CASE REPORT

Varicella zoster meningoencephalitis without exanthem: immunocompetent host

Shafaq Saleem[1], Hafiz Muhammad Motsim Tariq[2]

Abstract

In an immunocompetent person, varicella zoster virus (VZV) is an uncommon cause of aseptic meningoencephalitis. Reactivation of the latent varicella zoster virus from nerve infection results in shingles, a condition marked by rash, intense pain, and dermal involvement in immunocompromised hosts. We present an unusual case of a 22-year-old immunocompetent male diagnosed as VZV meningoencephalitis without exanthem. Workup revealed no risk factors for contracting VZV nor was there any childhood history associated with it. The patient responded to the treatment given and became symptom-free thereafter.

Keywords: Varicella meningoencephalitis, Aseptic meningitis, Acyclovir, Immunocompetent, Varicella vaccines.

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Introduction

Encephalitis can be caused by several viruses including HSV 1, arboviruses, and enteroviruses. Neurological complications of VZV includes nerve palsies, maculopathy, vasculopathy, myelopathy, cerebellitis, meningoencephalitis, and radiculopathy without rash. The complications of VZV in the absence of rash is difficult to diagnose and a challenge to healthcare professionals.[1,2] Encephalitis is a rare complication of VZV infection; however, it is more commonly reported in immunocompromised patients.[1,3] Presentation without rash commonly involves individuals in an immunocompromised state. Most common VZV-associated meningoencephalitis are associated with rash or more frequently occurs after post-herpetic neuralgia. Varicella zoster virus along with causing aseptic meningitis and meningoencephalitis can also lead to vasculopathy which can manifest as ischaemic strokes or haemorrhagic infarcts, aneurysms, arterial ectasias, and carotid dissection.[1] Immunocompromised status like diabetes, asplenism, HIV, steroids, chemo-radiotherapy, extremes of age, head trauma, IV drug use are all predisposing factors for atypical presentations of Varicella zoster virus.[1] However, in an immunocompetent individual, varicella zoster encephalitis is an uncommon presentation. Despite being an uncommon diagnosis, recently cases involving immunocompetent patients are increasing for which physicians are using high-sensitivity molecular panels to confirm the diagnosis; in Pakistan such high-cost laboratory tests are not readily available, which delays the diagnosis and treatment of this treatable condition. Here, we report a unique instance of acute meningoencephalitis in a healthy adult male without cutaneous lesions or dermal neuralgia related to VZV.

Case scenario

We present the case of a 22-year-old student of master's programme who presented to the emergency department, Aga Khan University Hospital, Karachi, on November 2022, with complaint of high-grade fever and vomiting for three days. This was followed by altered sensorium on the day of presentation. The patient had visited a farmhouse where he went swimming. Later, the same day he developed symptoms. Two days later, the patient developed altered sensorium progressing to drowsiness. No clinical seizure was witnessed. Headache was continuous, generalised throbbing which was partially relieved by painkillers. He has no prior history of developing varicella exanthem. Medication history was significant for receiving treatment with Cefixime and Paracetamol for the current symptoms. The patient denied any use of illicit drugs or addictions. He had chicken pox in his childhood which was resolved without any treatment.

On examination, the young male was agitated, disoriented, and was not following commands. His pupils were 2mm bilateral equally reactive, while extraocular movements were normal. Cranial nerve examination was unremarkable. His speech was coherent though confused, neck was rigid, but range of motion was

[1]Department of Neurology, Aga Khan University Hospital, Karachi, Pakistan; [2]Department of Anaesthesiology, Aga Khan University Hospital, Karachi, Pakistan.

Correspondence: Hafiz Muhammad Motsim Tariq.

