Journal of Acute Medicine 10(2): 96-97, 2020
DOI:10.6705/j.jacme.202006_10(2).0007
Make Your Diagnosis

Influenza A-Associated Acute Necrotizing Encephalopathy

Wen-Lan Yen, Kuan-Hsien Lee, Hsin-Ju Huang, Ming-Jen Tsai*
Department of Emergency Medicine, Ditmanson Medical Foundation Chiayi Christian Hospital, Chiayi, Taiwan

Case Presentation

An 8-year-old previously healthy girl presented to the emergency department (ED) with chief complaint of fever on and off for one day. On arrival, lethargy consciousness, fever (39°C), tachycardia (123 beats per minute), a respiratory rate of 25 breaths per minute without respiratory distress, a blood pressure of 103/69 mmHg, and warm and non-mottled skin were found. Physical examination only showed injected throat. Blood tests showed no leukocytosis (8087/μL) and normal C-reactive protein (0.178 mg/dL). After use of intravenous fluid and diclofenac suppository, her consciousness and activity recovered. She was treated initially as upper respiratory tract infection. Antipyretics, antitussives, and antihistamines were prescribed. However, at the same day after discharge from the first ED visit, drowsy consciousness was noted during a fever attacked. She was sent back to the ED. On arrival, she was febrile (42°C) and unconscious (Glasgow Coma Scales: E2V2M3). Neurologic examination showed intermittent decerebrate posture, isocoric pupils of 3-mm diameter with light reflex, positive oculocephalic reflex, slightly increased deep tendon reflex, and negative Babinski sign. Fever workup showed leukocytosis (17210/μL), elevation of alanine aminotransferase (99 U/L), positive influenza A test, but normal urinalysis, chest radiography and ammonia level. The head computed tomography (CT) (Fig. 1B) revealed hypodense in bilateral thalami (arrows) and edematous change in white matter compared to previous normal CT performed nine months ago (Fig. 1A). The cerebrospinal fluid (CSF) study showed increased protein level (360 mg/dL) without pleocytosis. Because of deterioration of consciousness, the second CT was performed (Fig. 1C) six hours after the first CT and showed diffuse brain swelling and ischemic change. The electroencephalography showed diffuse cerebral dysfunction. Despite the support of mechanical ventilation, use of peramivir, mannitol, empiric antibiotics and inotropic agents, patient was expired at the same day. Finally, only the influenza A virus was detected in the CSF virus culture, no other pathogen was isolated from the CSF, throat and rectal swab.

Discussion

Influenza-associated acute necrotizing encephalopathy (ANE) is a rare, lethal and rapidly deteriorating disease, which is more prevalent in East Asia, including Taiwan, Japan and South Korea than in Western countries.[1] The neurologic symptoms usually developed rapidly within one day after the first fever episode. Consciousness disturbance and convulsion are the most common initial presentation.[1] The hallmark of neuroradiologic manifestations of influenza-associated ANE is multifocal, symmetric brain lesion especially affecting the thalamus, cerebral white matter, brain stem and cerebellum. Bilateral thalami are particularly involved in all reported patients with ANE, which serves as a distinctive and early neuroradiologic feature of ANE.[2,3] In addition to the above characteristics, Mizuguchi also described the diagnosis criteria for ANE which include increased CSF protein without pleocytosis, elevation of serum aminotransferase without hyperammonemia and exclusion

Received: July 23, 2019; Revised: December 6, 2019 (2nd); Accepted: January 6, 2020.
*Corresponding author: Ming-Jen Tsai, MD, Ph.D, Department of Emergency Medicine, Ditmanson Medical Foundation Chiayi Christian Hospital, No. 539, Zhongxiao Rd., East Dist., Chiayi City 600, Taiwan. E-mail: tshi33@gmail.com

