



Extreme delta brush activity: Could it be a marker for early diagnosis and prognosis of anti- NMDA (*N*-methyl-D-aspartate) encephalitis?

Aşırı delta brush aktivitesi anti-NMDA (*N*-metil-D-aspartat) ensefalitinde erken tanı ve prognoz için bir belirteç olabilir mi?

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Abstract

Autoimmune encephalitis should be excluded in unexplained encephalitis. A significant portion of autoimmune encephalitis in childhood is anti- NMDA encephalitis. However, neuroimaging and routine diagnostic tests are inadequate, diagnosis should be confirmed by the demonstration of autoantibodies. The treatment may be delay in this process. Extreme delta brush waves are unique electroencephalography pattern, seen in some of Anti-NMDA encephalitis, useful for early diagnosis. Extreme delta brush activity is associated with prolonged hospitalization and illness. Despite of these, the specificity and sensitivity of this pattern is not-known clearly. We present a five years old boy with the loss of consciousness, involuntary movements, intermittent generalized tonic clonic seizures and extreme delta brush activity in electroencephalography.

Keywords: Anti-NMDA encephalitis, early diagnosis, extreme delta brush, prognosis

Öz

Açıklanamayan ensefalit kliniği ile başvuran hastalarda otoimmün ensefalitler dışlanmalıdır. Çocukluk çağında otoimmün ensefalitlerin önemli kısmı anti-NMDA (*N*-metil-D-aspartat) ensefalitidir. Ancak nörogörüntüleme ve rutin tetkikler tanıya yetersiz kalmakta, kesin tanı otoantikörlerin gösterilmesi ile konulmaktadır. Bu süreçte tedavide gecikme olabilmektedir. Anti-NMDA ensefalitli olgularının bir kısmında erken dönemde elektroensefalogramda saptanan özgül bir örneği olan aşırı delta 'brush' tanıda gecikmeyi önlemektedir. Aşırı delta 'brush' aktivitesi, uzamış hastalık ve hastanede kalma süresi ile ilişkilendirilmiştir. Tüm bu bilinenlere rağmen bu örneğin özgüllüğü ve duyarlılığı tam olarak bilinmemektedir. Bu yazıda bilinç kaybı, istemsiz hareketler ve sık jeneralize tonik klonik nöbetler ile başvuran, elektroensefalografisinde aşırı delta 'brush' gözlenen beş yaşında erkek bir hasta sunuldu.

Anahtar sözcükler: Anti-NMDA ensefaliti, aşırı delta brush, erken tanı, prognoz

Introduction

Autoimmune encephalitis is responsible for about 50% of all cases of encephalitis with unknown cause and anti-NMDA (*N*-methyl-D-aspartate) encephalitis is the most common cause of autoimmune encephalitis in childhood (1, 2). Absence of specific clinical and laboratory findings may cause delayed diagnosis. The most helpful results in the diagnosis include specific auto-antibodies measured

in the cerebrospinal fluid (CSF) and serum. However, treatment delays occur in autoimmune encephalitis because detection of autoantibodies may take days. Here, we present a case of anti-NMDA encephalitis, for which early diagnosis and prognostic factors are still controversial, after obtaining informed consent from the patient's family. We think that delta brush activity, which is a specific pattern on electroencephalogram (EEG), can be used in early diagnosis and as a prognostic factor in anti-NMDA encephalitis.

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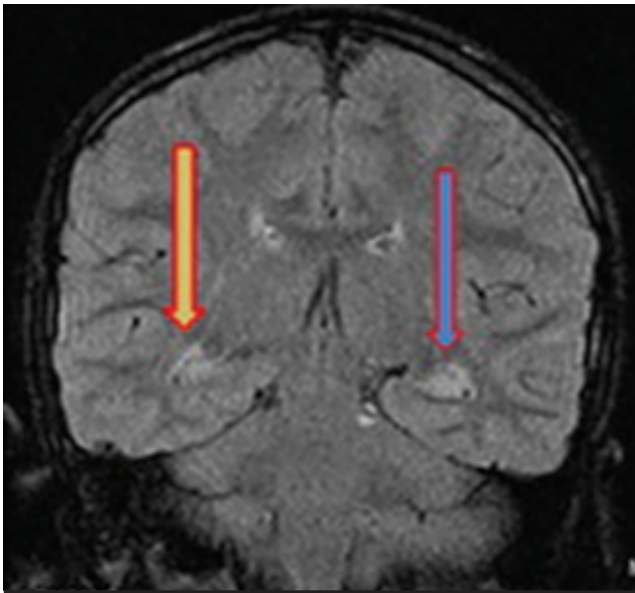


