Case Report

Adult Influenza A (H1N1) Related Encephalitis: A Case Report

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Abstract

The year 2009–2010 saw H1N1 influenza outbreaks occurring in almost all countries of the world, causing the WHO to declare it a pandemic of an alert level of 6. In India, H1N1 influenza outbreaks were again reported in late 2014 and early 2015. Since then, sporadic cases of H1N1 influenza have been reported. H1N1 influenza usually presents itself with respiratory tract symptoms. In a minority of patients, abdominal symptoms may occur as well. Acute influenza-associated encephalopathy/encephalitis mostly occurs in the pediatric population, whereas in adults, it is a rare complication. The incidence of neurological complications appears to have increased after the 2009 H1N1 influenza A virus pandemic. We would like to draw attention to an adult patient case who initially presented with respiratory symptoms but then deteriorated and developed encephalitis, which is rarely reported. As per literature reviewed by Victoria Bangualid and Judith Berger on PubMed, only 21 cases of neurological complications were found in adult influenza A patients, out of whom 8 had encephalopathy.

Keywords: Adult, encephalitis, H1N1

Introduction

Influenza is an acute, usually self-limited, febrile illness caused by infection with influenza type A or B virus. While respiratory symptoms are the most common, myositis, rhabdomyolysis, myoglobinuria, myocarditis, pericarditis, and central nervous system (CNS) involvement have all been described with influenza virus infections.[1] Influenza related encephalitis/encephalopathy is more common is paediatric population, however neurological complications appears to have increased after 2009 pandemic.[2-3] Only eight cases with adult influenza A related-encephalopathy has been reported by Victoria Bangualid and Judith Berger.[4] CNS complications may manifest as encephalopathy, seizures, and Guillain–Barré Syndrome.[5-8] The diagnosis is difficult because there is no uniform clinical presentation; influenza virus is rarely detected in cerebrospinal fluid (CSF) and may no longer be detectable in respiratory samples when the patient presents with neurological symptoms.[9] We would like to report a patient with adult H1N1 influenza, who developed encephalitis.

Case Report

A 76-year-old , an elderly female in her mid 70s, was admitted to our Intensive Care Unit with chief complaints of sore throat, sneezing, and fever for the last 7 days, along with oliguria during the last 3 days. She was initially treated at a district hospital with macrolides, antipyretics, and aminoglycosides. Oseltamivir 75 mg bd was initiated 1 day prior to admission. Her comorbidities included hypertension and rheumatoid arthritis.

The patient was on tablet methotrexate which she had left 2 months prior to admission. Her chest radiograph was suggestive of right-sided pneumonia.

On admission, she was conscious, alert, hypotensive, and maintaining saturation on room air. Her mean arterial pressure improved after fluid resuscitation. Her initial laboratory results showed thrombocytopenia (63,000/μl), a deranged renal profile (blood urea nitrogen – 38 mg/dl, creatinine 2.1 mg/dl), and hyponatremia (124 mg/dl). Her total leukocyte count, liver functions, and coagulation profile were within normal limits. Chest X-ray showed bilateral homogenous opacities in all lung fields. Her antibiotic regimen was modified to

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Quick Response Code:

Website: www.ijccm.org

DOI: 10.4103/ijccm.IJCCM_344_17

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How to cite this article: Midha D, Kumar A, Vasudev P, Iqbal ZA, Mandal AK. Adult influenza A (H1N1) related encephalitis: A case report. Indian J Crit Care Med 2018;22:384-7.

intravenous carbapenems and doxycycline along with oral oseltamivir. Sputum samples were sent to rule out viral pneumonia. A high-resolution computed tomography (CT) was made which showed multiple areas of crazy paving, dense consolidation in the right lower lung lobe along with mediastinal lymphadenopathy, and bilateral axillary lymph nodes [Figure 1].

On day 2 of admission, she developed respiratory distress. Viral myocarditis was ruled out with a negative troponin T and raised pro-BNP levels (1300 pg/ml). She was supported with noninvasive ventilation and diuretics. She did show clinical improvement with the above interventions.

She was reported to be real-time polymerase chain reaction positive for pandemic influenza A (H1N1) in 2009. Her antibiotics were de-escalated and she was continued on tablet oseltamivir 150 mg bd. Sequential chest X-rays showed worsening with bilateral consolidation. She developed severe acute respiratory distress syndrome (ARDS) requiring invasive ventilation. She was kept sedated and paralyzed with fentanyl, midazolam, and vecuronium infusion in view of p/f ratio <100 suggestive of severe ARDS. She developed hemodynamic instability which was managed with fluids and vasopressors.

