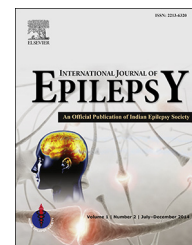


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Case Report

Status epilepticus as presenting manifestation of H1N1 infection



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ABSTRACT

Background: During the global H1N1 pandemic, neurological complications were reported in approximately 6–10% of children suffering from H1N1 infection, but only rarely in adults. Generalized convulsive status epilepticus (GCSE) as a presenting manifestation of H1N1 infection in an adult is exceedingly rare and has not been reported in literature. We report a patient who presented to us with GCSE as a presenting manifestation of H1N1 infection who improved following appropriate antiviral treatment.

Methods and results: This 20-year-old gentleman presented to us with history of fever followed by GCSE of 24 h duration. He was treated symptomatically and was evaluated in detail. He was diagnosed to be suffering from H1N1 infection based on appropriate serological tests. After start of antiviral therapy, he improved and is doing well at 4 months follow up. **Conclusion:** This case report further expands the spectrum of clinical findings associated with sporadic H1N1 infection. A possibility of H1N1 infection should be considered in all patients who present with GCSE without any obvious cause so that appropriate diagnostic tests and treatment can be carried out at the earliest.

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1. Introduction

In April 2009, a novel influenza A (H1N1) virus was reported from Mexico. Worldwide spread of virus within a few weeks led World Health organization (WHO) to declare a pandemic.¹

By the time this pandemic subsided in August 2010, approximately 18,000 deaths had occurred worldwide. Despite subsidence of pandemic, sporadic cases are still encountered throughout the world. Though H1N1 infection is associated with neurologic complications in about 6% of cases, these usually occur later during the course of the disease following respiratory symptoms, rather than as presenting com-

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plaint.^{2,3} Generalized convulsive status epilepticus (GCSE) as presenting manifestation of H1N1 infection has not been reported in literature so far. We report a patient with H1N1 infection, who presented to us with GCSE as presenting complaint.

2. Case report

A 20-year-old gentleman presented to emergency services of our institute with fever of 5 days and recurrent generalized tonic clonic seizures (GTCS) of 24 h duration. There was no history of any other systemic or neurological symptoms. The past and family histories were noncontributory. There was no history of any addictions. His general physical and systemic examinations were normal. On neurological examination, he was having GCSE. There were no obvious focal deficits. He was immediately given intravenous lorazepam 0.1 mg/kg (6 mg over 3 min) along with other supportive measures and was shifted to intensive care unit (ICU) for further management. He was loaded with phenytoin (20 mg/kg intravenously (IV) over 25 min followed by 10 mg/kg IV over 10 min). As seizures did not subside, he also received valproate (20 mg/kg over 10 min), followed by phenobarbitone (20 mg/kg IV over 25 min). Subsequently as status epilepticus was still persisting, he was started on propofol [2 mg/kg loading followed by 5 mg (300 mg/h) infusion with invasive arterial blood pressure monitoring. Subsequently, he was also given levetiracetam in a loading dose of 20 mg/kg followed by 500 mg three times a day. He was investigated in detail. His hematological and biochemical parameters were normal. Gadolinium enhanced magnetic resonance imaging (MRI) of brain and detailed cerebrospinal fluid (CSF) analyses (cell count, glucose, proteins, fungal serology, HSV PCR, TB PCR and malignant cytology) were normal. Chest X-ray revealed right upper lobe infiltrates. In view of normal MRI brain and CSF, a diagnosis of new onset status epilepticus of unknown cause was made and he was empirically given IV immunoglobulin 2 g/kg over 3 days. Subsequently his H1N1 RT-PCR turned out to be positive (fifth admission day) and he was treated with oseltamivir 150 mg twice daily for 5 days following which he improved. His sensorium started improving three days following start of oseltamivir, though he continued to be drowsy. He continued to have occasional focal twitching of right side of face for up to 4 days after starting oseltamivir, which subsided thereafter. In view of contribution of antiepileptic drugs to drowsiness, antiepileptic drug dosages were decreased and he was discharged 3 weeks later on phenytoin and levetiracetam. Phenytoin was gradually tapered off after 3 months as he developed severe gum hyperplasia. At 120 days follow up, he is fine on monotherapy with levetiracetam without any further seizures.

3. Discussion

During the H1N1 pandemic, neurological complications occurred in 6–10% of pediatric cases, though most of the available data is limited to small clinical series. The commonest neurological complications of H1N1 infection include

seizures (febrile or nonfebrile) and/or encephalopathy. Most of the patients who develop neurological complications have a pre-existing medical (usually neurological) ailment. Other neurological complications which are commonly associated with H1N1 infection include aseptic meningitis, acute necrotizing encephalopathy, transverse myelitis, extrapyramidal syndromes such as chorea or dystonia, acute disseminated encephalomyelitis and Guillain Barre Syndrome.

