Cerebellar involvement is usually self-limiting, and symptoms improve in 1–3 weeks. Presence of viral antigens or antibodies in the CSF suggests a direct viral infection of cerebellum. CSF is most often normal but may show lymphocytic pleocytosis (<100 cells) and mildly elevated proteins in 20–30% of cases.[3]

Diffuse cerebral encephalitis is one of the most serious complications of VZV infection. It is estimated to occur in about 1–2 patients per 10,000 cases.[4] Symptoms most often occur during the first week of appearance of rashes. There are no characteristic symptoms or signs that point towards VZV infection. Onset of these symptoms may be sudden or gradual with seizures reported in 29–52% of the patients with encephalitis.[5] Abnormal CSF finding include elevated CSF pressure, lymphocytic pleocytosis and mildly elevated proteins with normal glucose. Imaging of the brain shows areas of low attenuation consistent with demyelination.[6] Mortality occurs in 5–10% of patients with this complication.[7] Intravenous infusion of acyclovir is the treatment of choice in both the conditions.

3.2. Herpes zoster

VZV reactivation usually presents as painful vesicular eruptions that have a dermatomal distribution and may be associated with dysesthesias. It is common in elderly because cell-mediated immunity gets weakened, aiding the reactivation of previously latent virus.

Postherpetic neuralgia (PHN) is the most common neurological complication of the reactivated virus. Dermatomal distribution pain that persists three months after the infection constitutes PHN. There is no proper treatment guideline for this condition. In day-to-day practice, tricyclic antidepressants, gabapentin, pregabalin and topical lidocaine patches are commonly used for treating this severely painful condition. Percutaneous peripheral nerve field stimulation is a potentially promising treatment, which is being developed.[8]

VZV meningitis, encephalitis and cerebellitis have similar pathophysiology, and diagnosis is usually confirmed by demonstration of viral antigens or antibodies in the CSF. They may present with or without a rash.

VZV vasculopathy is due to progressive infection of the cerebral arteries that may present as a transient ischaemic attack or overt stroke. This condition is believed to be more common than described in literature, which reports a 30% increased incidence of stroke in patients with herpes zoster infection and a 4.5-fold increased risk in patients with ophthalmic-distribution zoster.[9,10] Nagel et al.[11] studied 30 patients with VZV vasculopathy and reported that rashes were seen in 63% of individuals, CSF pleocytosis in 67% and imagining abnormality in 97%. In their study, 50% of the times, both large and small arteries were affected.[11] This is one of the reversible causes of stroke, which is often missed because a zoster rash is absent in at least one-third of patients. Treatment involves intravenous infusion of acyclovir. There are reports of multifocal VZV vasculopathy which may resemble giant cell arteritis.[12]

VZV myelitis is another uncommon complication that occurs weeks after acute varicella reactivation. This so-called post-infectious myelopathy is self-limiting in immunocompetent individuals. Usually, nerve roots are involved which may result in spastic paresis with or without sensory abnormality. Steroids are used in the treatment of these patients although spontaneous recovery may also occur. In immune-compromised individuals, this condition is usually severe and sometimes fatal. The spinal cord may also be involved. MRI spine reveals a longitudinal serpiginous pattern in such cases. Diagnosis is confirmed by demonstration of viral antigen or antibody in both the scenarios. Treatment in severe cases should involve intravenous infusion of acyclovir.[13,14]

Zoster sine herpete is a condition in which radicular pain occurs in the absence of rashes. This is due to nerve root infection by the varicella virus or due to ganglionitis. There are reports of multiple patients with this condition in our literature. This is diagnosed again by demonstration of the viral antigen or antibody in the CSF. In case of ganglionitis, pathological and virological analysis of the ganglionic mass is warranted for the diagnosis.[15,16]

Multiple cranial neuropathies are another known complication after the zoster infection. They may occur several days after the zoster rash, sometimes even in the absence of rashes. Clinical

