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Case Report

Simply influenza A (H3N2)-associated encephalitis with seizure

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ABSTRACT

Influenza-associated acute encephalopathy (IAE) is more prevalent in children than in adults and often results in neurological sequelae or even death. Diagnosis of IAE is difficult as clinical presentation varies significantly and the influenza virus is rarely detected in cerebrospinal fluid. Moreover, seizures in adults due to influenza infection are rare. Herein, we describe the case of an adult presenting with both acute encephalitis and seizures.
A 38-year-old female was admitted to the emergency department with acute respiratory symptoms and fever, followed by quick progression to stupor within 24 h. A rapid antigen test was influenza A-positive, and polymerase chain reaction of nasal secretions confirmed the H3N2 subtype. Brain magnetic resonance imaging showed bilateral water restriction lesions at the thalamus and the cerebellum and an electroencephalogram showed frequent episodic generalized sharp-and-slow waves over the bilateral frontal region. Based on the neuroimaging and laboratory findings, we diagnosed the patient with adult influenza A (H3N2)-related encephalitis complicated by seizure. Treatment with oseltamivir and anticonvulsants led to complete neurologic recovery by day 14. This report describes two unusual neurological manifestations of influenza A, i.e., encephalitis and seizures, in an adult. We emphasize that, in adults presenting with acute viral encephalitis, clinicians should consider influenza infection as part of the differential diagnosis, and that typical neuroimaging in conjunction with laboratory detection of influenza virus and/or intrathecal antibody production suggestive of IAE, may help establish an accurate diagnosis.

Influenza virus infection is a common etiology of acute respiratory illnesses that can also result in multiple systemic complications. Central nervous system (CNS) involvement is rare but well-described and manifests as altered consciousness, disorientation, seizures, or even death, but usually after the onset of fever and respiratory symptoms. Influenza-associated encephalopathy/encephalitis (IAE) is more prevalent in children than in adults [1]. Even though complex clinical scenarios can complicate recognition [2], adult cases are infrequently reported and poorly characterized, and diagnosis is hampered by significant variation in clinical presentation and difficulties in virus detection in the cerebrospinal fluid (CSF) [3]. Influenza A H1N1-associated encephalopathy is better described than others, but recognizing H3N2-related encephalitis is important given its increasing prevalence [4]. Here, we describe a rare case of H3N2 influenza in a 38-year-old woman presenting with both encephalitis and seizures.

A 38-year-old woman presented to the emergency department (ED) with a 2-day history of prodromal acute respiratory symptoms, fever, and significant fatigue. Her medical and family histories were unremarkable.

Vital signs at presentation were temperature 38 °C, pulse rate 102 per minute, respiratory rate 22 per minute, and blood pressure 116/77 mmHg. The chest plain film, routine blood and biochemical analyses showed insignificant findings. Polymerase chain reaction (PCR) of nasopharyngeal aspirate (rapid antigen test) identified influenza A. As the present symptoms and clinical entity of the patient did not meet the criteria of high risk of complications from influenza [5], antipyretics were administered. Two days later, she presented again with refractory fever and gradually reducing consciousness. Upon arrival to the ED, neurologic examination revealed lethargy with a Glasgow Coma Scale score of 11 (eye opening: 3, best verbal response: 3, and best motor response: 5), equivocal meningeal irritation signs, slow-reactive but equal pupils, and intact bilateral Babinski reflexes. Laboratory data showed normal white blood cell count (5140/μL), but excessively elevated levels of aspartate aminotransferase (197 U/L), alanine aminotransferase (145 U/L), creatine kinase (2577 U/L), and procalcitonin (14.44 ng/mL). Brain computed tomography (CT) revealed bilateral

Abbreviations: IAE, influenza-associated encephalopathy; CNS, central nervous system; CSF, cerebrospinal fluid; ED, emergency department; PCR, polymerase chain reaction; CT, computed tomography; MRI, magnetic resonance imaging.

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hypodense lesions over the cerebellum and the thalamus, and magnetic resonance imaging (MRI) demonstrated corresponding water restriction lesions (Fig. 1A). CSF analysis was insignificant except for elevated protein (165 mg/dL). Broad-spectrum antimicrobial agents, intravenous ceftriaxone and acyclovir, were initiated for presumed infectious meningitis. However, further microbiologic workup of CSF was negative for bacteria, fungi, and acid-fast bacilli, and PCR was negative for influenza virus. Within 24 h of admission, she became stuporose and required endotracheal intubation, while, PCR of nasal secretions identified the presence of influenza A H3N2-subtype. She underwent additional gadolinium-enhanced brain MRI on day 2 which demonstrated interval progression with central necrosis in the cerebellum and the thalamus (Fig. 1B). Therefore, a diagnosis of influenza A (H3N2)-associated acute necrotizing encephalopathy was made based on characteristic MRI findings, clinical presentation, and lack of a clear alterative etiology, and twice-daily treatment with oral oseltamivir 75 mg was initiated. Intravenous betamethasone pulse therapy (2 mg daily for 3 days) was started on day 3, followed by a slow tapering of oral prednisolone. An electroencephalogram acquired on the same day showed frequent episodic generalized bilateral sharp-and-slow waves over the frontal region, indicating non-convulsive seizures. After a 5-day course of 75 mg oseltamivir and intravenous levetiracetam 500 mg twice-daily, she gradually regained consciousness by day 7, was successfully weaned from mechanical ventilation, and almost completely recovered with only slight disruption of daily life by day 14. Her mental status returned to normal and she was discharged without any subsequent encephalitic or neuropsychiatric manifestations.

