

Case Report

A rare case of varicella zoster virus encephalitis in a 16 years old unvaccinated girl

Abdul Wali Khan^{1*}, Abad Khan², Muhammad Ishaq¹, Irfan Ullah^{3,4}, and Marhami Fahriani⁵

¹Department of Medicine, Hayatabad Medical Complex, Peshawar, Pakistan; ²Khyber Teaching Hospital Peshawar, Pakistan; ³Kabir Medical College, Gandhara University, Peshawar, Pakistan; ⁴Undergraduate Research Organization, Savar, Dhaka, Bangladesh; ⁵Medical Research Unit, School of Medicine, Universitas Syiah Kuala Indonesia, Banda Aceh, Indonesia.

*Correspondence:

Abdul Wali Khan
Department of
Medicine, Hayatabad
Medical Complex,
Peshawar, Pakistan

E-mail address:
abdulwalikhan801@yahoo.com

Abstract

We reported a 16-year-old girl, with diffuse vesicular rashes all over the body, presented to the emergency department with altered mental status, irritability, persistent fever and one episode of a generalized tonic-clonic seizure. After thorough evaluation and investigations, the case was a varicella zoster-associated encephalitis in an unvaccinated patient. Appropriate treatment was initiated, the patient was then shifted to the critical care and subsequently discharged with no sequelae. Early diagnosis and treatment should be emphasized as they play an important role in the clinical outcome of chickenpox-associated encephalitis.

Keywords: Chickenpox, encephalitis, neurological complication, varicella, VZV

Introduction

Varicella or chickenpox is predominantly a disease of children, usually occurs in pre-school and school-age children. It is a viral infection caused by a member of herpes virus family, varicella-zoster virus (VZV). The primary infection manifests in generalized vesicular rashes in unvaccinated children, accompanied by fever and pruritus. It is a highly contagious disease and spreads rapidly in unvaccinated children, usually in outbreaks. After the vesicle crusted, the patient becomes less contagious and eventually would be fully recovered.

Complications of chickenpox may arise, for instance, bacterial skin infections, pneumonia, lower respiratory tract infection (LRTI), and neurological complications among the various others. Neurological complications following primary chickenpox infection occur extremely rare (about 0.01% to 0.03%) (Yilmaz and Çaksen, 2005). In children below 15 years of age, cerebellar ataxia is the most common neurological complication, while in adults and infants, encephalitis is more frequent (Giriya et al., 2007). The diagnosis of varicella-associated encephalitis should be suspected in individuals with neurological symptoms during chickenpox primary infection. Prompt diagnosis and treatment are important in improving the clinical outcome and quality of life of the patient (Granerod et al., 2010). The aim of this report was to present a case of varicella-associated encephalitis and to demonstrate that prompt diagnosis, laboratory investigation and proper treatment are required in order to improve the clinical outcome of the patient.

Case summary

A 16-year-old girl presented with high grade fever, altered mental status, and an episode of generalized tonic-clonic seizure one day prior to admission. Patient was also complaining of headache and lethargy. On examination the patient had altered mental status, ataxia, hyperreflexia and bilateral up-going plantar. A week ago, the patient had fever along with burning itching sensations followed by vesicular rashes all over the body (Figure 1). She was diagnosed as a case of chickenpox by the primary health care provider and paracetamol and antihistamines were prescribed. The patient showed initial improvement with the treatment (fever subsided, rash became non pruritic and crusting). However, on the 4th day, she developed high grade fever and became irritable

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with intellectual ability gradually deteriorated. On the 6th day of rash eruption, the patient experienced disorientation and a generalized tonic-clonic seizure. She experienced few episodes of generalized tonic-clonic seizure in the hospital. Her past and family medical history was insignificant except no vaccination history on her medical record.



Figure 1 Crusting vesicular rashes on the leg of the patient.

Routine blood chemistry was within normal limits except for elevated total leukocyte count of 12,600 cells/mm³ with polymorph 85% and lymphocytes 8.9%. No evidence of hepatitis B and C virus infection. The levels of D-dimer and alkaline phosphatase were raised (Table 1). Brain magnetic resonance imaging (MRI) was normal and no pathologic finding on fundoscopy. Lumbar puncture was performed with cerebrospinal fluid (CSF) findings supporting viral encephalitis (Table 1). Real-time polymerase chain reaction (RT-PCR) of CSF, targeting *ORF62* gene, came back positive for VZV, confirming the diagnosis of varicella zoster-associated encephalitis. No aerobic or anaerobic bacteria were grown from CSF culture and no acid-fast bacillus (AFB) seen in Ziehl-Neelsen staining smear of CSF.

