



Case report

A rare case of influenza A in a hospitalized adult presenting with encephalitis and a seizure

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ABSTRACT

Influenza A in hospitalized adults uncommonly may present with neurologic manifestations, e.g., encephalitis. Encephalitis is the most common influenza related neurologic complication in adults. However, seizures in hospitalized adults due to influenza are extremely rare. This is a case of a 58 year old female hospitalized for influenza A. On admission, she was confused and obtunded. Her EEG showed diffuse global slowing indicative of encephalitis. On hospital day (HD) #2, she had a seizure. She had no history of a seizure disorder, and was not febrile at the time of the seizure. While seizures are not uncommon in children (febrile seizures) with influenza B, but in adults with influenza A, only a few cases of seizures have been reported. This case was most interesting in having both encephalitis and seizure complicating influenza A. If present, neuropsychiatric manifestations may be due to oseltamivir, but encephalitis and seizures are not among the neurologic adverse effects of oseltamivir. In adults hospitalized with influenza A, clinicians should be alert to the possibility of neurologic complications.

Introduction

Influenza is a common cause of viral pneumonia in hospitalized adults. Among viral influenza like illnesses (ILIs), influenza is the most severe. Death due to influenza, usually influenza A, is most often due to respiratory failure from severe hypoxia. Less commonly, influenza A may be complicated by concurrent bacterial co-infection (*S. aureus*), or subsequent co-infection (*S. pneumoniae*, *H. influenzae*) [1].

In adults, neurologic complications of influenza A in adults are rare [2]. In children, neurologic complications are common and unlike adults, may experience febrile seizures. Influenza associated neurologic complications (IANC) include 5 clinical syndromes, e.g., encephalitis, myopathy, chorea, transverse myelitis, Guillain-Barre syndrome. Autoimmune post-infectious acute disseminated encephalomyelitis (ADEM) is a late rare complication (Table 1) [3–12]. In hospitalized adults with influenza A, influenza associated encephalitis (IAE) is rare, and potentially lethal complication. However, the pathophysiology of IAE is not well understood [13–15]. In admitted adults with influenza A, seizures are reportedly rare [16,17]. Seizures, in children are most often febrile seizures [3,5,16]. Adults with influenza may rarely present with seizures alone as the sole neurologic manifestation of influenza [1–16].

We present a most interesting case of influenza in an admitted adult

complicated by both encephalitis and a seizure.

Case

A 58 year old female was admitted with fever, chills, severe myalgias, profound malaise, and mental confusion. She had no past medical history of seizures. Three days prior to admission (PTA), she was febrile (T = 101 °F) with chills. Two days PTA, she had prominent fatigue and remained febrile. One day PTA, she saw a doctor and a nasal swab PCR was positive for influenza A. She was given oseltamivir. The next day, the day of admission, her mental confusion had worsened, her fever and chills continued, and she was hospitalized. On admission, her temperature was 102.9 °F with a pulse of 104 bpm. Her physical examination was unremarkable except that she was completely confused. Her white blood cell (WBC) count was 3.9 K/uL with 12% lymphocytes (n = 21%). Erythrocyte sedimentation rate (ESR) was 33 mm/h and C-reactive protein (CRP) was 4.46 mg/L (n = 3 mg/L). Respiratory viral PCR swab was positive for Influenza A. She was diagnosed with encephalitis due to influenza A and was admitted to the neurological unit for monitoring. Oseltamivir 75 mg q12h was given. Brain MRI was unremarkable. Her electroencephalogram (EEG) showed bilateral diffuse global slowing, diagnostic of encephalitis.

On hospital day two (HD # 2), she had a seizure and was transferred

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Table 1
Complications of Influenza.