Figure 1. Hyperintense areas in bilateral hippocampal white matter on T2-weighted coronal sections

Case

A five-year-old boy who had normal personal and familial history and normal psychosocial (cognitive) and motor development was followed up in the neonatal intensive care unit because of generalized dyskinesia, which was specifically prominent in the orolingual region, generalized tonic-clonic seizures, and blurred consciousness (Glasgow coma score 9). In his history, it was learned that he had symptoms including an inability to understand

what was being said, insomnia and restlessness for two days, and seizures began after these symptoms and he was followed up in another hospital for two days. When his general status worsened, he was referred to our division. A physical examination revealed the following findings: body weight: 17.5 kg (10–25p), height 112 cm (50–75p), head circumference: 49.5 cm (50p), apical heart rate: 126/min, respiratory rate: 28/min, and blood pressure: 105/65mm Hg. He had confusion, dyskinesia in the whole body more prominent in the face and arms, normal muscle strength, increased muscle tonus, and normoactive deep tendon reflexes. Examinations of the other organ systems revealed no pathology.

The patient's complete blood count, acute-phase reactants, and other biochemical values were found to be normal. Cranial magnetic resonance imaging (MRI) revealed hyperintense areas in bilateral hippocampal white matter on the T2 coronal sections (Fig. 1). An electroencephalogram (EEG) revealed diffuse slow waves and rapid activity (delta brush activity) observed on top of these slow waves (Fig. 2). Delta “brush” activity, which was found in the first week after the patient's symptoms began, continued until the 10th week. Biochemical and microbiologic tests of the cerebrospinal fluid were found to be normal. Considering specific EEG finding [extreme delta brush (EDB)] and the clinical status, a prediagnosis of anti-NMDAR encephalitis was made and methylprednisolone was administered at a dosage of 1 mg/day for five days and intravenous immunoglobulin (IVIG) was administered at a dosage of 1 kg/kg/day for two days. At this stage, herpes

