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Case Report

Acute Necrotizing Encephalopathy Caused by Influenza B in a 6 Years Old Healthy Girl: Case Report

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Abstract

Influenza associated neurological compilations such as encephalitis or encephalopathy are more common in children and are mostly caused by influenza A, and less commonly by influenza B. We report a case of 6-years old girl, previously well child, who was admitted with acute necrotizing encephalopathy (ANE) secondary to acute viral infection by influenza B. She presented to emergency department with seizure, fever and rapid decline in consciousness. Non-contract computed tomography scan (CT) of the brain demonstrated bilateral thalamic hemorrhagic changes with surrounded edema and hypodensities in cerebellum which is keeping with acute meningoencephalitis and acute necrotizing encephalopathy. She was treated with intravenous ceftriaxone, vancomycin and acyclovir along with oseltamivir which was added next day with immunoglobulin and intravenous dexamethasone. An electroencephalography (EEG) analysis showed no electrical brain activity. Unfortunately, the child had rapid deteriorating course over 7 days in the pediatric intensive care unit and she deceased. This case report highlight the fatal neurological complication of influenza B in a previously healthy child.

Keywords: *Influenza B; Acute Necrotizing Encephalopathy; Encephalopathy; Encephalitis; Children*

Introduction

Influenza associated neurological compilations are variable and include encephalitis or encephalopathy which are more common with influenza A compared to influenza B [1]. Influenza virus A and B both are associated with alterations in neuraminidase and neurovirulence effect [2]. Most common presentations of influenza viruses are fever, upper respiratory infection. They can also present with central nervous system (CNS) manifestation like irritability, seizure, hemiparesis and coma. In Japan, during the period of influenza epidemic noticed that influenza encephalopathy was widely recognized and estimated as 100 - 500 case per years [2]. Whereas in US during 2000 - 2004 the incidence of neurologic complications associated with influenza based on retrospective study was reported as 4 cases per 100,000 children-years aged between 2 and 4 years [3]. In Oman, several studies about influenza viral infection were conducted but non-showed the neurological complications [4-6]. Therefore, the neurological manifestations associated with influenza virus infection are still not well understood and the frequency is underestimated. Neurological complication of influenza can manifest as acute necrotizing encephalopathy/encephalitis, Reye syndrome, Guillain-Barre syndrome, transverse myelitis, and seizures. Acute hemorrhage leukoencephalopathy is another neurological complication of influenza [7]. Seizures is considered as the most frequently reported neurologic complication [3,7].

Case Presentation

A previously healthy 6-years old Omani girl, presented in August 2018 with history of fever, cough and runny nose for almost 2 days. She was diagnosed with upper respiratory tract infection and was treated symptomatically with antipyretic. The next day, she developed vomiting, became unresponsive and stiff over few hours after which she started to have generalized seizure. She presented late to medical services because her parent took her to traditional healer for herbal treatment, they did think that her condition was related to abnormal behaviors and black magic but the child didn't improve and continued seizing with unresponsiveness. Then they decided to take her to pediatric emergency department (ED) at tertiary hospital.

In the ED, she was unresponsive with continuous generalized tonic-clonic seizure. She was treated with diazepam, midazolam and loading dose of phenytoin. Then she was intubated due to low Glasgow Coma Scale. Child started to bleed from endotracheal tube and nose and blood products (packed red blood cells(PRBC), platelet and crypipataicated) were given to her. Family denies any past medical illness and her immunizations were up-to-date.

Blood gas revealed metabolic acidosis: pH 7.27, paCO2: 32 mmHg, HCO3: 16 mmol/L] with high lactate of 4. Child was admitted to Pediatric intensive care unit. Initial laboratory investigations showed deranged renal function (creatinine 142 umol/L and urea 17.1 mmol/l), deranged coagulation profile: high Prothrombin time 16.1s, Active thromboplastin time: 61.2s and international normalized ratio of 1.6) and raised liver enzymes: Alanine aminotransferase: 69 iu/L); a picture of disseminated intravascular coagulation (DIC). Other liver function parameter were within normal range which included Alkaline phosphatase: 269 iu/L, protein: 80 g/L, albumin: 41 g/l and total bilirubin of 6 umol/L

Other blood investigations were all within normal. Respiratory virus panel was sent along with serology tests for most common viruses including Dengue, enterovirus, adenovirus, herpes virus, cytomegalovirus (CMV), Epstein Barr virus (EBV), Crimean Congo hemorrhagic fever virus (CCHFV). Respiratory virus panel came positive for influenza B. Lumber Puncture deferred as child remained critically sick.

Non-Contrast Computed tomography (CT) head scan revealed bilateral focal thalamic lesions which is surrounded by brain edema with possible hypo-densities in cerebellum and right temporal lobe possibilities due to meningoencephalitis with dilated of ventricles (Figure 1). Few days later another CT head revealed multiple supra and infra tentorial hypo-densities could be most due to ischemia change and less likely to isolated encephalitis. Brain Magnetic Resonance Imaging (MRI) was not done due to the critical condition of the child. Furthermore, chest radiograph was suggestive of aspiration pneumonia at right upper lobe with consolidation with streaky opacities.

