Case Report

Post-varicella Multiaxial Nervous System Involvement in an Immunocompetent Adult Female: an Unusual Presentation

Bhupender Kumar Bajaj*, Prahlad Karki**

Abstract

Post-chickenpox neurological complications have been reported mostly in paediatric population and immunocompromised adult individuals. Extensive multiple site neuraxis involvement is not common in immunocompetent adults. Treatment of these complications of varicella zoster infections is not settled as the exact pathogenesis is still elusive. We report a case of 28-year old immunocompetent female who presented with sensory and cerebellar ataxia with autonomic dysfunction and non-paralytic squint 2 weeks after the onset of fever associated with chicken pox eruptions. The patient was managed with steroids and acyclovir with favourable response.

Key words: Chickenpox; varicella-zoster virus; cerebellum; neuritis; polyradiculoneuropathy; dysautonomias

Introduction

Neurological complications like cerebellitis, disseminated encephalomyelitis, myelitis and Guillain-Barré syndrome (GBS) have been mostly reported as isolated complications of chickenpox predominantly in paediatric population. Immunocompromised individuals are more likely to have extended period of severe cutaneous lesions and visceral dissemination of varicella zoster virus leading to involvement of lungs, liver and central nervous system. There are no reports of extensive multiaxial central as well as peripheral nervous systems involvement after chicken pox particularly in immunocompetent adults. Pathogenesis of these neurological complications is not established. Direct infections of the nervous system by the virus as well as autoimmune response to preceding infection are the implicated mechanisms of these complications. The management of neurological manifestations is ambiguous. The present patient, an immunocompetent adult female developed complications related to involvement of multiple sites of neuraxis following chickenpox infection.

Report of case

A 28-year old previously healthy female developed 100-101°F fever associated with multiple itchy exanthems over trunk and face. The eruptions were initially macular followed by papular and vesicular transformation over next four days. Fever subsided spontaneously within four days of onset. She was diagnosed to have chickenpox by a local practitioner in her village and received no specific therapy for the condition. The patient developed tingling sensation in all the limbs about two weeks after onset of fever. Over the period of next 24 hours, she had difficulty in getting up from squatting position, slurring of speech and limb and gait ataxia. She was bed-confined within a couple of days and presented in this condition. Her husband, who was accompanying her, had noticeable hyperpigmented lesions in the distribution of ophthalmic division of trigeminal nerve. Further inquiry revealed that he suffered from herpes zoster ophthalmicus three weeks prior to development of febrile episode in the patient. The patient did not give any history suggestive of chicken pox or herpes zoster infection in the past. Patient's examination at presentation revealed regular pulse of 88/minute, blood pressure of 120/100 mm Hg and, excoriated and scarred lesions all over body, predominantly the trunk. Neurological assessment revealed conscious,

* Department of Neurology, PGIMER & Dr. RML Hospital, New Delhi, India.
Formerly, Assistant Professor (Neurology) at BP Koirala Institute of Health Sciences, Dharan, Nepal
** Department of Medicine, B. P. Koirala Institute of Health Sciences, Dharan, Nepal

Corresponding Author: Dr. B. K. Bajaj, Department of Neurology, PGIMER & Dr. RML Hospital, New Delhi
Email : docbajaj@yahoo.co.in
Received : 08-07-2010 | Accepted : 11-09-2010 | Published Online : 15-09-2010

cooperative and anxious looking lady who had manifest squint with intact cranial nerve functions. There was no double vision or restriction of eye movements and an impression of non-paralytic strabismus was made. Inquiry from family members and patient revealed that the squint was of recent onset. The patient did not have weakness of cranial musculature or restriction of tongue movements. She had cerebellar dysarthria and motor system examination revealed marked hypotonia, Medical Research Council grade 3-4/5 power in all the limbs proximally and 5/5 power distally with generalised areflexia and flexor plantar response. The patient had impaired joint position and vibration sense with normal pain and temperature sensation in lower and upper limbs. Finger nose and heel-knee-shin tests were positive with no improvement in performance of these tests with visual cues. On the next day, a self-retaining indwelling urinary (Foley's) catheter was placed when patient developed retention of urine. MRI-brain did not reveal any abnormality while nerve conduction study showed absence of sensory nerve action potentials in all the limbs. Distal latencies, amplitudes of compound muscle action potentials (CMAPs), conduction velocities and F-responses were within normal limits in all the limbs. However, F responses were inconsistent in bilateral common peroneal nerves. Lumbar puncture was done and it revealed, raised protein (183 mg/dL), normal glucose (60 mg/dL) and mild lymphocytic pleocytosis (total cells = 24/ mm3; all lymphocytes). Microbiological examination including Gram staining, ZN staining and India ink preparation revealed no organisms. Bacterial culture of cerebrospinal fluid revealed no growth. ELISA for HIV was negative. The patient was started on intravenous methylprednisolone for 3 days followed by rapidly tapering oral prednisolone alongwith oral acyclovir 800 mg five times a day for 2 weeks. Meanwhile, her pulse rate and blood pressure showed fluctuations. After second day of therapy, the patient felt significantly relieved of paraesthesiae. At the end of three days of therapy, she could sit unsupported for a few minutes. She had to be given laxatives for constipation. Meanwhile, her two children who were staying at the patient's home place developed chickenpox. The patient could stand with little support on the tenth day of admission when she was discharged. On follow up, two weeks after discharge, we found that her speech had recovered; she could feed herself with some difficulty and could stand and walk with support. However, the squint, generalised hypotonia, areflexia and mild ataxia persisted. Two months later, she was normotensive with no postural hypotension, and had normal bowel and bladder control. She could carry out all the activities of daily living without help. She had persistent non-paralytic squint, impaired joint position sensation, areflexia and residual sensory ataxia. Her repeat nerve conduction study revealed persistently absent sensory nerve action potentials.