Table 1. Laboratory investigation both blood and CSF of patient

Specimen	Parameters	Normal range	Patient result
Blood	Blood urea	10-50 mg/dl	28.8 mg/dl
	Glucose (random)	70-140 mg/dl	135 mg/dl
	Total bilirubin	0.1-1.0 mg/dl	0.08 mg/dl
	Alanine transferase	10-50 U/l	21.5 U/l
	Alkaline phosphatase	<187 U/l	205 U/l
	Creatinine	0.3-0.9 mg/dl	0.55 mg/dl
	D-dimer	0.25-139 µg/ml	1002 µg/ml
CSF	Volume		2 ml
	Turbidity	Nil	Nil
	Colour	Clear	Pale yellow
	Protein	20-40 mg/dl	39 mg/dl
	Glucose	50-90 mg/dl	89 mg/dl
	White blood cells count	0-5 cells/mm ³	72 cells/mm ³
	Red blood cells count	0-10 cells/mm ³	2 cells/mm ³
	Neutrophil	0%	22%
	Lymphocytes	100%	78%

The patient was treated with intravenous acyclovir (infusion in 5% dextrose) 30 mg/kg/day in three divided doses, prophylactic antibiotic (intravenous ceftriaxone

75mg/kg/day in two divided doses), and intravenous dexamethasone 4mg. Patient was also given intravenous valproic acid 20mg/kg/day in two divided doses.

The patient was shifted to the critical care unit where her condition improved and then subsequently discharged on the 10th day of admission. On discharge the patient was fully conscious and oriented to time, place, person and events. Her deep tendon reflexes were normal and there were no focal neurological deficits.

Discussion

The nature of chickenpox complications varies with age. For children less than 5 years of age, infections of skin and respiratory tract are the most common causes of hospitalization; for children between 5 and 14 years, the common ones are varicella encephalitis and Reye Syndrome, while varicella encephalitis and pneumonia are the most common causes for hospitalization among adults (Mofenson et al., 2009). In the majority of cases, these complications present at a median time of 5 days after onset of rash (Science et al., 2014). The underlying mechanisms for the neurological complications associated with chickenpox have been attributed to direct neurological insult, vasculopathy, and immune system activation (Amalnath et al., 2016).

The development of neurological complications associated with chickenpox are rare (0.01% to 0.03%) and may occur without rash (Yılmaz and Çaksen, 2005). These complications range from encephalitis, cerebellitis, cortical venous thrombosis, arterial strokes, isolated seizures, Guillain-Barre Syndrome, acute disseminated encephalitis and Ramsay Haunt syndrome (Amalnath et al., 2016; Science et al., 2014). Early diagnosis of these cases and proper antiviral therapy is important to decrease the associated morbidity and mortality. Routine follow-up is also needed to identify any sequelae experienced by the patient after being discharge. A study report that patients that survived varicella zoster encephalitis still presented with moderate to severe sequelae even after 3 years hospitalization (De Broucker et al., 2012). In our patient, clinical presentation (fever, vesicular rash, seizure and altered mental state), CSF findings and RT-PCR result established the diagnosis of varicella-zoster associated encephalitis. The brain imaging showed normal findings which is similar to other study (Pahud et al., 2011); it is in line with the neurological symptoms of the patient (disturbance of consciousness, disorientation, general seizure, and irritability) that suggested a diffuse encephalopathy as no focal neurological symptoms exhibited by the patient.

The epidemiology of chickenpox has changed significantly in countries where VZV vaccine was added to national vaccination program. In Germany, universal varicella vaccination was introduced to decrease the incidence of varicella-associated neurological complications, which resulted in an approximately 60% reduction in varicella-associated neurological complications. It showed a continuous decrease from an incidence of 2.8 per 100,000 children less than 17 years of age to 1.2 over a period of 7 years after the universal vaccination was introduced (Streng et al., 2017). In the US, the incidence of chickenpox declined dramatically with an average of 97.4% (from 1993–1995 to 2013–2014) compared to pre-vaccine years (Lopez et al., 2016). Milder cases (less than 50 vesicular lesion, shorter duration and lower incidence of fever) was reported in vaccinated persons compared with symptoms seen in unvaccinated persons (Chaves et al., 2008). Our patient showed rapid progression of CNS complication related to VZV and longer duration of illness which is typical in unvaccinated person. In our region, as chickenpox vaccination is not a routine vaccination program during childhood, we need to emphasize that the incidence of chickenpox and its associated complications might continue to rise in the following year.

Conclusion

This case described a successful rapid diagnosis and treatment in primary varicella zoster infection with CNS complication in unvaccinated patient. Appropriate antiviral medication has showed improvement in the patient's outcome with no sequelae presented after discharge. Therefore, we highlight the importance of prompt diagnosis, laboratory investigation and proper therapy. We also emphasize that VZV vaccination should be include in the national program to decrease the mortality and morbidity of chickenpox and its complication.

Authors' contributions

Conceptualization: AWK and IU; Data Curation: AWK, AK and MI; Resources: IU; Validation: AWK, AK, MI, IU and MM; Writing – Original Draft Preparation: AWK and IU; Writing – Review & Editing: AWK, AK, MI, IU, and MM.

Consent for publication

The patient guardian given written consent to the inclusion of material about patient.

Conflict of interest

No potential conflict of interest was reported by the authors.

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