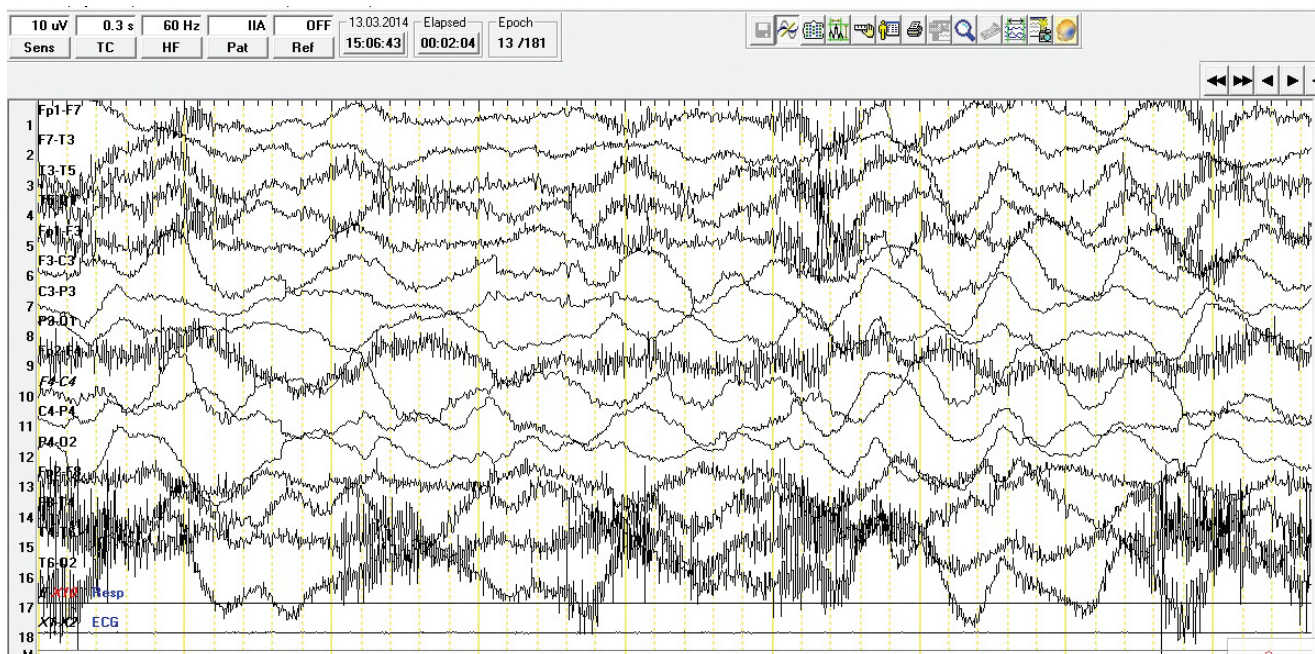


Figure 2. Diffuse slow waves superimposed with rapid delta “brush” activity

simplex virus (HSV), enterovirus, and mycoplasma pneumonia were found to be negative in a serologic examination of the patient’s cerebrospinal fluid (CSF). N-methyl-D-aspartate antibodies were found to be positive in a CSF examination and his treatment was planned such

that corticosteroid was administered at a dosage of 1 mg/kg/day and IVIG was administered at a dosage of 1 g/kg every three weeks for 6 months. Although levetiracetam treatment was initiated for his seizures, generalized seizures continued 1–2 times daily. Thus, valproic acid