Davis LE³ reviewed 32 published cases of encephalopathy in association with H1N1 infection. Most of the cases were in children. Approximately 50% of these had seizures. Patients usually complained of fever, cough, and myalgias from 1 to 4 days prior to the onset of encephalopathy. CSF was normal in most. MRI brain was normal in 62% of patients. It revealed focal brain edema in 31% and bilateral thalamic lesions in 19% of patients. The duration of encephalopathy was less than 1 week with good recovery in most of the patients. In another series, Khandaker et al⁴ reported neurologic complications in 10% of children suffering from H1N1 infections. 42.8% of these children had pre-existing neurologic illness. At the time of presentation, 36.7% had triad of cough, fever and coryza, whereas 38.7% had only one or no respiratory symptoms. Seizures were the commonest neurological complication (7.5%). Death occurred in two patients (4.1%) and most survivors recovered without sequelae.

The mechanism whereby influenza virus causes neurological dysfunction is unknown. A leading hypothesis is that respiratory viral infection triggers proinflammatory cytokines that reach brain via blood. The main point in favor of this hypothesis is that the highest level of cytokines is seen in children with severe encephalopathy.⁵ A second theory suggests that neurological manifestations result from central nervous system damage consequent to a postinfectious immune-mediated process, which is unlikely, as influenza encephalopathy begins early in infection and not during recovery phase. A third hypothesis, which suggests that encephalopathy results from severe systemic respiratory infection, is unlikely as many patients do not have respiratory symptoms. A fourth theory suggests direct viral infection of brain endothelial cells. In this context, H1N1 has occasionally been isolated from damaged nervous tissues, but conclusive proof of this has been lacking.³

The risk of neurological complications is adults with H1N1 infection is much less when compared to children. In contrast to children, where neurological complications occur in approximately 6%, H1N1 infection is rarely associated with seizures or alteration in consciousness level in adults.^{6,7}

Though seizures and status epilepticus have been described previously in association with H1N1 infection, this is the first case report of an adult patient presenting with generalized convulsive status epilepticus in association with H1N1 infection. Another unique feature in our patient is that he did not complain of any respiratory symptoms at the presentation. Our case further expands the clinical spectrum of neurological complications associated with H1N1 infection. It also stresses on need to actively screen all patients of new onset status epilepticus for H1N1 infection in the absence of other obvious causes.

The influenza virus is very rarely isolated from CSF and mainstay of diagnosis is prompt suspicion and appropriate testing (RT-PCR for H1N1 in sputum or tracheal aspirates/other specimens).⁸ In our patient also CSF examination was noncontributory.

Antiviral medications have ten improvements and reduce the risk of complications and should be started as quickly as possible.⁹ As testing often takes time, it is prudent to start treatment empirically if clinical suspicion is strong.⁶ In keeping with the available evidence, our patient also improved significantly following treatment with oseltamivir.

4. Conclusion

GCSE as a presenting manifestation of H1N1 infection is a novel finding. One needs to keep this rare presentation in mind while evaluating patients with new onset status epilepticus and carry out appropriate diagnostic tests so that specific treatment can be initiated at the earliest.

Conflicts of interest

All authors have none to declare.

REFERENCES

1. Novel Swine Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza virus (H1N1) in humans. *N Engl J Med*. 2009;360:2605–2615.
2. Ekstrand JJ, Herbener A, Rawlings J, et al. Heightened neurologic complications in children with pandemic H1N1 influenza. *Ann Neurol*. 2010;68:762–766.
3. Davis LE. Neurologic and muscular complications of the 2009 influenza A (H1N1) pandemic. *Curr Neurol Neurosci Rep*. 2010;10:476–483.
4. Khandaker G, Zurynski Y, Buttery J, et al. Neurologic complications of influenza A(H1N1): surveillance in 6 pediatric hospitals. *Neurology*. 2012;79:1474–1481.
5. To KK, Hung IF, Li IW, et al. Delayed clearance of viral load and marked cytokine activation in severe cases of pandemic H1N1 2009 influenza virus infection. *Clin Infect Dis*. 2010;50:850–859.
6. Kitcharoen S, Pattapongsin M, Sawanyawisuth K, Angela V, Tiamkao S. Neurological manifestations of pandemic (H1N1) 2009 virus infection. *Emerg Infect Dis*. 2010;16:569–570.
7. Yeo LL, Paliwal PR, Tambyah PA, Olszyna DP, Wilder-Smith E, Rathakrishnan R. Complex partial status epilepticus associated with adult H1N1 infection. *J Clin Neurosci*. 2012;19:1728–1730.
8. Morishima T, Togashi T, Yokota S, et al. Encephalitis and encephalopathy associated with an influenza epidemic in Japan. *Clin Infect Dis*. 2002;35:512–517.
9. Kaiser L, Wat C, Mills T, Mahoney P, Ward P, Hayden F. Impact of oseltamivir on influenza related lower respiratory tract complications and hospitalizations. *Arch Intern Med*. 2003;163:1667–1672.