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VENOUS STROKE SECONDARY TO VARICELLA ZOSTER VIRUS INFECTION

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ABSTRACT:

This is a case of cerebral venous sinus thrombosis (CVST) as a rare complication of varicella Zoster infection. A young male with no significant medical history presented with generalized tonic clonic seizures preceded by vesicular rash on the face diagnosed as Varicella zoster infection. The MRI showed bilaterial superficial hemorrhagic infarcts involving frontal and temporal lobes and MR Venogram was consistent with extensive CVST involving superioir sagittal, right transverse and superficial veins. After initial treatment with antiepileptic and anticoagulant, he showed marked improvement in symptomatology and made complete recovery subsequently with recanalization of sinuses seen on a follow up MRV done at fourth month. Our case emphasizes on having a high suspicion of Varicella Zoster infection in patient who presents with CVST with an underlying ongoing Rash or a prior history of recent body Rash.

CASE PRESENTATION

A 36 years old previously healthy male with no co-morbids and no significant past medical history, presented to a local hospital ER with new onset seizure. He had a history of vesicular rash involving multiple dermatomes 2 weeks ago. During the illness he developed high grade intermittent fever up to 102 ˚F along with severe diffuse headache. He was treated conservatively with antipyretics and was discharged home. In the second week of his illness, he suffered three brief episodes of generalized tonic clonic seizures. He was taken to ER where he was given intravenous Diazepam and loaded with Leviteracetam.
On general physical exam the patient had cutaneous lesions that was partly crusting, was diagnosed as “shingles” by our infectious disease expert. On neurological examination he was drowsy and disoriented with right hemiparesis. Brain MRI showed bilaterial superficial hemorrhagic infarcts involving frontal and temporal lobes and MRVenogram showed extensive CVST involving superioir sagittal sinus, right transverse sinus and superficial veins. The laboratory investigations revealed a high Total Leukocyte Count (20.8 x109). Liver function tests, hepatitis B and C serology, cerebrospinal fluid (CSF) analysis were all within normal limits. Polymerase chain reaction tests for Herpes simplex virus (HSV) Mycobacterium tuberculosis and, India ink stain, cryptococcal antigen and bacterial cultures of CSF were negative. CSF showed presence of IgG varicella antibodies. Protein C and S levels were normal but serum homocysytiene level was elevated (32 mc moles/L). He was given intravenous Acyclovir with adequate hydration and was continued on oral Levetiracetam. He was started on low molecular weight heparin (1 mg/kg SQ every 12 hours). His general condition improved gradually. He became afebrile and the cutaneous lesions continued to crust. His headache disappeared and no seizure recurrence was observed. He became alert and oriented while hemiparesis improved. A follow up MRI showed recanalization of venous sinuses after 4 months with no lesions in brain parenchyma. He was continued on anticoagulation for 3 months with an unremarkable course of recovery.

DIAGNOSTIC AND TREATMENT ALGORITHM

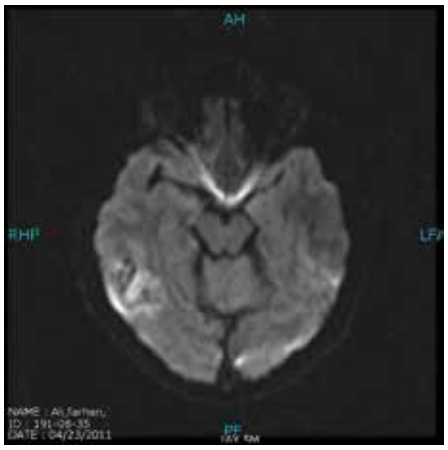
Stroke and CVT is a well-known complication of VZV. It must be suspected in all patients with typical skin lesions and neurological findings especially focal neurological deficits. Brain imaging is a must preferably contrast MRI and MR venogram. Meningoencephalitis is not uncommon in patients with neurological involvement. A lumbar puncture should be done unless contra indicated in all patients. Cerebral VZV infection can be identified by IgG antibodies against VZV. Many

diagnostic kits (for example Biofilm array) include VZV in their panel for meningoencephalitis. If not included in panel, it could be ordered separately. These antibodies are considered diagnostic for cerebral VZV infection.
VZV infections are effectively treatable with acyclovir IV(10 mg per kg three times a day) for 10-14 days. CVT is treated with anticoagulation (Low Molecular weight heparin) for 3-7 days followed by oral anticoagulation. Newer anticoagulants are currently preferred choice for long term anticoagulation as compared to warfarin. In the absence of any hypercoaguable state most patients require 3-6 months anticoagulation. Seizure are treated with anti-epileptic drugs for six months or more. Most patients with acute CVT and seizures do not require long terms (2-23 years) AEDs.

DISCUSSION

Varicella Zoster virus (VZV) is known to cause a benign self-limiting exanthem in children rarely with any neurological manifestations. However, with increasing incidence of VZV in adult population, severe neurological manifestations have been reported with cerebellar ataxia and encephalitis being the most common. VZV is also associated with cerebral vasculopathy including cerebral artery stenosis, vasculitis, large artery disease, aneurysm, subarachnoid hemorrhage and cerebral venous sinus thrombosis (CVST) [1]. Venous thrombosis secondary to VZV is rare and may occur both during primary infection as well as reactivation of virus. Patel et al. report the case of a 25-year old male with recent history of VZV infection presenting with severe throbbing headache and status epilepticus. CT revealed significant thrombosis in left transverse, straight and sigmoid sinuses confirming the diagnosis of CVST [2]. Headache and seizure history were also present in our case. Siddiqi et al. described two cases of CVST associated with VZV in protein C and S deficient patients [3]. Other cases of CVST associated with VZV have also been reported in literature and one patient was reported to have both CVST and pulmonary embolism secondary to VZV due to widespread thrombosis [4-6]. VZV associated cerebral venous sinus thrombosis is attributed to blood vessels providing an anatomic pathway for virus to spread, direct endothelial damage by the virus hence provoking thrombosis. There also has been a temporal link postulated between development of skin lesions and thrombotic complications. The latency period of 2-3 weeks is the time during which endothelial damage occurs leading to a widespread thrombotic process [4]. Patients with a pro-coagulant state like protein C and S deficiency and raised homocysteine level have also shown high occurrence of thrombosis [3]. In VZV vasculopathy patients may not always have VZV DNA in cerebrospinal fluid (CSF) but diagnosis can be confirmed with anti-VZV antibodies in CSF [2]. Our patient not only had high homocysteine levels making him more susceptible to CVST, but also showed presence of IgG varicella antibodies in CSF. This report provides an insight into rare manifestations of varicella infection in adults. Studies investigating the possible mechanism of development of CVST would allow for improved management and therefore better outcomes in these patients.

Figure 1; FLAIR image of brain showing right temporal hemorrhagic infarct



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Asma Akbar Ladak; data collection, data analysis, manuscript writing, manuscript review
Salman farooq; data analysis, manuscript writing, manuscript review