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CASE REPORT

Acute necrotizing encephalopathy: a case report

Waleed Altwaijri[1], Salman Sultan J. Alshahrani[2*], Anfal Muaddi Alshalan[3]

ABSTRACT

Background: Acute necrotizing encephalopathy (ANE) is a neurological complication of influenza infection. ANE is characterized by periventricular white matter, brainstem, and multifocal symmetric brain lesions in the thalamus and cerebellum. ANE is a rare and severe form of H1N1 encephalopathy.

Case Presentation: The presented case was of an 11-year-old boy who was diagnosed with ANE, the patient was clinically examined and several laboratory investigations, magnetic resonance imaging, as well as reverse transcription polymerase chain reaction for H1N1 was done. The patient was found to be H1N1 positive and was treated with Oseltamivir, intravenous Igs, and corticosteroids. The patient was discharged after 5 weeks.

Conclusion: Combination of Oseltamivir, corticosteroid, and intravenous Igs are the effective treatment for the children having ANE and results in complete recovery.

Keywords: Acute, necrotizing encephalopathy, H1N1.

Introduction

Influenza A H1N1 was first identified in 2009 in Mexican town of La Gloria, Veracruz [1]. Besides the respiratory consequences of the influenza infection, it has been associated with a wide range of neurologic complications [2]. Neurologic manifestations of influenza include acute necrotizing encephalopathy (ANE), encephalitis, acute disseminated encephalomyelitis, transverse myelitis, and Guillian–Barre syndrome [3]. ANE is characterized by periventricular white matter, brainstem, and multifocal symmetric brain lesions in the thalamus and cerebellum [4]. The clinical presentation of ANE develops rapidly including fever, cough, and vomiting combined with neurological dysfunction such as seizures and rapid alteration of mental status [4]. In most severe cases of influenza associated with ANE, the patient develops altered mental status either with or without seizures and then progresses rapidly to comatose state within 24–72 hours from the onset of upper respiratory symptoms and fever [5–7]. Death occurs in 30% of the cases and it results from either complications or cardiorespiratory compromise from ventilation [5]. A case series from US in 2009 reported an association between H1N1 influenza and encephalopathy [8]. In 2011, a case was reported from Turkey [4] and it was the first case to report the association between H1N1 and ANE. It was stated that ANE is a rare and severe form of H1N1 encephalopathy [9].

Case Presentation

The case under study is of an 11-year-old Saudi boy who was referred to the hospital from the periphery of Riyadh with sub-acute onset of dizziness, gradual aphonia, tremoring, and general stiffness with mild fever (38.8°C), no other associated respiratory symptoms were found. Brain magnetic resonance imaging (MRI) was performed for the patient (Figure 1) and it revealed necrotizing encephalopathy. Basic investigations were performed for the patient including complete blood count (CBC), blood glucose, blood gases, renal and liver function tests, electroencephalogram test (EEG), cerebrospinal fluid (CSF), erythrocyte sedimentation rate, C-reactive protein, and ophthalmologic consultation. All these investigated parameters were normal. The metabolic investigations included blood gas and blood glucose, ammonia, serum lactate and pyruvate, CSF lactate, and all of them were normal. Serum ceruloplasmin, serum, and 24 hours urine copper also were normal. Organic acids pattern in

Correspondence to: Salman Sultan J. Alshahrani
*Medical Intern, King Khalid University, Abha, Saudi Arabia.
Email: Salman.alawashiz@gmail.com
Full list of author information is available at the end of the article.
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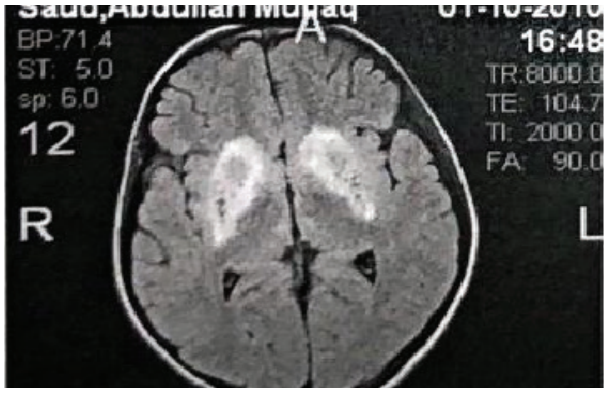

