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Case Report / Olgu Sunumu

Uncommon Organic Psychosis: an Adolescent Case of Anti-N-Methyl-D-Aspartate Receptor Encephalitis

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ABSTRACT

Uncommon organic psychosis: an adolescent case of Anti-N-Methyl-D-Aspartate receptor encephalitis

Psychotic symptoms may present in many neurological and general medical conditions in which, diagnosing is sometimes difficult. We reported a 16-year-old female presenting acute psychotic symptoms and diagnosed with Anti-N-Methyl-D-Aspartate Receptor (Anti-NMDAR) encephalitis. In this case report, main characteristics of anti-NMDAR encephalitis were highlighted and reviewed. Clinicians, especially psychiatrists, should consider a differential diagnosis of anti-NMDAR encephalitis in young, female patients with acute onset of psychotic symptoms, disorganized behaviors, decreased level of consciousness and new onset seizures, and remember that laboratory and imaging tests can be negative for a period of time.

Key words: Adolescence, Anti-N-Methyl-D-Aspartate receptor encephalitis, psychosis

ÖZET

Nadir organik psikoz: Bir ergen Anti-N-Metil-D-Aspartat reseptor ensefaliti olgusu

Psikotik belirtiler tanılamanın bazen güç olduğu çok sayıda nörolojik ve genel tıbbi durumlarda ortaya çıkabilir. Olgu sunumunun konusu, akut psikotik belirtilerle gelen ve Anti-N-Metil-D-Aspartat Reseptor (Anti-NMDAR) ensefaliti tanısı alan 16 yaşında kızdır. Bu olgu sunumunda, Anti-NMDAR ensefalitinin ana özellikleri vurgulandı ve gözden geçirildi. Klinisyenler, özellikle psikiyatristler, akut psikotik belirtiler, dezorganize davranışlar, azalmış bilinç düzeyi ve yeni başlayan nöbetleri olan genç kız hastalarda Anti-NMDAR ensefaliti ayırıcı tanısını düşünmeli ve bir süre laboratuar ve görüntüleme testlerinin negatif olabileceğini hatırlamalıdırlar.

Anahtar kelimeler: Ergenlik, Anti-N-Metil-D-Aspartat reseptor ensefaliti, psikoz

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INTRODUCTION

Psychotic symptoms may present in many neurological and general medical conditions such as autoimmune and infectious diseases (1). It is important for clinicians to primarily identify whether there is a medical condition associated with psychosis since it can be easily curable with early diagnosis, but can be life-threatening otherwise.

Anti-N-methyl-D-aspartate receptor (Anti-NMDAR) encephalitis is a recently recognized uncommon autoimmune type of encephalitis that may classically manifest in a combination of psychiatric (mainly psychotic), neurological, and autonomic features (2). It is potentially reversible if diagnosed early (3). As the disease can cause life-threatening autonomic instability, central hypoventilation, and permanent neurological disability, it is important to have a high suspicion for anti-NMDAR encephalitis, especially in cases presenting with psychotic symptoms.

The purpose of this case report was to highlight some remarkable characteristics of anti-NMDAR encephalitis and to increase the awareness and knowledge of it among psychiatrists and other clinicians.

CASE

A 16-year-old girl was brought to our hospital's emergency department by her parents because of acute onset of withdrawal and talking to herself. According to the history that was taken from the parents, she had begun to display symptoms such as withdrawal, undressing herself, fear, plucking hair from her body, and talking to herself, 20 days earlier. In addition to these, she had insomnia and reluctance to eat and go to school in the last 10 days. Her speech decreased progressively during the last 20 days and she had a seizure 3 days ago. After neurological examination and tests at a neurology department of a different hospital, levetiracetam treatment had been planned but the family rejected this antiepileptic treatment. Results from cranial magnetic resonance imaging (MRI) were normal. No electroencephalogram (EEG) was obtained. In addition to all the symptoms, the patient progressed to mutism within the last 2 days. She was brought to the emergency department by her parents and admitted to the child and adolescent psychiatric inpatient unit with a preliminary diagnosis of acute psychotic disorder. There was no significant medical history. There was no history of alcohol or illicit drug usage, or reported social stressors.

At the first psychiatric evaluation in the inpatient service, she had no eye contact or speech and appeared hallucinated. Although she was conscious, the doctors could not get her to cooperate with them. She had no orientation and could not take simple commands. Her affect was very superficial. Because of her mutism, her opinions and the context of her opinions could not be evaluated. At first sight, it was clear that her psychomotor activity had increased. Moreover, her plucking of hair on her head and genital area and undressing herself were evaluated as disorganized behaviors. Physical examination was normal. Neurological examination could not be conducted due to limited cooperation and increased psychomotor activity.

While she was in the inpatient unit for 5 days, she sometimes experienced excitations that needed haloperidol (10mg/day) and biperidene (5mg/day), intramuscularly. These medications were given on an as-needed basis for her excitations. During severe episodes of agitation and increased psychomotor activity, she received lorazepam (1mg/day orally). Although pharmacological treatment was applied, there was no change in the clinical features. On the 3rd day of hospitalization, the fluctuations in consciousness and ataxic gait were observed in addition to previous symptoms. During the first 3 days of hospitalization, no organic pathology was suspected according to neurological evaluation by a neurologist. Initial laboratory testing, imaging procedures, and EEG failed to provide any evidence. Findings from cranial MRI carried out on the 5th day of hospitalization were compatible with acute ischemia or encephalitis or spongiform encephalopathy. Thereafter, the patient was transferred to the inpatient service of neurology. On the same day, she was discharged from the neurology service upon demand of her family.