Discussion

Infection caused by varicella-zoster virus still remains of medical significance. Varicella-zoster pneumonia and neurological manifestations are important complications of chickenpox infection. While pneumonitis is an early complication of chicken pox, neurological manifestations present about 2-4 weeks after chickenpox. Central nervous system complications are known to occur in less than 1% cases of chickenpox [1,2]. In a hospital based study of children admitted for varicella related complications, 23% had CNS involvement [3]. In a recent study from United Arab Emirates, authors reported 17.6% neurological complications in children with chickenpox requiring admission [4]. There are only isolated reports of peripheral nervous system involvement after chickenpox. These complications are presumably autoimmune in origin. There are, however, reports of pre-eruptive neurological manifestations of varicella zoster [5,6]. Tsolia et al [6] reported acute hemiplegia, cerebellar ataxia and dysarthria in a child, 24 hours prior to eruptions of varicella exanthem. The child had multiple ischaemic infarcts on MRI. Takeuchi et al [7] reported recurrent and pre-eruptive acute cerebellar ataxia likely due to direct invasion by varicella-zoster. The literature is replete with cases of cerebellitis and encephalitis after chickenpox. However, there are no reports of involvement of central as well as peripheral nervous system. Our patient presented with acute onset predominantly sensory, large fibre type sensorimotor polyradiculoneuropathy as evidenced by proximal motor weakness, joint position and vibration sense impairment with marked sensory ataxia. Absent sensory nerve action potentials and inconsistent F responses in bilateral common peroneal nerves confirmed this. The patient had dysarthria and ataxia which did not improve with visual cues suggesting cerebellar involvement. Non-paralytic squint also suggests central nervous system involvement. However, MRI brain did not

demonstrate any abnormality. The patient developed acute retention of urine, constipation and fluctuating blood pressure suggesting a possible associated involvement of autonomic nervous system. Central myelitis leading to bladder and bowel dysfunction cannot be excluded. However, there was no clinical evidence of long tract signs suggestive of spinal cord involvement. Significance of different neurological presentations lies in determination of presumed pathogenesis of the complications. Different types of antibodies have been associated with different presentation of neurological complications [8,9]. Autoantibody assay could not be performed at our centre because the facility was not available.

Pre-eruptive neurological complications are believed to be due to initial viraemia leading to vasculopathy and are not due to autoimmune mechanism. Detection of varicella zoster virus DNA by polymerase chain reaction (PCR) suggests direct viral invasion of nervous system leading to the complications [10]. However, autoimmune mechanisms are suggested by detection of autoantibodies against neural elements in patients with postvaricella neurological complications and occurrence of neurological complications two to four weeks after chickenpox. Management of neurological complications of chickenpox is not yet settled [11]. There are no controlled therapeutic trials for treatment of these complications. Steroids have been used with success in post-varicella neurological complications like acute disseminated encephalomyelitis and myelitis [12], and non-neurological complications like thrombocytopenia [13]. Intravenous immunoglobulins have been used in patients with Guillain-Barré syndrome after varicella zoster infection. Acyclovir therapy alongwith steroids have been successfully used for neurological complications like cerebellitis and myelitis [10] because of the suspicion of direct invasion of virus. The present patient had not received acyclovir for her chickenpox during her initial contact with local practitioner. It was decided to administer acyclovir along with methylprednisolone therapy in view of appearance of neurological complaints early in post-chickenpox phase and progression of deficit. This patient showed improvement in bladder and bowel function, stabilisation of blood pressure and improvement in ataxia and dysarthria. Persistent sensory ataxia and electophysiological confirmation of absent sensory nerve action potentials suggests incomplete response. Immunoglobulins are probably better choice for post-varicella polyradiculoneuropathy as seen in cases of GBS. Our patient was disabled mainly because of sensory ataxia, cerebellar ataxia, dysarthria and autonomic dysfunction. The neuroelectrophysiological findings revealed normal CMAPs contrary to findings in Acute Motor Sensory Axonal Neuropathy. Further, the patient had not only peripheral, but central nervous system involvement as well. There are no defined guidelines or evidence of superiority of intravenous immunoglobulins over steroids. In the sensory variant of GBS, steroids are known to be useful. Steroids have been used and found effective for central neurological complications of chicken pox including acute disseminated encephalomyelitis and cerebellitis. Intravenous immunoglobulins can be used for these conditions as well. While intravenous immunoglobulins were considered for administration, but the high cost involved proved to be a hinderance in this patient who belonged to poor socio-economic status. There is a need to further understand pathogenesis of the post-varicella neurological complications and define their treatment.

