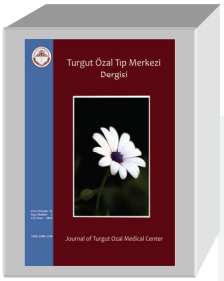

OLGU SUNUMU/CASE REPORT
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Acute Necrotizing Encephalopathy of Childhood Associated With A Novel Influenza Type A Virus: A Case Report

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Abstract
Acute necrotizing encephalopathy of childhood is a rare, clinically distinct entity of acute encephalopathy triggered by acute febrile diseases, mostly viral infections. This syndrome is characterized by the presence of multifocal symmetrical brain lesions involving mainly thalami, brainstem, cerebellum and white matter. The most common abnormalities are an increased level of serum aminotransferase activity and cerebrospinal fluid protein. The etiology and pathogenesis remain unknown and there is no specific therapy or prevention. The prognosis is usually poor and less than 10% of patients recover completely. Diagnosis is made mainly by the characteristic findings of neuroimaging. We describe a case of a young child who was infected with a novel influenza A virus and displayed the characteristic clinical features and neuroimaging findings of acute necrotizing encephalopathy. Influenza is generally considered as a benign illness, but phsysicians should be aware of this unusual presentation of influenza infection.
Key Words: H1N1; Acute Encephalopathy; Child.

Nekrotizan Ensefalopati: Bir olgu sunumu

Özet
Akut Nekrotizan Ensefalit, akut ateşli hastalıkların sıklıkla da viral enfeksiyonların tetiklediği nadir görülen bir ensefalopati formudur. Bu sendrom özellikle talamus, beyin sapı, beyincik ve beyaz maddeyi içeren multifokal simetrik beyin lezyonların varlığı ile karakterizedir. En yaygın anormallikler artmış serum aminotransferaz aktivitesi ve artmış beyin omurilik sıvısı proteini düzeyidir. Hastalığın etyolojisi ve patogenezisi tam olarak bilinememektedir ve spesifik bir tedavisi ve korunma yöntemi yoktur. Prognoz genellikle kötüdür ve hastaların %10'undan azı tamamen iyileşir. Tanı genellikle karakteristik nörögörüntüleme bulguları ile konulur. Biz İnfluenza A enfeksiyonun neden olduğu ve Akut Nekrotizan Ensefalitin tipik klinik ve radyolojik özelliklerini taşıyan 8 yaşındaki olguyu sunarak, influenza enfeksiyonlarının bu nadir ve ciddi formuna dikkat çekmek istedik.
Anahtar Kelimeler: H1N1; Akut Ensefalopati; Çocuk.

INTRODUCTION

Acute necrotizing encephalopathy of childhood (ANE) is a rare disease that predominantly affects infants and young children. The clinical characteristics of this disorder are fever, vomiting, seizures, acute encephalopathy, and rapid alteration of consciousness after a nonspecific viral illness (1).

The hallmark of ANE is multiple symmetrical lesions affecting the thalami; other brain lesions can be located in the brainstem, periventricular white matter, and cerebellum (1,2). Herein we describe an 8 year old boy who presented with fever, headache and ANE confirmed after previous diagnosis with Influenza A (swine origin H1N1 serotype) that was detected in a nasopharyngeal swab specimen.

CASE REPORT

An 8 year old previously healthy boy presented to our emergency department with a three-day history of fever, rhinorrhea, cough a one-day history of projectile vomiting, bitemporal headache and drowsiness. His medical history was negative for recent travel, exposure to other drugs and family history of neurological disorders. His routine immunizations were fully done, but had not received the seasonal influenza vaccine.

Physical examination of the patient on admission revealed, febrile and phrayngeal hyperemia. On neurologic examination he appeared confused, lethargic and had a bilateral extensor plantar response. Neck-stiffness was present, but Kernig's and Brudzinsky's signs were negative, all other findings on general examination were normal.

Laboratory investigations showed normal values of blood counts, chemistry, electrolytes, plasma lactate, ammonia, thyroid function tests. Although white blood cell count was low (3200/µL, normal value >4500), his serum C-reactive protein level and erythrocyte sedimentation rate were normal.

Cerebrospinal fluid examination showed normal glucose

and increased protein levels, without pleocytosis (glucose: 45 mg/dl (normal value, 60-120), protein: 298 mg/dl (normal value <45). A cerebrospinal fluid viral culture was negative as were PCR test of the CSF for HSV1 and 2, EBV, HHV-6, mycoplasma. His electroencephalography showed generalized 5-6 Hz theta wave slowing.

He was treated with ceftriaxone and acylclovir based on clinical and CSF findings that raised suspicions of meningitis or meningoencephalitis. On the third day following treatment he experienced persistent high fevers, and his mental status fluctuated and then progressively declined. Brain magnetic resonance imaging (MRI) on hospital day 3. revealed bilateral symmetric high signal intensities in bilateral thalami and external capsule (Fig. 1,2). We diagnosed the patient with ANE based on the clinical symptoms and MRI findings and intravenous gammaglobulin (IVIg) treatment 0.4 gr/kg/day for 5 days was started.