Over the next few days, the patient started showing signs of improvement with decreasing oxygen requirement. On day 7, however, she developed recurrent episodes of focal seizures involving both eyes and upper left lip. No immediate correctable cause was found on blood investigations and a drug chart review. Electroencephalography (EEG) showed a generalized burst suppression pattern with abnormal interictal comatose state. Her seizures were alleviated with leviteracetam and phenytoin along with a midazolam infusion. A CT of the brain showed no significant abnormality. However, an MRI of the brain done later on showed symmetrical areas of altered signal intensity appearing hyperintense on T2/fluid-attenuated inversion recovery sequences involving bilateral thalamic nuclei, midbrain, and pons, suggestive of encephalitis [Figure 2]. Ceftriaxone and vancomycin were added on suspicion of bacterial meningitis. Acyclovir was also added empirically and later withdrawn once the herpes simplex results were found to be negative. The CSF analysis showed a liquor white blood cell count of 30, with neutrophils of 70%, lymphocytes of 15%, and mononuclear cells of 15%. The protein CSF content was 292 and the CSF glucose was 69 mg/dl with corresponding blood sugars being 111 mg/dl. CSF tests for cryptoccal antigens, an India ink preparation, HSV antigens, and cultures were all negative.

She was given sedation vacation but then was found to be in a confused state with intermittent agitation and maximum response of E_4M_4Vt on Glasgow Coma Scale (GCS).

No correctable cause was found. On day 13, a repeat MRI brain was done which showed a significant reduction of abnormal signaling in the affected areas [Figure 3]. A repeat EEG was done which was suggestive of a generalized encephalopathy [Figure 4].

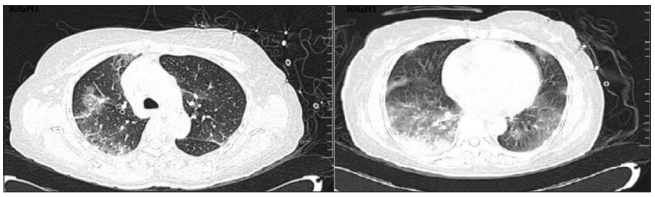

Figure 1: High-resolution computed tomography chest showing multiple areas of crazy paving and dense consolidation in the right lower lobe

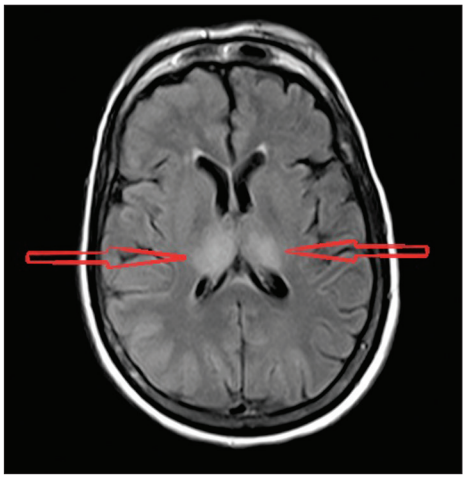

Figure 2: Magnetic resonance imaging brain showing symmetrical areas of altered signal intensity appearing hyperintense on T2/fluid attenuation inversion recovery involving bilateral thalami

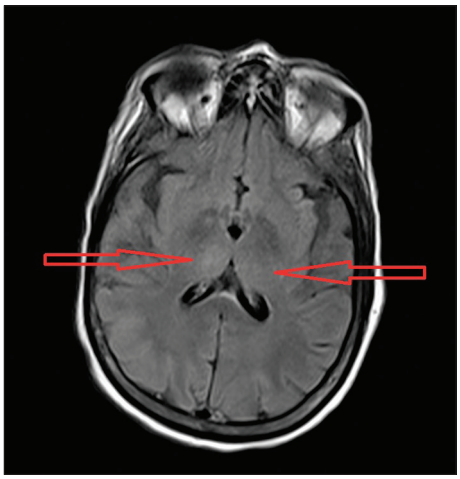

Figure 3: Repeat magnetic resonance imaging brain showing a significant reduction in abnormal signal in the affected areas

Tracheotomy was done and the patient continued to be in an encephalopathic state with fluctuating sensorium, between $E_3M_4V_T$ and $E_4M_5V_T$, and gave no meaningful eye contact. She was slowly weaned off ventilatory support over the next week. She was discharged after 29 days of admission with her tracheostomy *in situ*. At her time of discharge, she was still in