Key Points

- Post-chickenpox neurological complications are common in paediatric population and immunocompromised adults.
- Post-varicella multiaxial involvement in an immunocompetent adult has been reported. The patient presented as acute onset predominantly sensory, large fibre type sensorimotor polyradiculoneuropathy as evidenced by proximal motor weakness, joint position and vibration sense impairment with marked sensory ataxia; and also had dysarthria, cerebellar ataxia, non-paralytic squint and autonomic dysfunction.
- Although, treatment of such neurological complications of varicella zoster infections is unsettled, however steroids and acyclovir showed a favourable response in this patient. Intravenous immunoglobulins can also be an option though its high cost is a deterrent.

Conflict of interest: None declared.

Source of funding: Nil.

References

1. Girija AS, Rafeeque M, Abdurehman KP. Neurological complications of chickenpox. Ann Indian Acad Neurol 2007;10:240-6
2. Barnes DW, Whitley RJ. CNS Diseases associated with varicella zoster virus and herpes simplex virus infection. Neurol Clin 1986;4:265-283.
3. Tseng HW, Liu CC, Wang SM, Yang YJ, Huang YS. Complications of varicella in children: emphasis on skin and central nervous system disorders. J Microbiol Immunol Infect 2000;33:248-52.
4. Uduman SA, Sheek-Hussein M, Bakir M, Trad O, Al-Hussani M, Uduman J, et al. Pattern of varicella and associated complications in children in United Arab Emirates: 5-year descriptive study. East Mediterr Health J 2009;15:800-6.
5. Dangond F, Engle E, Yessayan L, Sawyer MH. Pre-eruptive varicella cerebellitis confirmed by PCR. Pediatr Neurol 1993;9:491-3.
6. Tsolia M, Skardoutsou A, Tsolas G, Karayanni C, Spyridis P, Sinaniotis C. Pre-eruptive neurologic manifestations associated with multiple cerebral infarcts in varicella. Pediatr Neurol 1995;12(2):165-8.
7. Takeuchi Y, Yoshihara T, Ishimura K, Amano T, Kadomoto Y, Swada T. Recurrent and pre-eruptive acute cerebellar ataxia: a rare case of varicella. Paediatr Neurol 1987;3:240-1.
8. Yoshikawa T, Suzuki K, Suga S, Miyata E, Yamamoto H, Hosokawa T, et al. Immune response to gangliosides in a case of Guillain-Barré syndrome after varicella. Arch Dis Child 2000;83:172-173.
9. Adams C, Diadori P, Schoenroth L, Fritzler M. Autoantibodies in childhood post-varicella acute cerebellar ataxia. Can J Neurol Sc 2000;27:316-20.
10. Puchhammer-Stockl E, Popow-Kraupp T, Heinz FX, Mandl CW, Kunz C. Detection of varicella zoster virus DNA by polymerase chain reaction in the cerebrospinal fluid of patients suffering from neurological complications associated with chickenpox or herpes zoster. J Clin Microbiol 1991;29:1513-6.
11. Steiner I, Kennedy PG, Pachner AR. The neurotropic herpes viruses: herpes simplex and varicella zoster. Lancet Neurol 2007;6:1015-28.
12. Rosenfeld J, Taylor CL, Atlas SW. Myelitis following chickenpox: a case report. Neurology1993;43:1834-6.
13. Aji DY, Altinkaya N, Guler A, Ayhan YI, Erginel A, Cenani A. The role of high-dose intravenous methylprednisolone in the treatment of varicella associated thrombocytopenic purpura. Turk J Paediatr 1993;35:69-73.