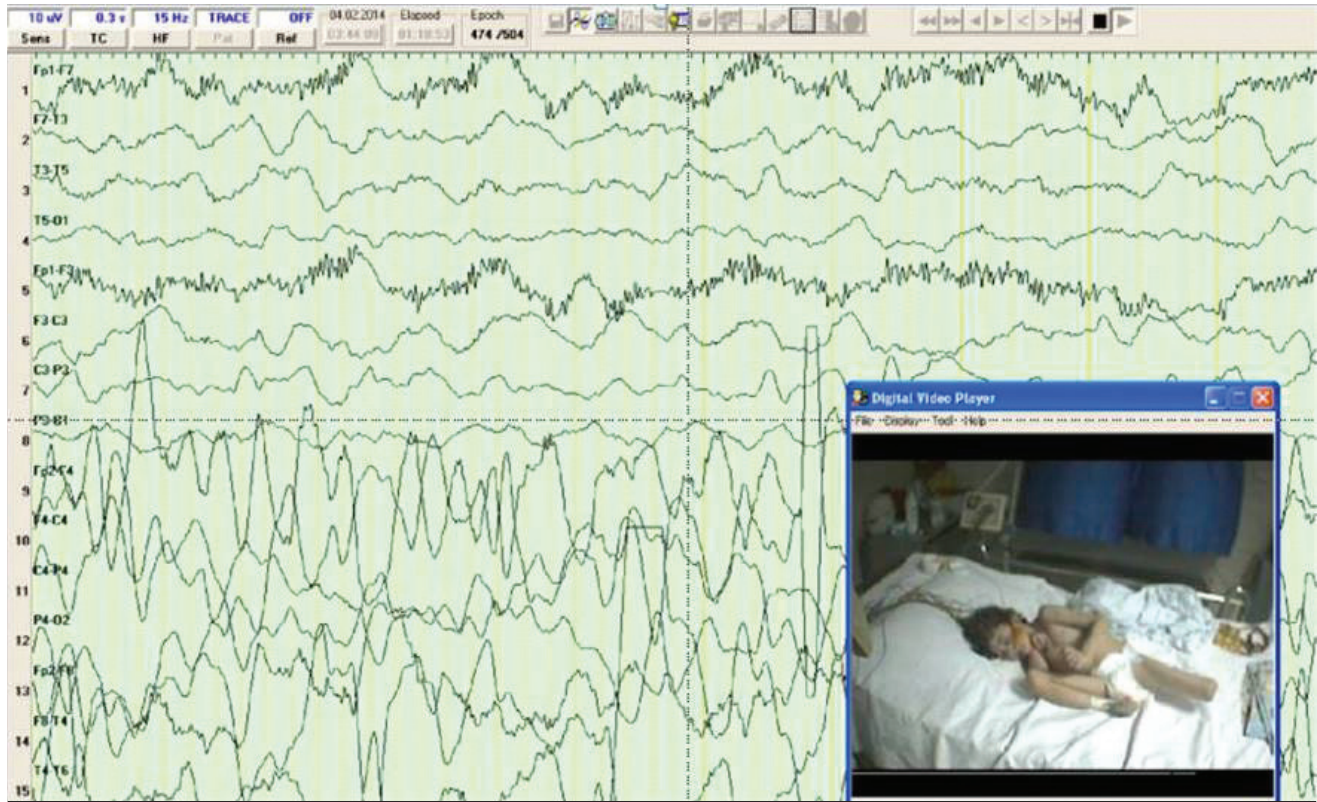


Figure 3. Delta “brush” activity localized in the frontal regions in bilateral hemispheres

