Adult Patient with Novel H1N1 Infection Presented with Encephalitis, Rhabdomyolysis, Pneumonia and Polyneuropathy

Ketan K Patel, Atul K Patel, Shalin Shah¹, Rajiv Ranjan, Sudhir V Shah¹

Infectious Diseases Consultant, Infectious Diseases Clinic, “VEDANTA” Institute of Medical Sciences, Navarangpura, Ahmedabad, ¹Neurology Department, Sterling Hospital, Memnagar, Ahmedabad, India

ABSTRACT

Neurological complications of influenza are well known. Influenza A is commonly associated with neurological complications. Neurological complications especially encephalitis is described in the pediatric age group of patients with current pandemic novel H1N1 infection. We are describing a case of novel H1N1 infection presenting with multi-system involvement (encephalitis, bilateral pneumonia, severe rhabdomyolysis leading to renal failure and polyneuropathy) in adult patient.

Key words: Encephalitis, Novel H1N1, Polyneuropathy, Rhabdomyolysis

INTRODUCTION

Influenza is an acute, usually self limited, febrile illness caused by infection with influenza type A or B viruses that occur in outbreaks of varying severity almost every winter. Symptoms are primarily related to the respiratory system, but myositis, rhabdomyolysis, myoglobinuria, myocarditis, pericarditis, and central nervous system (CNS) involvement has been described with influenza virus infection.[1-3] Involvement of the CNS in influenza virus infection is very rare, but serious manifestations like seizures, encephalitis, myelitis, Reye syndrome, and other neurologic disorders have been described previously in association with respiratory tract infection with seasonal influenza A or B viruses.[4-6] These findings indicate that, as with seasonal influenza, neurologic complications can occur with on going novel influenza A (H1N1) pandemic, but the frequency with which these occur is unknown. Encephalitis has been reported with novel H1N1 infection, mainly in children.[6] There has been only one case report of encephalopathy associated with novel H1N1 infection in adult.[7]

We are describing a case of novel H1N1 infection presenting with multi-system involvement (bilateral pneumonia, severe rhabdomyolysis leading to renal failure and encephalitis) in adult patient

CASE REPORT

A 27-year-old, male, immunocompetent patient presented with 5 days history of fever, running nose, dry cough, and sore throat. He also had complaint of breathless since 3 days. He had generalized tonic-clonic convulsion, altered sensorium and increasing breathlessness requiring ventilatory support after hospitalization. With this brief illness patient was transferred under our care with ventilatory support.

On examination, he was intubated and sedated, his limbs were swollen, pulse: 108/min, temperature: 37°C, and blood pressure was 138/84 mmHg. He was maintaining SpO₂ of 96% at 100% FiO₂ on controlled mode ventilation. CNS examination revealed sedated patient (receiving IV midazolam), pupils were normal size reacting to light, all deep tendon reflexes were absent, and there was generalized hypotonia. Auscultation revealed the presence of crepetitions in right infra scapular and infra-axillary regions of chest. Cardiovascular and abdominal system examination was unremarkable. Laboratory investigations on presentation to us showed hemoglobin: 14.42 gm%, total WBC counts: 1730 cells/cu.mm, platelet count: 1.25 lac/cu.mm, serum bilirubin total: 1.2 mg%, direct: 0.5 mg%, indirect: 0.7 mg%, SGPT: 200 IU/L, SGOT:
DISCUSSION

Neurological complications of seasonal influenza virus infection have been well described in Pediatric age group and young adults. Neurological complications usually occur early in the course of disease and include encephalopathy, encephalitis, seizures, Reye syndrome, and Guillain-Barre syndrome (GBS). Severity of complication ranging from mild and transient central nervous system alterations to severe forms associated with high mortality. The pathogenesis of influenza virus encephalitis is unclear. Whether the influenza virus invades the brain parenchyma is still a controversial issue. The viral RNA has been frequently detected in the CSF by RT-PCR. However, recent reports have indicated that viral RNA is not detected in the CSF of most patients with influenza-associated encephalitis. Findings of pathologic examination, including the lack of detectable viral antigen in brain...
tissues, also have suggested that direct viral invasion and inflammation are unlikely to be the causes of this disease. It has been hypothesized that the respiratory tract infection triggers immune system cytokines that result, in rare instances, in an inflammatory process in the brain, which can lead to neurologic squeal or fatal outcomes.[6]

Neurological complications with Novel H1N1 pandemic reported so far are seen in the pediatric age group and many patients have recovered from H1N1 and develop neurological complications (polyneuropathy, transverse myelitis, encephalitis).

