

Cerebral vein thrombosis complicating influenza A in a toddler

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ABSTRACT

We describe a child who presented with a respiratory illness in the influenza pandemic season and was found to be positive for the influenza A, he developed neurological manifestations of cranial nerve palsies and was found to have radiological evidence of cerebral sinus thrombosis. He received treatment with oseltamivir and supportive therapy and was discharged home free of long-term neurological sequelae. This is a rare complication which might have associated with this infection and has not been reported in children before as far as we are aware. Children who develop focal neurological signs during the course of flu epidemic should be evaluated for the possibility of cerebral sinus thrombosis.

Key words: Cerebral sinus thrombosis, Encephalitis, Influenza A

The incidence of neurological complications of seasonal influenza has been estimated at around 4 per 100,000 children per year [1]. Neurological complications have been reported more commonly in children <6 years of age [2]. Neurological complications including seizures, encephalopathy, and Reye's syndrome have been described previously in association with respiratory tract infection with seasonal influenza A or B viruses; however, we are not aware of such complications being reported with influenza A (H1N1) virus [2]. The pathogenesis of influenza-associated neurologic disease remains unclear.

Influenza RNA is rarely detected in the cerebrospinal fluid (CSF) of patients with encephalopathy; one possible hypothesis is a systemic immune response [3]. High levels of proinflammatory cytokines (such as interleukin [IL]-6 or tumor necrosis factor-alpha) have been demonstrated in the serum and in the CSF of children with influenza-associated encephalopathy. There is evidence from the literature that elevated serum IL-6 can be a predictor of a poor outcome in such patients [4]. Some authors have suggested that underlying metabolic disorders or genetic susceptibility may play a role in the pathogenesis [5]. We could not find any previous report of cerebral sinus thrombosis in patient of H1N1 influenza; therefore, we are reporting such case.

A patient with acute neurologic complications or signs of encephalopathy such as seizures or focal neurological signs associated with novel H1N1 virus infection having laboratory-confirmed novel H1N1 infection, in the absence of an alternative etiology, will support such diagnosis. Encephalopathy is defined as altered mental status lasting more than 24 h. The patients with encephalitis will have pyrexia of $\geq 38.0^{\circ}\text{C}$ focal neurologic signs, CSF pleocytosis, or abnormal neurophysiological or neuroimaging studies supportive of CNS infection [7,8].

Electroencephalogram abnormalities were commonly observed in seasonal influenza-related encephalitis (86%) of patients in review of Amin *et al.* [2]. They described evidence of either generalized or focal slowing in such patients. Neuroimaging findings in influenza-associated encephalopathy may be normal. In severe cases, abnormalities can include diffuse cerebral edema and bilateral thalamic lesions [7,8].

CASE REPORT

An 18-month-old female with a history of recent travel to Egypt presented with lethargy and fever of 2 days duration preceded with 1 week history of upper respiratory tract infection in Egypt. She was admitted our hospital for respiratory distress and poor feeding. On examination, she had labored breathing with grunting; she was commenced on antibiotics for concern about pneumonia. She was well hydrated with no evidence of dehydration or hypernatremia. On the 5th day, she developed a convergent squint more noticeable in the left side and fever. Rest of her neurological examination including fundus examination was normal. Her laboratory investigations were only significant for an elevated CSF protein at 0.45 g/l and no cells. Thrombophilia screen was not deemed necessary. She tested positive for H1N1 from her nasopharyngeal aspirate which was confirmed on the repeat sampling. Oseltamivir and further antibiotics were added.

Initial computed tomography (CT) scan following the neurological evaluation showed a low-density area in the left temporal lobe with bilateral ethmoidal and maxillary sinusitis. Magnetic resonance imaging (MRI) brain showed evidence of thrombosis of the left transverse sinus and superior sagittal sinus with hemorrhagic infarction involving part of the left temporal



Figure 1: Axial t1-weighted. Sequence showing thrombosed left transverse sinus (white arrow) and hemorrhagic infarct in the left temporal lobe of the brain (black arrow)

lobe (Fig. 1). She did not receive anticoagulation; however, a short course of aspirin was given initially.

She was managed conservatively; oseltamivir was used to treat her H1N1 infection and she was commenced on aspirin. Apart from the squint, she did not have any further neurological signs and she remained well neurologically throughout her hospital stay. Due to the concern about Reye syndrome, aspirin was discontinued on day 4 and she was discharged home on day 7 with no residual deficit. Follow-up at 3, 6, and 12 months showed normal neurological examination and normal development.

DISCUSSION

Pandemic H1N1 virus (2009) derives six genes from triple reassortant North American swine virus lineages and two genes (encoding neuraminidase and matrix proteins) from Eurasian swine virus lineages. Young children with 2009 H1N1 virus infection may have marked irritability, severe lethargy, poor oral intake, dehydration resulting in shock, and seizures. Other complications include invasive bacterial infections, encephalopathy or encephalitis (sometimes necrotizing), and diabetic ketoacidosis. Kimura *et al.* divided influenza-related brain changes into five categories based on the neuroimaging findings: Normal (category 1), diffuse involvement of the cerebral cortex (category 2), diffuse brain edema (category 3), symmetric involvement of the thalamus (category 4), and focal encephalitis (category 5). Our patient's CT findings are consistent with category 5, i.e., focal encephalitis.

Lyon *et al.* reported CT and MR imaging findings in a 12-year-old female infected with H1N1 whose clinical course was complicated by acute necrotizing encephalopathy. The authors reported T2 hyperintensity and restricted diffusion in the thalami, cerebellar hemispheres, and brain stem. Haktanir A. reported similar abnormalities and also bilateral perirolandic changes

and diffuse meningeal enhancements. A report from Texas by Maricich *et al.* in 2009 [8] identified four children with H1N1 Influenza who developed neurological sequelae; two of them developed seizures, but none had evidence of vascular disease or venous thrombosis. Kulkarni and Kinikar [9] reported the first case in India in pediatric age group manifested with seizure with full recovery.

We are not aware that cerebral venous thrombosis has been reported as a complication of H1N1 epidemic influenza in children. The good outcome is encouraging as is the case in most cases of venous thrombosis in infants and young children. Antiviral treatment should be initiated as soon as possible for any hospitalized patient with suspected seasonal influenza or novel influenza A (H1N1); especially, children who develop focal neurological symptoms or signs.

CONCLUSION

Various neurological complications can occur in patients with H1N1 influenza. Clinicians managing such children need to recognize the potential for neurological complications and include neurovascular imaging in their evaluation for children with focal signs.

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