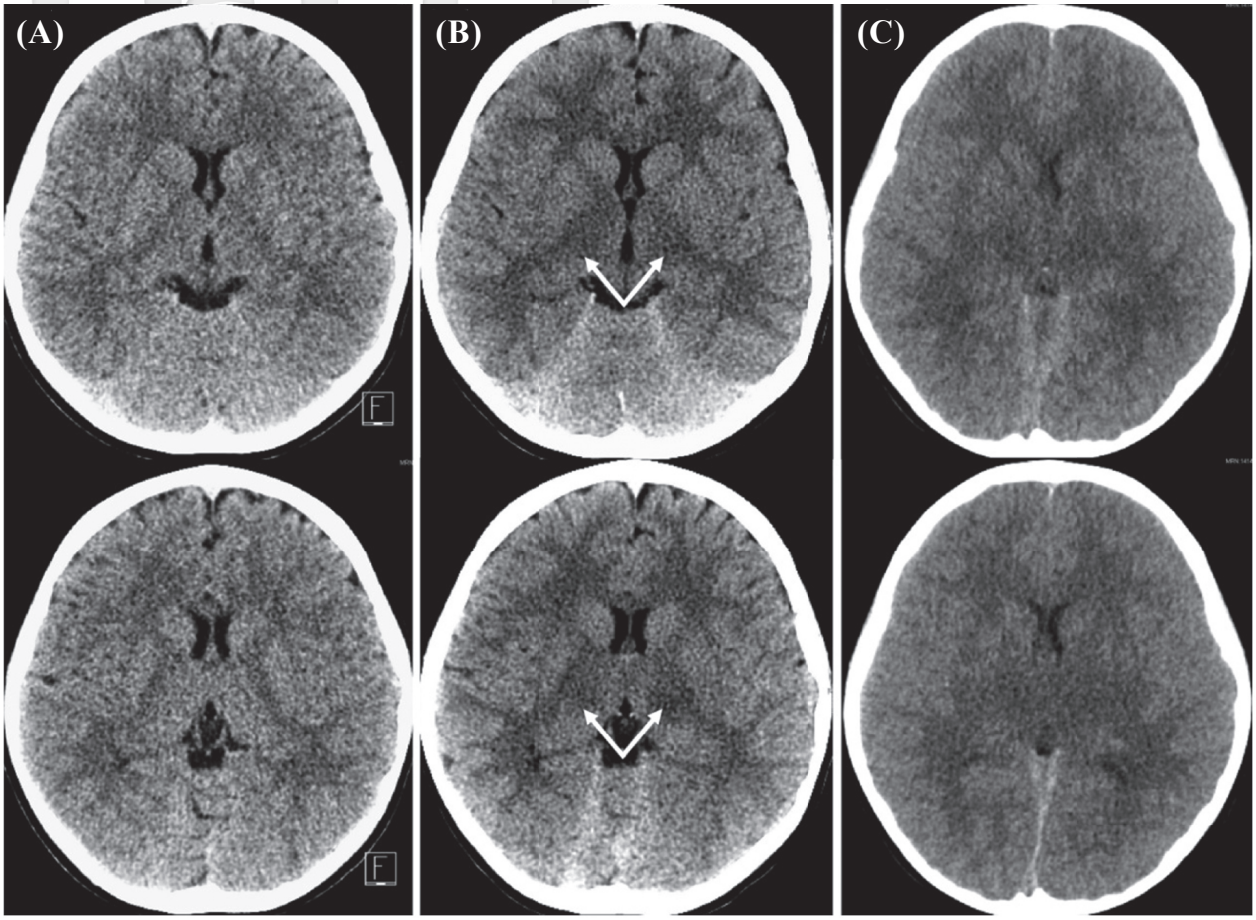

Fig. 1. (A) The previous brain computed tomography (CT) (nine months ago) shows the normal brain parenchyma. (B) The first CT scan of the emergency department shows bilateral thalami (arrows) and white matter edematous and hypodense change. (C) The second CT scan (six hours after the first CT scan) shows diffuse brain swelling and ischemic change.

of other resembling disease.[2-4] So far, there is still a lack of recommended therapies for influenza-associated ANE. In addition to the intensive care and antiviral therapy, the immunomodulatory agents, like glucocorticoids and immunoglobulin, and plasmapheresis were tested to treat the hypercytokinemia secondary to the viral infection.[2] Because of high mortality rate and usual underdiagnosis, keeping a high degree of awareness in influenza patients with consciousness disturbance or convulsion, familiarity with its initial radiologic features of involvement of bilateral thalami and managing with a tailored treatment strategy may be the key to treat this disease.

References

1. Chen LW, Teng CK, Tsai YS, et al. Influenza-associated neurological complications during 2014–2017 in Taiwan. *Brain Dev* 2018;40:799-806. doi:10.1016/j.braindev.2018.05.019
2. Wu X, Wu W, Pan W, Wu L, Liu K, Zhang HL. Acute necrotizing encephalopathy: an underrecognized clinicoradiologic disorder. *Mediators Inflamm* 2015;2015:792578. doi:10.1155/2015/792578
3. Mizuguchi M. Acute necrotizing encephalopathy of childhood: a novel form of acute encephalopathy prevalent in Japan and Taiwan. *Brain Dev* 1997;19:81-92. doi:10.1016/s0387-7604(96)00063-0
4. Mizuguchi M, Abe J, Mikkaichi K, et al. Acute necrotising encephalopathy of childhood: a new syndrome presenting with multifocal, symmetric brain lesions. *J Neurol Neurosurg Psychiatry* 1995;58:555-561. doi:10.1136/jnnp.58.5.555