These patients had relatively mild neurological symptoms associated with the infection.[6] Our adult immunocompetent patient presented with initial symptoms suggestive of influenza-like illness of 5 days duration before he develops encephalitis. There is one report of novel H1N1 encephalopathy in adult female. Symptoms of encephalopathy were mild and recover without any specific treatment. However our patient developed episodes of seizures with loss of consciousness with ongoing acute phase of influenza virus infection, which was suggestive of CNS involvement by influenza virus. Our patient developed CNS involvement with acute lung injury, these timing of neurological involvement is consistent with available information in literature.[11] Patient had loss of consciousness with flaccid quadriplegia suggestive of extensive brain damage. The clinical findings of severe encephalitis were confirmed by evidence of extensive involvement of brain parenchyma on MRI brain examination performed after he recovered from acute lung injury. Methyl prednisolone 120 mg/day intravenously was used on presentation in our patient for the acute lung injury associated with viral pneumonia. His pulmonary pathology responded to oseltamivir and IV methyl prednisolone. He does have improvement in sensorium with persistent neuromuscular weakness. EMG-NCV examination showed generalized predominantly pure motor, mixed axonal and demyelinating polyneuropathy. Demyelinating polyneuropathy of GBS type has been well known after acute viral infections. It is difficult to differentiate critical care neuropathy from viral associated neuropathy with available investigations in our patient. GBS has been reported after influenza virus infection or after administration of influenza vaccine.[5] Glucocorticoids and plasmapheresis had been used in some patients with success. As patient developed secondary bacterial pulmonary infection glucocorticoids were not reintroduced later because of intermittent fever spikes.

Only one case report of rhabdomyolysis in Novel H1N1 patient so far in the literature, though it was well described with seasonal influenza. Our patient also had severe myositis, swollen limbs with rhabdomyolysis and myoglobinuria.
(urinary myoglobin >1000 ng/ml) leading to renal failure on presentation. Myositis, rhabdomyolysis, and myoglobinuria are well known complication of influenza, although acute tubular necrosis and renal failure are not common.\textsuperscript{11,15-19}

During hospitalization, he also developed tachycardia requiring use of IV amiodarone, for which we were not able to point out any immediate cause, raising suspicion of myocardial involvement by influenza virus. Nearly 9% of patients with proven influenza infection develop evidence of myocarditis.\textsuperscript{20,21} Although the supportive investigations such as CPK MB, 2D echocardiography, and ECG were normal and we had not carried out any myocardial biopsy to confirm diagnosis of myocarditis. Generally, all these supportive investigations are inconclusive in most of the patients requiring myocardial biopsy for diagnosis.\textsuperscript{[22]} As the myocardial involvement is patchy in nature it may some time be difficult to prove the presence of myocarditis even after doing biopsy.\textsuperscript{[23]}

Severe inflammatory response generated by the body in response to influenza virus infection had led to more severe and extensive involvement of lung, muscle and brain. Our patient had multisystem involvement (pneumonia, encephalitis, neuropathy myositis, and possible myocarditis) from novel H1N1 influenza virus infection. Patient had incomplete recovery from all these insults with persistent neurologic dysfunction. This is probably first case report with multisystem involvement from novel H1N1 infection with significant post illness debility.

In conclusion, novel H1N1 infection can present with life-threatening multi-system involvement including encephalitis in adult patients.

