Case Report

Acute Cerebral Venous Sinus Thrombosis: A Rare Complication of Primary Varicella Zoster Virus Infection

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Varicella-Zoster is a benign self limiting exanthematous illness in pediatric population which can rarely present with severe neurological manifestations such as cerebral venous thrombosis(CVT). We report the case of a 17-years old adolescent male with left hemiparesis, cranial nerve palsies associated with primary Varicella infection. MRI revealed cerebral venous thrombosis involving right transverse sinus, sigmoid sinus, internal jugular vein and infract involving right cerebral hemisphere, Midbrain and Pons. The patient responded well to Acyclovir, cerebral decongestants and oral anticoagulant therapy. CVT is a rare but the most life threatening complication following primary Varicella infection and early diagnosis is essential for proper management of the patient.

Keywords: Cerebral venous thrombosis, varicella zoster virus, vasculopathy

INTRODUCTION

Varicella zoster virus (VZV) causes primary, latent, and recurrent infections. Although often a mild illness of childhood, it can cause substantial morbidity and mortality in otherwise healthy children. Primary varicella infection causing venous infarct is very rare. We report a case of an adult boy with primary varicella infection who developed hemorrhagic venous infarct in the absence of hypercoagulable state.

CASE REPORT

A 17-year-old adult boy presented with a history of fever and headache for 8 days followed by altered sensorium and paucity of movements of left upper and lower limb for 2 days. The patient had a contact history of chicken pox from his younger sibling 10 days back. There was no history of seizures. Past history was not significant.

At admission, the patient was drowsy but responding to verbal commands. General physical examination revealed centripetal lesions with scabbing and normal vital parameters. On neurological examination, neck rigidity was present, and Kernig’s sign was positive. Pupils were equal and reacting to light. Fundus examination revealed bilateral papilledema. Right 6 and 7 nerve palsies [Figure 1] and left 9, 10, 11, and 12 cranial nerve palsies were present. The patient had dysarthria. Motor examination revealed left hemiparesis with muscle power of 2/5, loss of superficial reflexes, brisk deep tendon reflexes, and extensor plantar response on the left side.

His routine investigations, including complete blood count, blood sugar level, renal parameters, liver function tests, electrolytes, coagulation profile, and blood culture, were normal. Serology for human immunodeficiency virus, hepatitis B surface antigen, and anti-hepatitis C virus were negative. Antinuclear antibodies, antiphospholipid antibodies, protein C, protein S, antithrombin III, and homocysteine levels were normal. Cerebrospinal fluid (CSF) examination...
showed lymphocytic pleocytosis with 25 cells/mm³, mildly raised protein 70 mg%, and normal glucose level (48 mg%); CSF was negative for Gram and Ziehl–Neelsen stain, and the culture was sterile. Magnetic resonance imaging (MRI) revealed cerebral venous thrombosis, involving right transverse sinus, sigmoid sinus, and internal jugular vein, and infarct, involving right cerebral hemisphere, midbrain, and pons secondary to vasculopathy [Figure 2]. Varicella-specific immunoglobulin G (IgG) was positive in the CSF and the blood with reduced CSF or serum ratios of VZV IgG. CSF VZV deoxyribonucleic acid (DNA) by polymerase chain reaction (PCR) was positive. Ultrasound Doppler of lower limbs was normal. Chest radiograph and two-dimensional echocardiography were normal.

The patient was treated with cerebral decongestants consisting of intravenous 20% mannitol and dexamethasone. Injection acyclovir was administered at 10 mg/kg for 10 days. Injection low-molecular-weight heparin was started for 10 days, followed by oral anticoagulation with warfarin, which was continued for next 12 weeks to maintain international normalized ratio between 1.5 and 2.5. The patient started recovering gradually over the next few days with improvement in sensorium and left hemiparesis. No history of worsening of symptoms or any bleeding manifestations was observed. After 6 months of treatment, the patient improved well, and he is on regular follow-up with monitoring of coagulation parameters.

**DISCUSSION**

Varicella is a highly contagious disease of childhood,[1] with neurological complications following both primary infection and reactivation of VZV, including encephalitis, aseptic meningitis, transverse myelitis, acute cerebellar ataxia, Reye’s syndrome, Ramsay Hunt syndrome, ventriculitis, meningoencephalitis, and rarely stroke,[3] which are reported in less than 1% cases.[3] Primary VZV infection can cause vascular thrombosis approximately 6 weeks after primary infection. Arterial stroke is a recognized complication of VZV infection but occurrence of venous stroke has been very rarely described in the literature.

Unifocal large-vessel vasculopathy (granulomatous arteritis) usually affects immunocompetent patients, whereas multifocal vasculopathy occurs primarily in immunocompromised patients.[4-6] The pathogenesis behind this is considered to be a productive viral infection in the cerebral arteries, as evident by the histological evidence of granulomatous inflammation and stenosis of the involved cerebral arteries.[1]

The exact pathogenesis of varicella cerebral venous sinus thrombosis (CVST) is still not known but presumed to be similar to VZV arteriopathy. Afferent fibers from trigeminal and other ganglia to both intracranial and extracranial blood vessels provide an anatomical pathway for the transaxonal spread of virus, thereby infecting meninges and venous sinuses of brain.[7] The damage to venous sinus and consequent CVST can be due to direct endothelial damage by virus, thrombosis secondary to acquired protein S deficiency, immunologically mediated vasculitis, and underlying hypercoagulable state.[7,8] Moreover, people with prothrombotic conditions are shown to be prone to develop thrombosis after having any systemic infection, especially in children.[9,10]

Virological confirmation of VZV-associated cerebral vasculopathy includes CSF analysis for both VZV DNA and anti-VZV IgG antibody. Although a positive PCR for VZV DNA in CSF is helpful, a negative PCR does not exclude the diagnosis.[7]

Our case developed CVST in the stage of primary infection itself and had no risk factors for cerebral venous
thrombosis. VZV DNA was positive in our patient with positive Serum and CSF IgG but with reduced CSF/serum ratios of VZV IgG. These patients require antiviral treatment and symptomatic treatment with heparin and oral anticoagulants. Our patient had remarkable improvement with the aforementioned treatment.

**Conclusion**

CVST is a rare neurological complication associated with primary VZV infection. Early diagnosis of VZV-associated cerebral vasculopathy includes CSF analysis for both VZV DNA by PCR method and anti-VZV IgG antibody measurement. As the management of venous stroke is different than arterial stroke, a high degree or suspicion for venous stroke should be kept after primary VZV infection.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Figure 2:** Magnetic resonance venogram of the patient showing sagittal sinus, sigmoid sinus, and transverse sinus thrombosis
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Conflicts of interest
There are no conflicts of interest.

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