Email: hmotsimtariq@gmail.com

ORCID ID: 0009-0004-0716-5411

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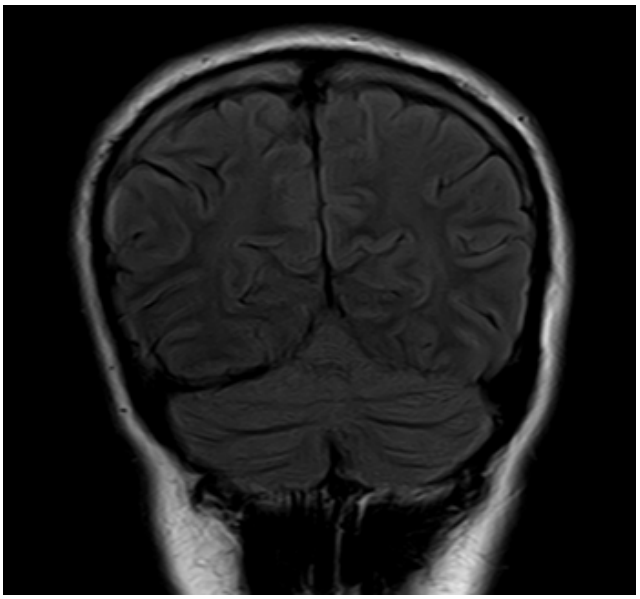

Figure-1: MRI of the brain without contrast, coronal section showing normal white and grey matter differentiation with no meningeal enhancement

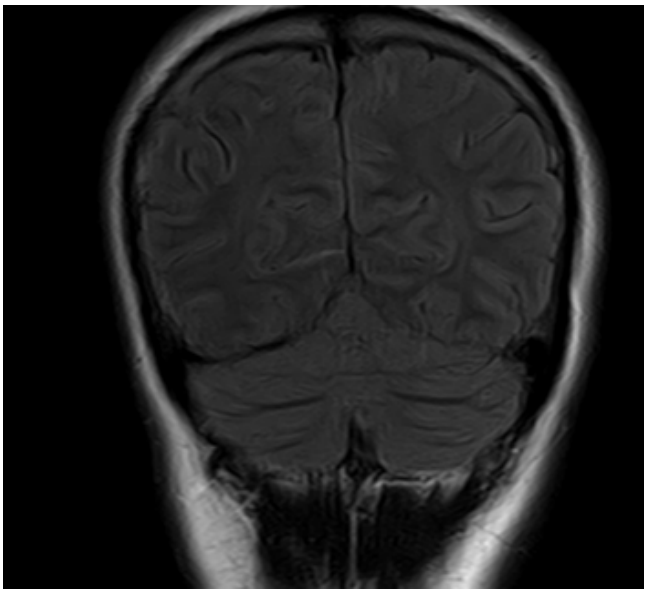

Figure-2: MRI brain post contrast FLAIR coronal section showing subtle meningeal enhancement right parieto-occipital parasagittal sulcus

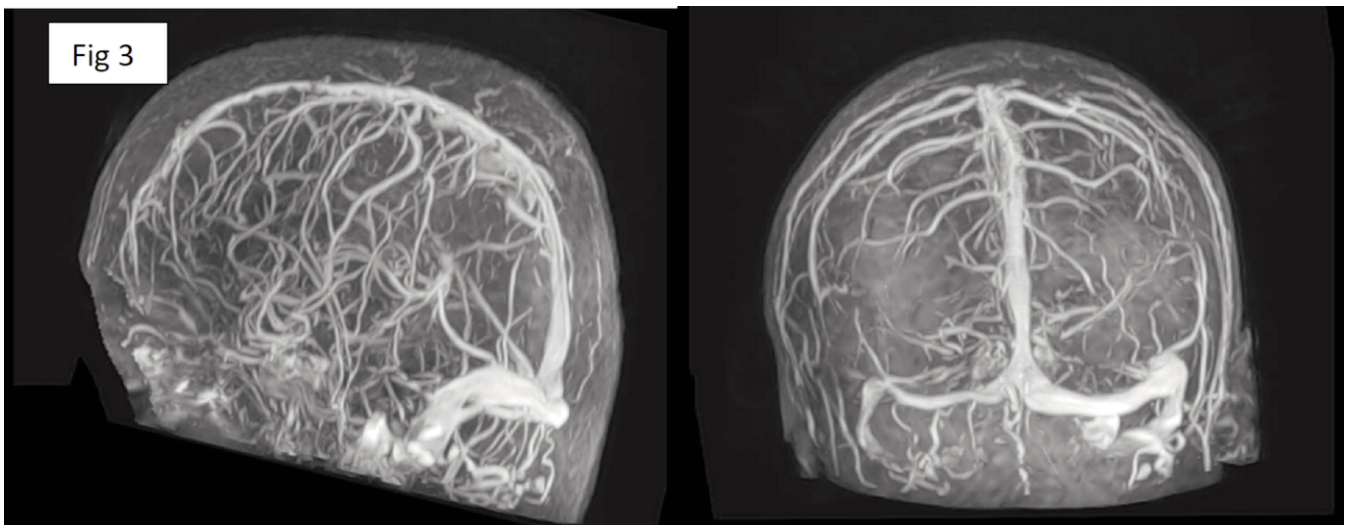

Figure-3: Post contrast images of MRV showing no filling defect in dural venous sinuses to suggest sinus thrombosis.