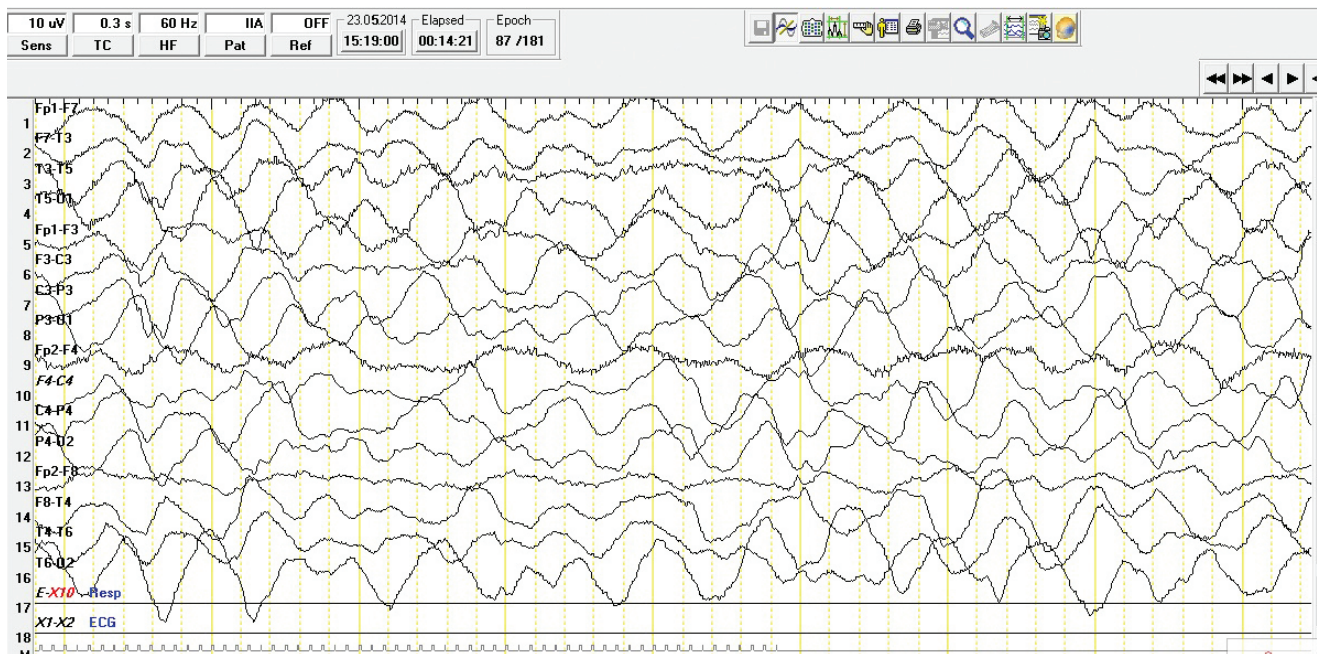


Figure 4. Electroencephalogram with predominance of diffuse slow waves

and phenytoin were added to treatment. The frequency of seizures decreased to every 2–3 days, but continued as short-term seizures. Subsequently, it was planned to initiate rituximab as a second-line treatment. However, the family did not give consent. EEGs performed intermittently revealed that extreme delta brush activity continued, but this specific pattern was observed only in the frontal regions of bilateral hemispheres at the end of the 8th week, and disappeared and gave way to EEG findings of predominant diffuse slow waves at the end of the 10th week (Fig. 3, 4).

The patient's seizures stopped and dyskinesia decreased after the 10th week of the follow-up. The Glasgow coma score increased to 11 after a total of 11 doses of IVIG and continuing steroid treatment. The patient was discharged after his antiepileptic treatment and nutrition were adjusted, to return for follow-up visits. At the 6th month follow-up visit, it was found that the patient, who could not even hold his head at the time of discharge, had no seizures, could sit without support, and eat table foods and make sentences of two words. Written consent was obtained from the patient's parents.

Discussion

In anti-NMDA encephalitis, early diagnosis is important in terms of decreasing sequelae. However, the fact that neuroimaging and CSF findings are not very helpful in the differential diagnosis causes delayed initiation of treatment (3). A specific finding that was found by Schmitt et al. (4) in the EEG of seven (30%) of 23 patients with anti-NMDA encephalitis, which was published by these authors in 2012, may be helpful for early diagnosis in these patients. This pattern was found in only one of six patients who were diagnosed as having autoimmune encephalitis in our clinic.

'Excessive delta brush' activity is defined as rhythmic delta activity at 1–3 Hz with superimposed bursts of rhythmic 20–30 Hz beta frequency activity. This activity mostly tends to occur diffusely. If it has focal appearance, it is mostly found in the frontal region. It is not influenced by sleep cycles and is continuous and symmetrical (4). Although there are authors who have proposed that this pattern emerges after status epilepticus, it has also been advocated that this pattern might be related to non-convulsive status considering that blurred consciousness continues in disease stages during which EDB is observed (5, 6). Our patient had delta waves with superimposed beta activity and this activity was observed to be diffuse on the initial investigations, and it was localized in the frontal region in the following weeks and disappeared in the 10th

week after the diagnosis was made. Benzodiazepine or barbiturate use, which could explain this activity, was not present in our patient.

This pattern has been observed in the early stages of the disease and generally disappears after the 3rd week (4, 7). Similarly, this pattern was found in the first week of the disease in our patient. Unlike the literature, however, its disappearance lasted longer. The pattern was diffuse in the first 8 weeks, and it was observed in the frontal region between the 8 and 10th weeks. It was observed that clinical improvement began after the disappearance of excessive delta brush activity. This suggests that EDB activity was directive in the prognosis.

In a study conducted by Veciana et al. (6), patients with anti-NMDA encephalitis who did and did not have EDB activity were compared and it was found that all patients who had EDB had seizures and were unresponsive to first-line treatment. Again, a significant difference was found between discharge times and modified Rankin scores at the time of discharge; no achievement was found at the 6-month follow-up, and the presence of EDB on EEG was specified as a poor prognostic factor in another comparative study (4). No response could be obtained to first-line treatment in our patient in the first weeks and the second-line treatment was not accepted by the family because of adverse effects.

More case reports are needed to determine the time of detection and disappearance of this pattern, which appears to be considerably helpful for early diagnosis, and its relation with clinical findings, when it exists.

Informed Consent: Written informed consent was obtained from the patients' parents.

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