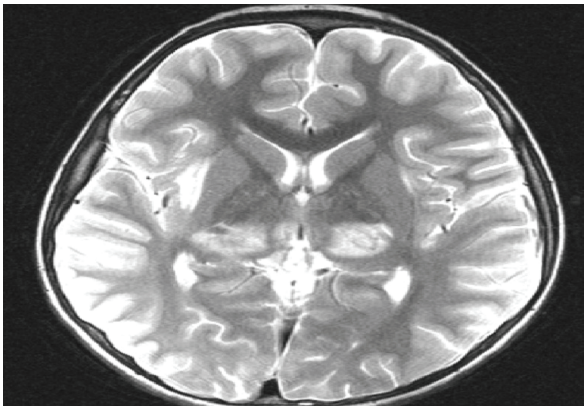

Figure 1. Axial T2-weighted image shows symmetric increased signal intensity in the thalami.

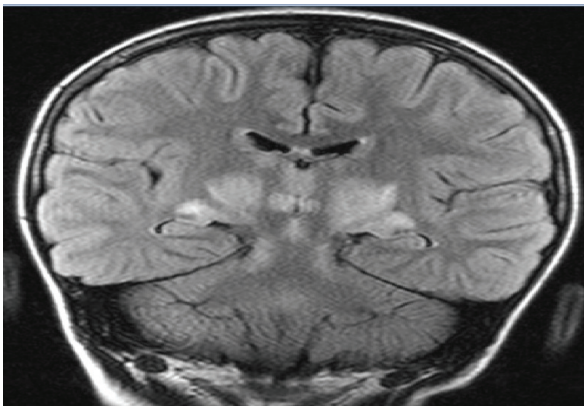

Figure 2. Coronal FLAIR image show symmetric increased signal intensity in the thalami.

Influenza A (swine origin H1N1 serotype) was detected in a nasopharyngeal swab specimen by enzyme immunoassay on day 4, and oseltamivir was administered to the boy. Leucopenia improved after oseltamivir treatment. On day 5 in the hospital, his mental status improved and he was discharged from the intensive care unit. We maintained oseltamivir for 10 days until the influenza virus polymerase chain reaction in nasopharyngeal swab specimen showed a negative result.

The patient was discharged upon retuning to his previous mental state after 14 days of hospitalization. Neurological examination was normal on follow-up visit at 3 months.

DISCUSSION

We describe here, the possible association between acute necrotizing encepahlitis (ANE) and influenza A (H1N1), in pediatric patient. Acute necrotizing encephalopathy (ANE), was first described in 1995 by Mizugachi et al., as an entity of acute encephalopathy characterized with alteration of mental status, seizures and coma during a viral upper respiratory infection (1).

Mizuguchi et al. proposed the following diagnostic criteria for acute necrotizing encephalopathy: a) acute encephalopathy following viral febrile disease with rapid deterioration in consciousness and/or convulsion; b) increased protein in cerebrospinal fluid (CSF) without CSF pleocytosis; c) Neuroimaging findings indicating multiple, symmetric brain lesions involving bilateral thalami, brainstem, periventricular white matter, internal capsule, putamen, and cerebellum; d) elevation of serum aminotransferases of variable degrees, but no hyperammonemia, and hypoglicaemia; e) exclusion of other resembling diseases

Our case presented these diagnostic criteria with the exception of elevated serum aminotransferases. The serum aminotransferases levels were not elevated in our case.

The etiology of ANE is unknown, various viruses have been reported as causative agents, and influenza A have been reported as the most commonly associated virus (1). The hallmark of this type of encephalopathy is it been multifocal, symmetric brain lesions affecting the thalamus bilaterally, brainstem tegumentum, cerebral periventricular white matter and cerebellum, which can be visualized best by MRI (1,2). Our patient had MRI findings consistent with those described in ANE, and influenza A virus was isolated from the upper respiratory tract.

ANE is associated with a significant morbidity and mortality, and its mortality reaches 30% and less than 10% recover completely. The prognosis is better in children older than 2 years and in those who have normal liver function tests, normal protein levels of cerebrospinal fluid and those without brainstem lesions on neuroimaging (3-6). Our patient carried all of these features with the exception of elevated CSF protein levels and recovered completely within 2 weeks.

The pathogenesis of ANE is not clearly understood. Tabarki et al. and other studies demonstrated high

proinflammatory cytokines in serum and cerebrospinal fluid in patients with ANE (7,8).

There is no specific therapy for ANE. Like any other acute encapholapthy, supportive and critical care management are essential. Because cytokine-induced neurotoxicity is one possible cause of poor prognosis, methylprednisolone and intravenous immunuoglobulin treatment may be useful (9,10). Our patient received IVIg 0.4 gr/kg/day for 5 days and oseltamivir treatment, because recent infection with influenza A was documented.

In summary, we describe a pediatric patient infected with influenza virus A, who presented with ANE. Influenza is generally a benign illness, but phsysicians should be aware of this unusual presentation of influenza infection.

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