normal. Kernig's and Brudzinski's signs were negative. Power was 5/5 on MRC (Medical Research Council) scale in all four limbs. Babinski was negative. No body exanthem or vesicular eruption was seen. On arrival, his vitals were within normal limits. The rest of the systemic examination was unremarkable.

He was given IV Tramadol 50mg, IV Nalbuphine up to 10mg, Midazolam 5mg and was started empirically on IV Ceftriaxone 2 gram q12hourly and IV Acyclovir 750 milligram q8hourly and Vancomycin 750mg q8hourly in meningitis doses and Ampicillin. CT of the head was unremarkable. Later, MRI of the brain with contrast showed meningeal enhancement along right parieto-occipital sulcus (Figures 1, 2, 3)

He was shifted to the neurology special care unit. Complete blood count, electrolytes were within normal range (Table 1). His lumbar puncture was performed after getting informed consent. CSF DR showed lymphocytic pleocytosis. Bio fire film showed growth of varicella zoster virus (Table 2). His ECG showed left ventricular hypertrophy, so his echocardiography was done which was normal. To rule out immunocompromised status his HIV and VDRL were done which were negative, his urine toxicology was negative. The infectious disease

Table-1: Baseline Laboratory and specific Investigations.

Investigation	Result	Normal Value
Haemoglobin	13.2	(12.3-16.6) g/dl
Total leucocyte Count Neutrophil'sLymphocytes	15.1 (N= 72%) (L=19.0%)	(4.8-11.3) * 10E9/L(34.9-76.2) %(17.5-45) %
Platelets	309,000	(154-433) * 10E9/L
Creatinine	1.1	(0.9-1.3) mg/dl
Sodium	140	(136-145) mmol/L
Potassium	3.5	(3.5-5.5) mmol/L
Chloride	104	(98-107) mg/dl
Bicarbonate	27.3	(20-31mmol/)
Procalcitonin	0.052	<0.5ng/ml low risk for sepsis>2.0 ng/ml high risk for sepsis
C reactive protein	0.70	0-10 mg/L
INR	1.0	0.9-1.2
Hepatitis viral markersHepatitis B Ag:Hepatitis C Ab:	negative Negative	
HIV	Not reactive	
VDRL/RPR	Non-reactive	
Urine Toxicology	Negative for amphetamine, benzodiazepine, opiates, cannabinoids, barbiturates, cocaine	negative
Blood Culture	No growth	No growth
Covid-19 PCR	Negative	negative

Table-2: Cerebrospinal Fluid (CSF) Results.

Investigation	Result	Normal Value
CSF Opening Pressure	20	5-25 cm H2o
CSF Glucose Blood glucose (after lumbar puncture	64 123	(40-70)
CSF Protein	178	(15-40)
CSF Leucocyte count	0.326 (N=05%) (L= 95%)	(0-0.005) N= 0.000 L= 100%
CSF culture		No growth
CSF bio fire		Varicella zoster detected

CSF Bio fire Film Array: negative for Naegleria Fowleri E. coli, Haemophilus Influenzae, Listeria monocystogenes, Neisseria meningitidis, Streptococcus Pneumoniae, streptococcus agalactiae, cytomegalovirus, enterovirus herpes simplex virus 1, 2, HHV 6, human parechovirus, cryptococcus neoformans

Medical abbreviations:

- VZV : Varicella zoster virus
- HSV : Herpes Simplex Virus
- HIV : Human Immunodeficiency Virus
- HHV : Human Herpes Virus
- IV : Intravenous
- VDRL: Venereal disease research laboratory test; Syphilis
- N : neutrophills
- L : lymphocytes
- CSF : Cerebrospinal Fluid
- CNS : Central Nervous System
- PCR : Polymerase Chain Reaction
- MRC : Medical Research Council
- CT : Computerized Tomography
- ECG : Electrocardiogram
- MRI : Magnetic Resonance Imaging
- Q8hourly: every 08 hourly
- Mmol/L: millimole per litre
- Mg/dl : milligram per decilitre
- Gm/l : gram per litre

department was taken on board for antibiotics adjustment, Ampicillin and other antibiotics were stopped, hyperosmolar therapy was tapered off and then stopped. He was shifted out from special care after two days and kept under observation in the ward. The patient showed improvement in symptoms over the course of the hospital stay. He was discharged after a stay of four days on IV Acyclovir 750mg q8hourly for a total of 14 days duration. On outpatient follow-up visit after one week, he showed complete improvement; currently, the patient is completely healthy and fine.

Discussion

Varicella zoster, pure neurotropic virus has recently shown an increase in diagnosed meningoencephalitis cases with the advent of detecting VZV DNA by real time PCR techniques. VZV rarely causes meningoencephalitis without exanthem in immunocompetent patients with a prevalence as low as 0.5 %.[1] Reactivation of latent virus in ganglia leads to various clinical symptoms of dermatomal shingles, meningitis, cranial nerve palsies, and ophthalmic involvement. This commonly occurs in patients who are immunocompromised secondary to post transplant, HIV positive patients,[2] correlating with prior history of chickenpox early in life.[3] Primary neurological involvement without dermatological manifestations is a

rare presentation posing diagnostic challenge to clinicians. In a study conducted in Brazil, immunocompetent patients diagnosed as VZV meningitis develop rash five days after meningism.[2,3] We report an unusual case of primary varicella meningoencephalitis without skin rash in an immunocompetent host with no prior history of varicella infection.

Nonspecific wide spectrum of neurological disease manifestations including altered mental status with drowsiness, irrelevant talk, headache, seizures, and focal neurological signs are commonly seen.[2] Senthilkumar U in his article mentioned seizure as an atypical presentation of aseptic VZV meningoencephalitis.[1] Pasedag T et al also highlighted a case of VZV encephalitis in an immunocompetent host with CSF picture disguising as bacterial picture.[4]

CSF testing remains crucial in diagnosing CNS infections. New diagnostic methods have led to more positive results and awareness among physicians. Raised protein with lymphocytic finding (aseptic meningitis) has been a common finding. High opening pressure with false localising sixth nerve palsy has also been reported.[5,6] Amplification of viral DNA or presence of IgG antibody in CSF confirms infective aetiology.[7] Infection spread is not just localised to meninges but can also involve vessels. Imaging showing vasculitis and vasculitis infarcts has also been reported. Aneline-Lefond C in her article has highlighted vasculopathy in both small and large vessels leading to vasculitic infarcts. White matter ischaemic and demyelinating lesions often occur. Though in majority of cases brain imaging do not show characteristic findings.[8,9] Vasculopathy with vasculitic infarcts is also a disease sequelae. Large vessel involvement can also occur without stroke with rarest manifestations with intraventricular haemorrhage and subdural haemorrhage.[6] However, literature has not yet identified any characteristic findings specific for VZV encephalitis.[10] Diagnosis still relies on growth of VZV on PCR testing.

Treatment of infection with Acyclovir results in complete neurological recovery.[11] Recovery in immunocompromised patients, such as HIV positive patients, has a survival rate of 63%.[2] However, they frequently suffer neurological sequel aseptic meningitis, encephalitis with vasculitis, ventriculitis, leukoencephalopathy.[2]

Conclusion

In conclusion, Varicella zoster virus previously known for reactivation of virus in immunocompromised states with and without rash, can also manifest as primary neurologic meningoencephalitis without preceding or anteceding exanthem. Patients presenting with encephalitis and meningitis should have their CSF tested for VZV even in the absence of risk factors as prompt treatment can favour good prognosis. Thus, institutions and laboratories testing for lumbar puncture results should include test VZV in their routine panel among suspected meningoencephalitides.

Consent: Consent of patient for publication of his case report was obtained as a written document.

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Authors' Contribution:
SS: Idea, literature search, final approval and agreed to be accountable for all aspects of the work.

HMMT: Literature search, writing, drafting and agreed to be accountable for all aspects of the work.