Frequency	Neurologic Complications	Neuropsychiatric Complications
Common	<ul style="list-style-type: none"> ● Encephalitis ● Seizures 	<ul style="list-style-type: none"> ● None
Uncommon	<ul style="list-style-type: none"> ● Cerebrovascular accident (CVA) ● Guillain-Barre syndrome ● Acute disseminated encephalomyelitis (ADEM) 	<ul style="list-style-type: none"> ● Hyperactive delirium ● Reproducible neuropsychiatric adverse effects of oseltamivir Hallucinations Reversible memory deterioration

to the neurologic ICU (NSICU) and was started on levetiracetam 500 mg (IV) q 12 h for her seizure. She remained febrile with a T = 103 °F and a pulse of 103 bpm and was given acetaminophen. Patient remained obtunded and encephalopathic without improvement. Lumbar puncture (LP) revealed a clear (non-xanthochromic) CSF with a WBC count of 9 WBCs/hpf (n < 5 WBCs/hpf) with 41% lymphocytes and 47% monocytes. CSF glucose was 64 mg/dL and CSF protein was 120 mg/dL (n = 8–32 mg/dL). CSF viral PCR was negative for cytomegalovirus (CMV), varicella zoster (VZV), and Herpes simplex virus (HSV) 1 and 2.

She had no further seizures, and completed a 5 day course of oseltamivir. On HD #5, her mental status returned to normal and she was discharged home without any subsequent encephalitic or neuropsychiatric manifestations.

Discussion

Rarely, acute viral encephalitis may also have neuropsychiatric manifestations (NPM). These NPMs may complicate the patient's recovery from influenza encephalitis. NPMs may also be due to oseltamivir, used in the treatment of influenza. The majority of neuropsychiatric effects are in the form of delirium and abnormal behavior with a higher incidence in children and adolescents. They are manifested as mild, short-lived, and reversible consciousness impairments. Most patients have varying levels of mental confusion accompanied by a hyperactive state and/or anxiety. Visual hallucinations have also been reported.

Most reports of neuropsychiatric effects in patients infected with the influenza virus were in Japanese children and adolescents. Children 5–15 years of age are most frequently affected, with a higher incidence in males. There is no clear relationship between oseltamivir use and the incidence of hyperactive delirium is noted in infected patients not treated with oseltamivir. Although several cases have reported neuropsychiatric manifestations 1–2 h after taking oseltamivir, the number of cases remains small and difficult to evaluate.

Psychiatric symptoms usually develop within 48 h of oseltamivir. However, a case report from Japan revealed an onset of psychiatric symptoms 5 days after oseltamivir therapy. In this case, a 22 year old male with no personal or familial psychiatric history, developed mood swings, suicidal feelings, auditory hallucinations, memory deterioration, and insomnia after taking oseltamivir, requiring admission to a psychiatric ward. He was treated with olanzapine with marked improvement in psychiatric symptoms. However, because the effects of influenza encephalitis is not well known, the authors were unable to conclude if the symptoms were due to the course of influenza encephalitis or oseltamivir use.

Overall, regardless of oseltamivir use, influenza encephalitis is rarely associated by mild reversible neuropsychiatric symptoms. The most common population affected were children under 10 years of age. Japanese teenagers have a high association with an increase in hyperactive delirium, but noted that some of the patients had a family history or personal history of parasomnia. Several studies have shown that oseltamivir may induce psychiatric symptoms, but the cause remains

controversial. Interestingly, the neuronal excitability is associated with the active metabolite, oseltamivir carboxylate. Further studies of psychiatric side effects are needed.

This case of influenza A is very rare in presenting with both a seizure and encephalitis. Neurologic manifestations in adults with influenza may also be complicated by neuropsychiatric (NP) symptoms, e.g., hyperactivity, visual hallucinations which may be due to the illness or treatment with oseltamivir. NP manifestations of oseltamivir usually occur within 2 days of treatment [18,19]. Importantly, oseltamivir does not cause encephalitis or seizures. Therefore, in this case, the patients NANC cannot be associated to oseltamivir, and were due to influenza A.

Conclusion

We believe this case of influenza A in a hospitalized adult was an extremely rare manifestation of two neurologic complications of influenza A, i.e., encephalitis, and a seizure. The take home lesson for clinicians is that, in adults, influenza A should be in the differential diagnosis of acute viral encephalitis. Furthermore, encephalitis occurs early during influenza. The other clinical point is that seizures are rare in influenza A in adults.

Author contributions

All authors were involved equally in the editing and writing.

Conflicts of interest

None of the authors have conflicts of interest to declare.

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