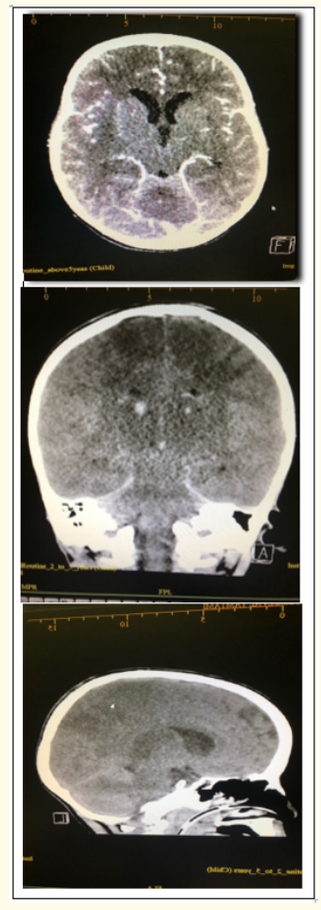

Figure 1: *Non-contract CT Brain demonstrated bilateral thalamic hemorrhagic changes with surrounded edema and hypo densities in cerebellum.*

Electroencephalograph (EEG) was done later as child has multiple frequent episodes of seizures despite been on multiple anti-epileptic drugs, and was reported as flat trace with no electrical discharge

Child was empirically treated as a case of meningoencephalitis with combination of antimicrobial regimen that include intravenous ceftriaxone, vancomycin, acyclovir and oseltamivir. Corticosteroid and immunoglobulin were added. Her condition continued to deteriorate further despite she was put on intensive supportive care with multiple blood product transfusion and ionotropic medications. Parents were counselled by multi-disciplinary team regarding the prognosis and outcome of their child condition. The patient remained comatose and intubated. Despite aggressive treatment and supportive measures, her condition rapidly deteriorated. On the seventh day after her intensive care unit admission, she died with cardiopulmonary arrest

Discussion

Acute necrotizing encephalopathy (ANE) was described by Mizuguchi in 1995 in japan as first case was reported there in same year [8,9]. Majorities of cases have been reported in Asia, mostly in Japanese and Taiwanese population and it was initially thought it was related to racial factor, but later increasing number of cases were reported in western countries and even affect the adult group but still the most common group is the children [1,2,9,10]. ANE is described as specific type of encephalopathy that affect infants and children following viral infection [8-10]. It is characterized by multifocal and symmetrical brain lesion mainly affect thalamus, cerebral and cerebellar white matter and brain stem [1,2,8,10]. These findings were found in neuroimaging of our patient. Bilateral thalami are typically involved in all patients with ANE, which consider as a distinctive feature of ANE [2,3,10].

The aeitology and the pathogenesis remain unclear, but it develops as a complication to viral infection which is commonly reported with influenza, parainfluenza virus, herpes virus 6 and 7 [9,10]. ANE is not considered as inflammatory process as known in encephalitis. The clinical Features of ANE is mostly nonspecific which include three stages: the first stage involves prodromal symptoms that occur due to viral infections (fever, signs of upper respiratory tract infections and gastroenteritis/vomiting). The second stage represents signs of shock, multiple organ failure and DIC. With the development of ANE, brain dysfunctions may present as seizures, alteration level of consciousness, and focal neurological deficits. The third stage represents neurological sequelae in most of the patients which could be either with long-term neurological sequelae or recovery [10].

There is no specific treatment recommended for ANE. Only supportive and symptomatic management that include empirical treatment with antiviral therapy and immunosuppressive therapy to counteract the hypercytokinemia state secondary to the infectious process [1,8-10]. Use of steroid, immunoglobulin, and plasmapheresis have been tried in treatment of ANE [8,10]. Some researchers reported that administration of steroids within 24 hours of onset or at the early stage of the disease was associated with better prognosis in those without brain involvement [10,11]. Even with the severity of presentation, the late administration of steroids found to have good outcome in some cases. Some researchers suggested that a trail of steroids should be given to all patients with ANE [3,10,12]. Another study, reported that ANE patients who was treated with steroids had a poor outcome [10,13-15]. Some studies has suggested high dose of oseltamavir (150 mg BID) with methylprednisolone in adult [1] but not in children. In our patient all this supportive management was initiated apart from plasmaphereses since the day of admission but still no improvement. ANE is a progressive disease and its prognosis varies from complete recovery to death regardless of treatment [2,9,10].

Conclusion

This case report highlight the fatal neurological complication of influenza B in a previously healthy child and the importance of early diagnosis. It emphasizes on the need for influenza vaccine and to increase the awareness of the public about influenza complications and the need for early presentation to health care facility. Further studies and research are recommended to come up with the best treatment recommendation for this clinical condition.

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