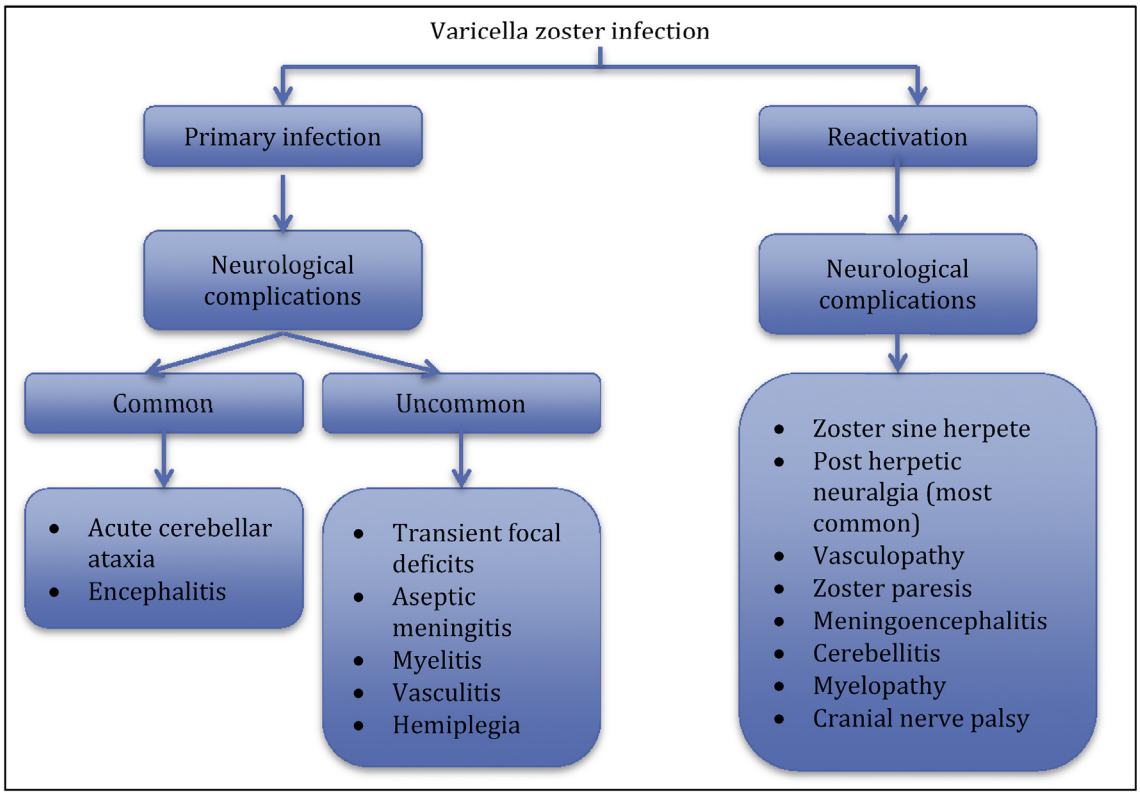

Fig. 2. Neurological complications of primary and reactivated VZV infection. VZV, varicella zoster virus.

presentation depends on the affected nerve. Diplopia and ophthalmoplegia occur in case of involvement of the third, fourth or sixth cranial nerves. Spontaneous tooth exfoliation and osteonecrosis may occur when the trigeminal nerve is involved, especially the maxillary and mandibular nerve. Ramsay Hunt syndrome is associated with tinnitus, nystagmus, sensorineural deafness and other symptoms of VIII cranial nerve involvement, along with lower motor neuron–type facial palsy. Lower cranial nerve involvement has also been described after the zoster infection.[8,16]

Optic neuritis and acute retinal necrosis are also some of the uncommon complications of VZV virus. In fact, VZV is the most common cause of progressive outer retinal necrosis, which is usually seen in people living with HIV/AIDS (PLHA). Treatment of this unusual condition includes ganciclovir, either as a monotherapy or in combination with foscarnet. This condition may also be preceded by other neurological complications of VZV such as aseptic meningitis, VZV vasculopathy or ophthalmic zoster.[17]

3.3. Prevention

Both varicella and zoster vaccines are live attenuated vaccines. Varicella vaccine is recommended in adults without any prior history of varicella infection and in PLHA with CD4 cell counts >200 cells/μl. It is administered as two subcutaneous doses (0.5 ml) 4–8 weeks apart. It can also be used in postexposure prophylaxis where a single dose is administered within 3–5 days of exposure. In the United States, zoster vaccine is recommended in elderly individuals (older than 60 years). It is administered in a single subcutaneous dose (0.65 ml). Trials show a 66% and 51% reduction in postherpetic neuralgia and herpes zoster, respectively, after the zoster vaccine.[18]

4. Conclusion

Most physicians readily recognize typical presentation of varicella infection. We present these two cases to create awareness among the physicians regarding the possibilities of some rare presentations. Irrespective of the puzzling and complicated nature of these presentations, we like to emphasize that they are completely reversible when a timely diagnosis is made.

Conflicts of interests

None.

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