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Acute Necrotizing Encephalopathy of Childhood: a Fatal Complication of Swine Flu

Muhammad Rehan Khan, Prem Kumar Maheshwari, Syed Asad Ali and Anwarul Haque

ABSTRACT

Acute necrotizing encephalopathy of childhood (ANEC) is a rare condition characterized by the presence of multifocal symmetrical brain lesions involving mainly thalami, brainstem, cerebellum and white matter. ANEC is a serious and life threatening complication of simple viral infections. We present a case of a young child who developed this condition with classical clinical and radiological findings consistent with ANEC, secondary to swine flu (H1N1). He needed ventilatory support and had profound motor and intellectual deficit on discharge. We report this case with aim of raising awareness about this fatal complication of swine flu which has become a global health care issue these days.

Key words: Acute necrotizing encephalopathy. Children. Swine flu. Symmetrical brain lesions. Thalami. Brainstem. Cerebellum. White matter.

INTRODUCTION

Viral illnesses contribute a major burden of infectious diseases. Influenza virus is usually associated with mild respiratory illnesses but rarely, influenza virus infections can result in severe neurological complications. Post-influenza encephalitis and acute encephalopathy have been described in literature since long. Acute necrotizing encephalopathy of childhood was first described by Mizuguchi *et al.* as possible subset of acute encephalopathy.¹ It is characterized by fulminant and monophasic clinical course along with classical radiological findings of the multifocal symmetrical lesions in the brain, affecting the thalami bilaterally, brainstem and cerebellum.² This disease usually affects young children and is associated with high morbidity and mortality.³ About 70% of the children with ANEC die within few days of onset of symptoms.⁴ Most of the cases of ANEC are reported to occur secondary to influenza-A (H3N2) or parainfluenza virus.

This is the first case of ANEC secondary to swine flu (H1N1) in Pakistan with classical clinical and radiological findings.

CASE REPORT

A two and a half years old, previously well, vaccinated according to EPI and developmentally normal child was admitted with acute history of cough and low grade fever followed by rapid progression of symptoms to high grade

fever, convulsions, irritability and drowsiness. On admission, he was febrile, drowsy with moderate disturbance of consciousness (Glasgow coma score of 7/15). There was hypertonia, exaggerated deep tendon reflexes, positive babinski reflex and decorticate posturing. The laboratory tests showed normal serum chemistry except for mildly elevated liver enzymes (SGPT 58 IU/L, SGOT 93 IU/L). LDH and CPK were also high i.e. LDH=1431 IU/L (normal range=253-548 IU/L), CPK=896 IU/L (normal range=17-176 IU/L) while ammonia and lactic acid were normal. Inflammatory markers were normal. Analysis of CSF showed a normal cell count and slightly elevated proteins. The clinical diagnosis of acute encephalopathy was made. CT scan of brain showed bilateral symmetrical low attenuation in dorsal part of brainstem, bilateral thalami and in deep white matter. Later on, similar findings were also documented on MRI brain (Figure 1 a and b), thus the diagnosis of ANEC was made on the basis of clinical and radiological findings.

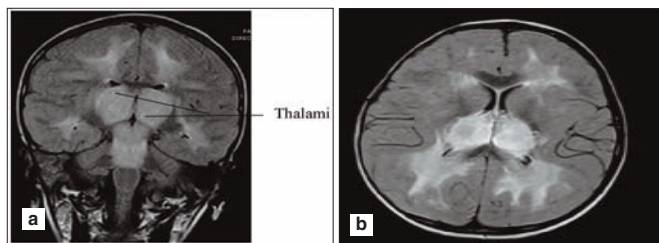


Figure 1 (a,b): Figures showing bilateral abnormal signals in dorsal part of midbrain, pons and thalami.

The child was placed on mechanical ventilation along with supportive care. He was treated with intravenous fluids and parenteral nutrition. Acyclovir was discontinued after the PCR test for herpes was found negative. Reverse transcription-PCR analysis of nasopharyngeal secretions confirmed the presence of swine flu (influenza-A, H1N1).

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The sample was confirmed positive by repeat RT PCR at National Institute of Health, Islamabad.

The child was treated with oseltamivir for 10 days. His conscious level gradually improved and was extubated after 10 days but he had profound motor and intellectual deficit at the time of discharge from the paediatric ICU.

DISCUSSION

The reported patient developed acute encephalopathy after 2-day prodrome of fever, vomiting and cough. Bilateral thalamic involvement with typical clinical and biochemical findings was consistent with the diagnosis of ANE, as reported by Mizuguchi *et al.*^{1,4} ANEC is a very specific type of encephalopathy, usually seen in very young children who are previously well and healthy. This disease is associated with severe neurological sequelae and profoundly high mortality.

Although the spectrum of neurological sequelae associated with ANEC is quite broad, children usually present with dramatic neurological deficits. Viral prodrome is followed by high grade fever, convulsions and sudden onset of severe neurological findings like hyperreflexia, positive Babinski's sign, decorticate/decerebrate posturing, miosis and papilledema on eye examination. There is rapid progression of symptoms into coma.³ Similar course of progression were observed in this patient with rapid neurological deterioration.

This condition is postulated to be immune mediated but the exact pathophysiology of this rare entity is still unknown.³ Disruption of the blood-brain barrier and extravasation of plasma takes place secondary to local vascular lesions. This is followed by destruction and necrosis of glial cells and neurons which is the pathognomic feature of ANEC.⁵

No specific laboratory parameters exist for the detection of influenza virus infection and ANEC. The patient may have raised level of liver transaminases and LDH while thrombocytopenia and deranged coagulation may also be rarely seen.⁶ The CSF examination is usually normal. MRI findings include symmetrically distributed brain lesions, specifically in the thalami, brain stem and cerebellum. Virological analyses are essential to prove that CNS complications are secondary to influenza.² This patient had elevated liver enzymes and LDH with normal CSF and typical radiological findings plus a positive PCR for swine flu.

Differential diagnosis of ANEC may include Reye syndrome, meningoencephalitis or Leigh disease. Both the Reye syndrome and Leigh disease usually have hypoglycemia, hyperammonemia and lactic acidosis which is absent in ANEC.^{4,7} This patient did not have hypoglycemia, hyperammonemia or lactic acidosis. Furthermore, ANEC has monophasic course while

Leigh disease usually has relapsing and remitting course. On the other hand, meningoencephalitis would result in pleocytosis in CSF and there will be lack of typical radiological findings.⁸

The treatment of ANEC is mainly supportive with use of anti-epileptic drugs for seizures and monitoring of intracranial pressure in ICU settings. Anti-viral agents like amantadine have been used since long as these drugs are effective against influenza-A virus with good bioavailability and efficient CSF penetration.^{9,10} However, there is no consensus whether anti-viral drugs have any beneficial effect in the CNS complications of influenza virus. This patient received Oseltamivir but still developed profound neurological sequelae.

Thus, ANEC is one of the deadly complications of swine flu which is now a well recognized epidemic throughout the world. The children are especially at the highest risk to acquire this viral infection. Vaccination and proper precautionary measures are the only available tools to prevent the swine flu. There is a need of awareness for influenza vaccination in population to prevent this disease and its life threatening complications like ANEC.

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