

# Unusual Presentation of *Varicella zoster* Virus Meningitis – Role of Molecular Rapid Diagnostics in Diagnosis and Antimicrobial Stewardship

Sir,

Viral meningitis may remain a diagnostic enigma without molecular techniques. Rapid molecular FilmArray assays are the great advancement for the diagnosis of difficult-to-grow pathogens such as viruses and thus can become a big tool in antimicrobial stewardship. We are reporting a case of unusual presentation of *Varicella zoster* meningitis which was diagnosed rapidly using molecular FilmArray assay which is based on syndromic approach covering various bacteria, viruses, and fungi in a single run rather than the detection of different pathogens using conventional/real-time polymerase chain reaction (PCR) assay.

A 24-year-old female medical student presented at our institute with severe throbbing, hemicranial right-sided headache with recurrent vomiting for 1 week. Initially, headache was mild, nonthrobbing, and without any accompaniments. After 3 days, headache worsened in severity and was localized to the right side and was associated with recurrent vomiting. The patient experienced a transient episode of facial asymmetry, dysarthria, and difficulty in holding objects with the right hand which lasted for 8 h. The patient was admitted to a local hospital where noncontrast computed tomography head revealed normal study, and the pain was relieved with nonsteroidal anti-inflammatory drugs. The patient continued to have severe headache with periodic exacerbations and vomiting, for which she was brought to our institute. On examination, the patient was conscious, lethargic, and photophobic. Blood pressure and pulse rate were normal. There was no fever, rash, pallor, cyanosis, and edema. Nervous system examination showed no focal neurological deficit and fundi were normal. Neck rigidity was not observed, and meningeal signs were absent. Cardiovascular, respiratory, and abdominal systems were also found to be within normal limits. There was no history of diabetes mellitus, hypertension, and tuberculosis. There was a history of needle prick injury from a sharp used on a HIV-infected patient 3 months prior, for which the patient took postexposure prophylaxis for 6 weeks. Her complete blood cell counts, liver function test, kidney function test, and thyroid function tests were within normal limits. Hepatitis B virus surface antigen, Hepatitis C virus antibodies, and HIV-I and II virus antibodies were nonreactive after 3 months. Cerebrospinal fluid (CSF) examination showed normal opening pressure, total leukocyte count 385/mm<sup>3</sup> (neutrophils 5% and lymphocytes 95%), glucose 50 mg/dl (corresponding blood sugar was 90 mg/dl) and proteins 47.1 mg/dl. Gram stain, AFB stain, and fungal smear examination of CSF were negative. *Cryptococcus* antigen and tuberculosis real-time PCR assay in CSF were also negative. Nested multiplex

PCR assay on CSF using FilmArray meningitis/encephalitis panel (Biofire Diagnostics, Biomerieux Inc, USA) detected *Varicella zoster* virus (VZV) DNA. FilmArray assay was negative for *Escherichia coli* K1, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, *Cytomegalovirus*, *Enterovirus*, *Epstein–Barr* virus, *Herpes simplex* virus 1, *Herpes simplex* virus 2, *Human herpesvirus* 6, *Parechovirus*, and *Cryptococcus neoformans/gattii*. The quantitation of VZV genome was done later by real-time PCR (Argene, Biomerieux, France), and it was quantitated as 3099 copies/ml. The patient was managed with intravenous acyclovir for 10 days followed by oral acyclovir for 4 days with prompt relief of headache and vomiting by the 3<sup>rd</sup> day of treatment.

The incidence of neurological complications produced by VZV have been found to be 1–3/1,000 cases, and these complications are usually associated with the appearance of skin rash.<sup>[1]</sup> The unusual clinical presentation and infrequent complication present a diagnostic challenge to the clinicians. The diagnosis of VZV meningitis/meningoencephalitis can be made by the detection of VZV DNA in CSF or in blood mononuclear cells, or the presence of anti-VZV IgG antibody in CSF or of anti-VZV IgM antibody in CSF or serum.<sup>[2]</sup> Table 1 compiles atypical presentations of *Varicella zoster* meningitis in literature where the patient was immunocompetent, and there was no history of skin rash.

In the cases described in Table 1, the cytological and biochemical examination of CSF was suggestive of bacterial meningitis. So, the antibiotics were administered before the detection of VZV DNA in patient's CSF. However, in our patient, since we could detect VZV DNA very rapidly using FilmArray meningitis/encephalitis panel, so no antibiotic was administered to the patient and it was a step in antimicrobial stewardship component of early and accurate diagnostics. In a retrospective study on VZV reactivation in central nervous system, Becerra *et al.* detected VZV DNA in 11 out of 519 CSF samples (2.1%), submitted from patients with a clinical diagnosis of viral meningitis or encephalitis. They observed eruption of skin lesions in only five patients (45%).<sup>[1]</sup>

VZV meningitis may occur in immunocompetent person without prodromal illness. Rapid molecular FilmArray tests can play a great role in antimicrobial stewardship in such cases by early accurate diagnosis curtailing administration of unnecessary antibiotics. It is also important to make clinicians aware about these newer diagnostic modalities for the timely management of the patients.