Figure 1. *MRI of the patient's brain.*

urine, the serum level of biotinidase enzyme activity, and tandem spectrometry metabolic screen showed that they all were normal. Very long chain fatty acids (peroximal panel), creatinine phosphokinase, lactate dehydrogenase (LDH), and UA were normal too. A blood sample was sent to Germany to investigate mitochondrial DNA mutations related to Leigh's disease and it was not detected. Virologic investigations included serology of different viruses including: HIV, measles, rubella, mumps, cytomegalovirus, Epstein Barr virus, Varicella zoster, Herpes Simplex virus (HSV) 1, HSV2, influenza A and B, mycoplasma pneumonia, toxoplasmosis, Echovirus, enterovirus, and parainfluenza, which were negative to acute infection by the detection of IgM. Polymerase chain reaction (PCR) of adenovirus, DNA (serum PCR), HSV1, HSV2, and tuberculosis (TB) (CSF) were negative too. Reverse transcription (RT)-PCR of influenza A H1N1 had been detected from nasopharyngeal swab 1 month after the disease onset. The PCR of H1N1 from CSF and serologic study of it were not available. Oseltamivir was initiated in oral therapeutic doses and management of acute disseminated encephalomyelitis (ADEM) acute disseminated encephalomyelitis disease of pulse methylprednisolone of pulsive and maintenance therapy and intravenous immunoglobulin (IVIG) were performed. The patient showed very well clinical improvement, where the patient vocalized and spoke comprehensible speech and was discharged after 5 weeks. After 11 weeks from disease onset on follow up, the patient could stand up, walk with limping, understandably talk, symmetrically smile, and laugh. The patient thoroughly remembered all the previous events that he had experienced during the hospitalization and could write using the right hand. Nearly, 3.5-kg weight was also gained post-discharge.

Discussion

The presented case was of necrotizing encephalopathy patient with H1N1 positive detection. It was stated that ANE follows viral febrile illness and it is characterized by alteration in mental status, multifocal symmetric lesions seen on MRI in the thalamaus, cerebellar medullae, cerebral and brainstem, coma during upper respiratory infection, seizures and elevation of serum aminotransferases, the absence of heperammonia, and hyperglycemia. ANE progresses rapidly where patient experiences fever with non-specific symptoms such as cough and diarrhea [3,4]. Also, it was reported that measles, rubella, varicella, parainfluenza, mycoplasma, and influenza A and B were associated with ANE [4]. In the present case, MRI showed presence of ANE, some of the previous ANE characteristics were found and detected in the present case including sub-acute onset of dizziness, fever, normal blood glucose, and ammonia; however, the patient had normal aminotransferases and showed negative results for measles, rubella, varicella, and mycoplasma, RT-PCR showed positive influenza A H1N1. The association between ANE and H1N1 was reported in the previous case reports, one of them [3] was 7-year old presented with H1N1 and showed well-described features of ANE, but progressed to brain death. Another case was from Turkey [4] which showed similar results to the present case. Another case [10] was a 2-year-old girl who was treated with oseltamivir, acyclovir, and methylprednisolone, after 12 days of disease onset the girl showed improvements. It was mentioned that there was no definitive treatment for ANE and the management depended on the supportive care for neurologic failure, but in Japan, Oseltamivir, intravenous Igs, and corticosteroid were used to treat ANE cases that showed varying degrees of improvements [3]. It was found in one study that steroid within 24 hours of the disease onset was associated with better outcomes in patients with ANE in those without brainstem lesions [11]. In the present case, Oseltamivir was initiated in oral therapeutic doses, pulse methylprednisolone of pulsive and maintenance therapy, as well as intravenous Igs. The patient showed well clinical improvements, he could vocalize and speak and was discharged after 5 weeks, and after 11 weeks, the patient was normal with no presence of any clinical problems. It was reported that ANE prognosis is usually poor as less than 10% recover completely and mortality reaches 30%; however, the prognosis is better in children older than 4 years who have normal LDH and aminotransferases [12,13]. This was in agreement with the current case as the present patient was 11-year old with normal enzyme levels and recovered after 5 weeks, whereas in a previous case report [4], the case recovered within 3 weeks and this can be attributed to the difference in regimen used in their patient and the present patient.

Conclusion

H1N1 infection could result in ANE in children and it is a rare case. RT-PCR is necessary to investigate H1N1 infection, and to diagnose ANE several investigations could be performed including MRI, clinical examinations, and laboratory investigations. Combination of Oseltamivir, corticosteroid, and intravenous Igs are the effective treatment for the children having ANE and results in complete recovery.

List of Abbreviations

ANE	Acute necrotizing encephalopathy
CMV	Cytomegalovirus
CPK	Creatinine phosphokinase
HSV	Herpes simplex virus
LDH	Lactate dehydrogenase
RT-PCR	Reverse transcription polymerase chain reaction

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication

Informed consent was obtained from the patient.

Author details

Waleed Altwaijri[1], Salman Sultan J. Alshahrani[2], , Anfal Muaddi Alshalan[3]

1. Assistant Professor, KSAU-HS, Riyadh, Saudi Arabia; Director, Pediatric Neurology Residency Program; President, Saudi Pediatric Neurology Society; Chairman, Scientific Committee of Pediatric; and Neurology Residency Program in Saudi Council
2. Medical Intern, King Khalid University, Abha, Saudi Arabia
3. Northern Border University, Arar, Saudi Arabia

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