REFERENCES

1. Rothberg MB, Haessler SD. Complications of seasonal and pandemic influenza. Curr Care Med 2010;38:e91-7.
2. Maritch SM, Neul J, Lotze TE, Cazau AC, Uyeki TM, Demmler GJ, et al. Neurologic complications associated with influenza A in children during the 2003-2004 influenza season in Houston, Texas. Pediatrics 2004;114:e626-33.
3. Morishima T, Togashi T, Yokota S, Okuno Y, Miyazaki C, Tashiro M, et al. Encephalitis and encephalopathy associated with an influenza epidemic in Japan. Clin Infect Dis 2002;35:512-7.
4. Salonen O, Koshkinien M, Saari A, Myllylä V, Pyhältö R, Airolainen L, et al. Myelitis associated with influenza A virus infection. J Neurol 1997;233:85-5.
5. Wells CE, James WR, Evans AD. Guillain-Barre syndrome and virus of influenza A (Asian strain); report of two fatal cases during the 1957 epidemic in Wales. AMA Arch Neurol Psychiatry 1959;81:699-705.
6. Centers for Disease Control and Prevention (CDC). Neurologic complications associated with novel influenza A (H1N1) virus infection in children-Dallas, Texas, May 2009. MMWR Morb Mortal Wkly Rep 2009;58:773-8.
7. Gonzalez BE, Brust DG. Novel influenza A (H1N1) presenting as an acute febrile encephalopathy in a mother and daughter. Clin Infect Dis 2009;49:1966-7.
8. Flewett TH, Hoult JG. Influenzal encephalopathy and postinfluenzal encephalitis. Lancet 1958;2:11-5.
9. Lyon JB, Remigio C, Milligan T, Deline P, Katoh T, et al. PCR on cerebrospinal fluid to show influenza-associated acute cerebellar ataxia or encephalitis. Lancet 1998;352:873-5.
10. Ito Y, Ichiyama T, Kimura H, Shibata M, Ishiwea N, Kuroki H, et al. Detection of influenza virus RNA by reverse transcription-PCR and proinflammatory cytokines in influenza-virus-associated encephalopathy. J Med Virol 1999;58:420-5.
11. Deharo L, Middleton PJ. Influenza A virus associated with acute encephalopathy. Am J Dis Child 1979;133:822-4.
12. Fujimoto S, Kobayashi M, Uemura O, Iwasa M, Ando T, Katoh T, et al. PCR on cerebrospinal fluid to show influenza-associated acute cerebellar ataxia or encephalitis. Lancet 1998;352:873-5.
13. Ito Y, Ichiyama T, Kimura H, Shibata M, Ishiwea N, Kuroki H, et al. Detection of influenza virus RNA by reverse transcription-PCR and proinflammatory cytokines in influenza-virus-associated encephalopathy. J Med Virol 1999;58:420-5.
14. McAlpin HD, Reid AH, Taubenberger JK. Influenza RNA not detected in archival brain tissues from acute encephalitis lethargica cases or in postencephalitic Parkinson cases. J Neuropathol Exp Neurol 2001;60:565-704.
15. Ayala E, Kagawa FT, Wehner JH, Tan J, Upadhyay D. Rhabdomyolysis associated with 2009 influenza A(H1N1). JAMA 2009;302:1863-4.
16. Carrillo-Esper R, Ornelas-Arroyo S, Perez-Bustos E, Sanchez-Zuniga J, Uribe-Esquível M. Rhabdomyolysis and acute renal failure in human influenza A H1N1 mediated infection. Gac Med Mex 2009;145:519-21.
17. D’Silva D, Hewagama S, Doherty R, Korman TM, Buttery J. Melting muscles: Novel H1N1 influenza A associated rhabdomyolysis. Pediatr Infect Dis J 2009;28:138-9.
18. Foulkes W, Rees J, Sewry C. Influenza A and rhabdomyolysis. J Infect 1990;21:303-4.
19. Kessler HA, Trenholme GM, Harris AA, Levin S. Acute myopathy associated with influenza A/Texas/1/77 infection. Isolation of virus from muscles: Novel H1N1 influenza A associated rhabdomyolysis. Pediatr Infect Dis J 2009;28:138-9.
20. Foulkes W, Rees J, Sewry C. Influenza A and rhabdomyolysis. J Infect 1990;21:303-4.
21. Kessler HA, Trenholme GM, Harris AA, Levin S. Acute myopathy associated with influenza A/Texas/1/77 infection. Isolation of virus from a muscle biopsy specimen. JAMA 1980;243:461-2.
22. Sano T. Influenza myocarditis and pericarditis. Nippon Rinsho 1979;37:178-81.
23. Kizura Y, Deguchi H, Terasaki F, Ukimura A, Morita H, Tatsumi T. Influenza myocarditis-pathophysiology and developmental mechanism of myocarditis. Nippon Rinsho 2003;61:1945-52.