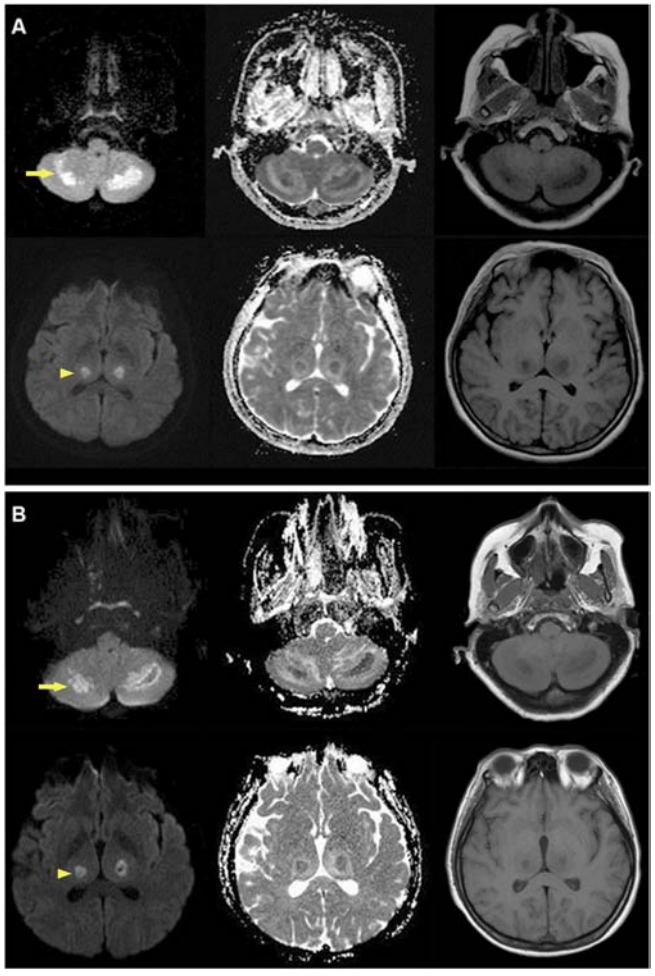

Fig. 1. (A) Brain MRI (axial view) revealed symmetrical bilateral hyperintense lesions in the cerebellum (arrows) and the thalami (arrowheads) on diffusion-weighted imaging (left), associated hypointense on the apparent diffusion coefficient-map (center), and T1 weighted imaging (right) in the corresponding areas at initial diagnosis of influenza-associated acute encephalopathy. (B) Central necrosis of these lesions was seen in the brain MRI series 48 h after onset.

Influenza A viruses are RNA viruses of the Orthomyxoviridae family, are capable of infecting multiple species, are known etiological agents of seasonal outbreaks, epidemics, and pandemics, and can manifest with a wide range of neurological complications, including Reye syndrome, generalized encephalopathy, seizures, aseptic meningitis, and postinfectious acute disseminated encephalomyelitis [6-9]. IAE is more common in children, especially with subtype H1N1 influenza A infection, and although not specifically typed, our case of IAE can be attributed to seasonal influenza A (H3N2). Acute IAE is characterized by rapid and progressive loss of consciousness as seen in our patient and brain imaging revealed hallmark IAE findings of initial bilateral hypodense areas on CT followed by characteristic symmetrical bilateral hyperintense MRI signals, both in the thalamus [10-12]. Few adult cases of seasonal influenza A-related meningoencephalitis have been reported. Burke et al. [13] described a 51-year old man with IAE presented with febrile and altered mental status. Similar to our case, PCR of an admission nasopharyngeal swab was positive for influenza A but not CSF samples, and he was successfully managed with antiviral treatment. In addition, the influenza A-subtype was not specifically identified, and H3N2 was presumed by a process of elimination: both H3N2 and H1N1 were co-circulating of the pandemic strain, and the complete blood count exhibited lymphocytosis (the feature of H3N2) rather than relative lymphopenia and thrombocytopenia (the features of H1N1). Unlike our case, electroencephalogram was not utilized for possible epileptic seizure detection. The brain CT produced unremarkable results rather than characteristic neuroimaging of IAE as in our case. The IAE was diagnosed based on his clinical and CSF findings. However, there are limited cases associated with such clinical settings of influenza A-H3N2, and diagnosing IAE is difficult as CSF-based detection of influenza is rare [14].

In adults presenting with acute viral encephalitis, influenza infection should be considered as a differential diagnosis. Routine neuroimaging, in conjunction with laboratory detection of influenza virus and/or intrathecal antibody production suggestive of IAE, may help establish an accurate diagnosis. Thus, this case is instructive because the patient presented with critical CNS complications and positive serial MRI findings due to seasonal influenza A (H3N2) infection.

Data sharing

No additional data.

Contributorship

All of the authors contributed to planning, conduct, and reporting of the work. All contributors are responsible for the overall content as guarantors.

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Declaration of Competing Interests

All of the authors have no conflict of interest.

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