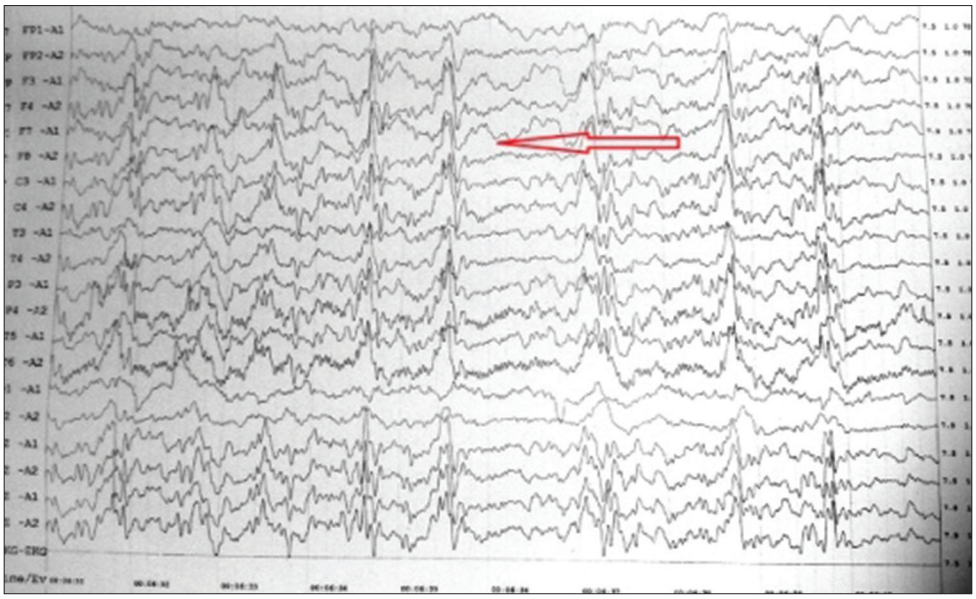

Figure 4: Electroencephalography suggestive of generalized encephalopathy

a confusional state with no meaningful eye contact, having a GCS of $E_4M_5V_T$.

Discussion

Seasonal influenza-related neurological manifestations have been reported in literature before. CNS complications may manifest as encephalopathy, seizures, and Guillain–Barré syndrome.[5-8] Acute influenza-related encephalopathy/encephalitis is a syndrome characterized primarily by symptoms associated with a rapidly progressive consciousness disorder in influenza patients. The true pathogenesis of influenza-associated neurologic disease remains unclear as influenza RNA is rarely detected in the CSF of encephalopathic patients.[9] High levels of pro-inflammatory cytokines (such as interleukin-6 or tumor necrosis factor alpha) have been demonstrated in the serum and the CSF of children.[10]

Acute encephalitis and encephalopathy appear to be very variable in severity, ranging from case reports showing no residual sequelae to severe residual signs and symptoms. There is also a subset of patients who follow a malignant clinical course characterized by high morbidity and mortality.[11-14] Our patient here did have significant residual neurological manifestations. Three out of four patients in a CDC report had abnormal EEG.[15]

Kimura *et al*. divided influenza-related brain changes into five categories based on the MR imaging and CT findings: (1) normal, (2) diffuse involvement of the cerebral cortex, (3) diffuse brain edema, (4) symmetric involvement of the thalamus, and (5) postinfectious focal encephalitis.[14] Our patient probably fell in category 4 with bilateral symmetrical involvement of the thalamic nuclei, midbrain, and pons, reflecting hyperpermeability of the cerebral blood vessels followed by severe edema with or without micro hemorrhages.[12]

In a study on patients with influenza-associated encephalopathy/encephalitis, Meijer *et al*. found influenza virus in the CSF in just 5 (16%) out of 32 patients. In the same study, the CSF analyses done in 38 patients were found to be abnormal in 26 (68%). An elevated white blood cell count and an elevated protein concentration were observed most commonly, in 16 and 9 patients, respectively.[9] We could not send CSF for influenza virus isolation because of nonavailability. CSF routine analysis was more in favor of viral encephalitis in our case

Conclusion

To the best of our knowledge, there are very few case reports of adult H1N1 influenza-related encephalitis reported worldwide.[3] This case report could serve to remind the clinician of the existence of adult H1N1 influenza-related encephalitis, especially in patients presenting with altered behavior in the setting of H1N1 influenza.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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