Four days after discharge, the patient was brought to an emergency service of a tertiary health unit with aggression and tonic clonic seizures, which lasted for half an hour. She could not walk without support for the last two days. The patient was evaluated as having status epilepticus and taken to the intensive care unit. The patient received phenobarbital (20mg/kg; maintenance dose 5mg/kg daily) intravenously. Extensive laboratory and imaging investigations of the central nervous system, and metabolic, infectious, toxic, autoimmune, and psychiatric disorders were performed. The previous cranial MRI results of the patient were re-evaluated by neuroradiology department and interpreted in favor of encephalopathy. Contrast and diffusion MRI were performed again and showed elevated T2 FLAIR (fluid-attenuated inversion recovery) signal intensity, reduced diffusivity, and minimal contrast enhancement in cortico-subcortical white matter of the bilateral (marked in the left) temporal region. According to the new radiologic findings, the lesion progressed gradually, when compared to the previous one. Based on these observations, the patient was started on ceftriaxone (100mg/kg/day, 3 times per day) and acyclovir (10mg/kg/day, 3 times per day). During this

period, the patient received further examinations and evaluations. The patient's vital signs were stable. Results of extensive laboratory investigations, including that of anti-NMDAR antibodies, were negative except for cerebrospinal fluid (CSF) protein levels of 148mg/dL. The antibiotics were discontinued, when her blood and CSF cultures returned negative. She continued on acyclovir to treat the presumed viral encephalitis of unknown etiology. After auto-immune encephalitis was diagnosed based on clinical and radiologic tests, intravenous immunoglobulin (IVIG) and steroid therapy was administered. She responded to treatment and was transferred to another inpatient unit in her country upon demand of her parents. In her country, anti-NMDAR receptor antibody markers in her serum and CSF were positive and she continued receiving IVIG and steroid therapy. While receiving the treatment, her parents subjectively reported gradual improvement in her clinical symptoms. According to the phone conversation with her parents, it was reported that the patient was conscious, cooperative, and location- and person-oriented, although orientation was only for a limited time. Her speaking skills were improving. She could form sentences with three words and could take simple commands. She regained her walking skills. Any disorganized behavior, aggression, or convulsion could not be detected after treatment. However, she experienced some compulsive behaviors such as washing dirty clothes. During the IVIG and steroid therapy for two months, the clinical features of the patient regressed and hence, her doctors decided to keep her on the same therapy for one more year with the support of physical rehabilitation.

DISCUSSION

Anti-NMDAR encephalitis is an anti-neuronal antibody–mediated disease, which is characterized by rapid clinical deterioration. The disease process has some sequential phases that usually begin with bizarre behavior and psychotic symptoms, followed by seizures and movement disorders, and lastly, decreased levels of consciousness and autonomic dysfunction. The most frequent clinical presentation is acute psychosis (4). In our case, disease history is consistent with the literature (3,5,6). Although our case replicated phases of the disease, the overall pattern was not clearly differentiated. As in our case, prodromal phases of fever, headache, or viral-like symptoms often goes unnoticed in most cases (6).

Most of the patients (80%) have abnormal CSF findings including CSF pleocytosis, increased protein, and CSF-specific oligoclonal bands (3). However, imaging and biochemical tests are normal in most patients (3,7). It has been reported that some cases do not have laboratory findings for up to three weeks (2). In our case, after the onset of symptoms, MRI findings of the disease were detected on the 25th day, increased protein in CSF was seen as the first biochemical finding in the first month, and anti-NMDAR antibodies in the blood and CSF were determined around 35 days later.

EEG is abnormal in most cases with non-specific slowing or disorganized activity (3). Seizures can be seen although not demonstrated by EEG (8). Excessive use of antiepileptic drugs can be seen in patients with seizures that are not demonstrated by EEG (8). The present case had a seizure on 17th day, at which point the family rejected antiepileptic treatment, and was in status epilepticus on 29th day.

Anti-NMDAR receptor antibodies are diagnostic when found in the CSF (3,4). When antibodies are detected, malignancy, particularly ovarian teratoma, should be investigated. Only 31% of children under the age of 18, have ovarian teratoma (5). Diagnosis of Anti-NMDAR encephalitis is delayed generally by two weeks and sometimes, by more than a year (9). In our case, anti-NMDAR encephalitis was diagnosed 35 days after the onset of symptoms and a teratoma was not detected. It is reported that some tumors are detected many months after onset of symptoms and therefore, it is suggested that patients should undergo imaging periodically for at least 2 years (8).

Corticosteroids and IVIG or plasma exchange are used as first-line treatments (3). Most of the patients (75%) respond to initial treatment (5). Time of treatment initiation is very important for prognosis (3,5). Most young patients have a favorable prognosis of 29% full

recovery, 45% significant improvement, and 26% minor improvement (5). Initiating steroids and IVIG treatment according to presumed diagnosis of autoimmune encephalitis might have been better for prognosis in this case. Although the clinical symptoms were decreasing during the treatment process, neurological squeal remained. In the follow-up process, neurological and psychiatric examinations, and ultrasound and MRI of the pelvis and abdomen should be performed, and the levels of anti-NMDAR antibody titers in the serum and CSF should be measured (5,8).

In conclusion, a diagnosis of 'acute psychosis' can be only be made after all possible organic causes are excluded. This case indicates that anti-NMDAR encephalitis should be considered in young, female patients with acute onset of psychotic symptoms, disorganized behaviors, decreased levels of consciousness, and new onset seizures. Brain MRI and measurements of anti-NMDAR antibodies should be reapplied to psychotic patients with presumed diagnosis of anti-NMDAR encephalitis. Since the majority of patients are first seen by psychiatrists, the psychiatrists require having the information for early diagnosis and successful treatment. Awareness of this new and severe neuropsychiatric disease should be increased in the psychiatric settings.

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