**Table 1: Cases of atypical presentations of *Varicella zoster* meningitis in immunocompetent patients**

| References                                  | Age (years)/gender | Clinical symptoms/signs  | Diagnosis   | Outcome   |
|---|--------------------|--|---|-----------|
| Leahy <i>et al.</i> , 2008 <sup>[3]</sup>   | 14/male            | Headache, photophobia, vomiting, no skin rash. CSF cytology and biochemical examination were suggestive of bacterial meningitis  | Detection of VZV DNA by PCR   | Recovered |
| Habib <i>et al.</i> , 2009 <sup>[4]</sup>   | 26/female          | Throbbing, bitemporal headache, photophobia, nausea, and vomiting for 2 days. No history of fever, skin rash, neck stiffness. Hypoglycorrhachia present. CSF cytology and biochemical examination were suggestive of bacterial meningitis                  | Detection of VZV DNA by PCR in acute stage and detection of VZV IgG antibodies in CSF during the second week of illness | Recovered |
| Pasedag <i>et al.</i> , 2014 <sup>[5]</sup> | 18/male            | Acute headache, nausea, and vomiting. No history of fever, skin rash, neck stiffness. CSF cytology, and biochemical examination suggestive of bacterial meningitis   | Detection of VZV DNA by PCR and VZV antibody-specific index   | Recovered |
| Ibrahim <i>et al.</i> , 2015 <sup>[6]</sup> | 15/female          | Severe headache, new-onset diplopia, blurring of vision, nausea, and vomiting for 3 days. No history of fever, skin rash, neck stiffness. Signs of the left 6 <sup>th</sup> nerve palsy present. CSF cytology and biochemical examination were nonspecific | VZV DNA in CSF detected by PCR  | Recovered |

CSF=Cerebrospinal fluid, VZV=*Varicella zoster* virus, PCR=Polymerase chain reaction

### 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.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

Vinit Suri<sup>1</sup>, Leena Mendiratta<sup>2</sup>, Suranjit Chatterjee<sup>3</sup>,  
Raman Sardana<sup>2</sup>, Hena Butta<sup>2</sup>

Departments of <sup>1</sup>Neurosciences, <sup>2</sup>Microbiology and <sup>3</sup>Internal Medicine, Indraprastha Apollo Hospitals, New Delhi, India

**Address for correspondence:** Dr. Hena Butta, Department of Microbiology, Indraprastha Apollo Hospitals, New Delhi - 110 076, India.  
E-mail: henavasdeva@yahoo.com

### REFERENCES

1. Becerra JC, Sieber R, Martinetti G, Costa ST, Meylan P, Bernasconi E, *et al.* Infection of the central nervous system caused by *Varicella zoster* virus reactivation: A retrospective case series study. *Int J Infect Dis* 2013;17:e529-34.
2. Gilden D, Cohrs RJ, Mahalingam R, Nagel MA. Neurological disease produced by *Varicella zoster* virus reactivation without rash. *Curr Top Microbiol Immunol* 2010;342:243-53.
3. Leahy TR, Webb DW, Hoey H, Butler KM. *Varicella zoster* virus associated acute aseptic meningitis without exanthem in an

immunocompetent 14-year-old boy. *Pediatr Infect Dis J* 2008;27:362-3.

4. Habib AA, Gilden D, Schmid DS, Safdieh JE. *Varicella zoster* virus meningitis with hypoglycorrhachia in the absence of rash in an immunocompetent woman. *J Neurovirol* 2009;15:206-8.
5. Pasedag T, Weissenborn K, Wurster U, Ganzenmueller T, Stangel M, Skripuletz T, *et al.* *Varicella zoster* virus meningitis in a young immunocompetent adult without rash: A Misleading clinical presentation. *Case Rep Neurol Med* 2014;2014:686218.
6. Ibrahim W, Elzouki AN, Husain A, Osman L. *Varicella zoster* aseptic meningitis: Report of an atypical case and literature review. *Am J Case Rep* 2015;16:594-7.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

#### Access this article online

##### Quick Response Code:



**Website:**  
www.annalsofian.org

**DOI:**  
10.4103/aian.AIAN\_438\_17

**How to cite this article:** Suri V, Mendiratta L, Chatterjee S, Sardana R, Butta H. Unusual presentation of *Varicella zoster* virus meningitis – Role of molecular rapid diagnostics in diagnosis and antimicrobial stewardship. *Ann Indian Acad Neurol* 2018;21:168-9.

© 2006 - 2018 Annals of Indian Academy of Neurology | Published by Wolters Kluwer - Medknow