

EXTREME DELTA BRUSH EEG PATTERN IN A CASE WITH ANTI-NMDA RECEPTOR ENCEPHALITIS

Elif SÖYLEMEZ, Betül Tekin GÜVELİ, Dilek ATAĞLI, Merve YATMAZOĞLU, Turan ATAY, Cengiz DAYAN

Bakirkoy Research and Training Hospital for Psychiatry, Neurology, Neurosurgery, Department of Neurology, Istanbul, Turkey



English | <http://dx.doi.org/10.18071/isz.68.0357> | www.elitmed.hu

EXTRÉM DELTA-TÜSKE EEG-MINTÁZAT ANTI-NMDA-RECEPTOR-ENCEPHALITIS ESETÉBEN

Söylemez E, MD; Güveli BT, MD; Ataklı D, MD; Yatmazoğlu M, MD; Atay T, MD; Dayan C, MD

Idégygy Sz 2015;68(9–10):357–360.

Kapcsolódó



[cikk online](#)

Anti-N-methyl-D-aspartate receptor NMDA-R encephalitis is caused by antibodies against the NMDA-R and characterized by a severe encephalopathy with psychosis, epileptic seizures and autonomic disturbances. This disorder is often accompanied with malignancies, especially ovarian teratoma. Some patients' EEGs show a different pattern similar to the waveforms of premature infants and this pattern is specifically named as extreme delta brush (EDB). We report a 24-year-old female having anti-NMDA receptor encephalitis and EDB pattern.

Keywords: Anti-NMDA receptor encephalitis, EEG, extreme delta brush, prognosis

Az anti N-metil-D-aszpartát-receptor (NMDA-R) encephalitist az NMDA-R elleni antitestek okozzák, jellemzője a súlyos encephalopathia pszichózissal, epilepsziás rohamokkal és autonóm zavarokkal. A kórképet gyakran kísérik malignus daganatok, főleg az ovarium teratomája. Egyes betegek esetében az EEG-n a koraszülött csecsemők mintázatához hasonló hullámformák látszanak, ennek neve az extrém delta-tüske (EDB). Beszámolunk 24 éves nőbetegünkről, akinél anti-NMDA-receptor encephalitis és EDB-mintázatot láttunk.

Kulcsszavak: anti-NMDA-receptor-encephalitis, EEG, extrém delta-tüske, prognózis

Correspondent: Dr. Betül Tekin Güveli, Bakirkoy Research and Training Hospital for Psychiatry, Neurology, Neurosurgery, Department of Neurology, Istanbul, Turkey Phone: +90-5327848273, e-mail: betultekin2013@gmail.com

Érkezett: 2014. október 14. Elfogadva: 2015. január 5.

Anti-N-methyl-D-aspartate receptor (NMDA-R) encephalitis is an immune-mediated disorder that is often paraneoplastic, treatable, and can be diagnosed serologically. The disorder was recognized in 2007, has been increasingly identified as a significant cause of autoimmune and paraneoplastic encephalitis. Most patients with anti-NMDA-R encephalitis develop a multistage illness that progresses from initial psychiatric symptoms to memory disturbance, seizures, dyskinesia, and catatonia. It usually begins with a prodromal phase suggestive of an acute or subclinical upper respiratory tract

infection that lasts for up to two weeks¹⁻³. Within two weeks patients usually develop psychiatric symptoms. Neurological features include cognitive problems, oro-facial dyskinesias, limb and trunk choreoathetosis, dystonia, rigidity, autonomic instability and seizures^{1, 2}. Computed tomography and magnetic resonance imaging of the brain is unremarkable. Electroencephalograms (EEG) usually show nonspecific slowing of background activity. Extreme delta brush (EDB) is a recently described electroencephalographic pattern presented in only one third of patients and consists of a nearly contin-

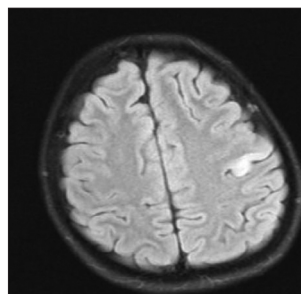
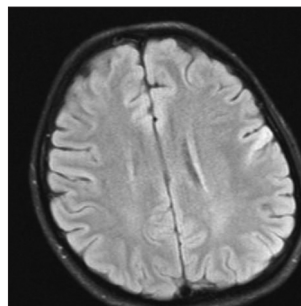
uous combination of delta activity with superimposed fast activity, usually in the beta range, in patients taking no sedative or anesthetic medications^{4,5}. Definitive diagnosis of anti-NMDA receptor encephalitis is established by demonstrating NMDA-R antibodies in patients' serum or cerebrospinal fluid (CSF). Management of anti-NMDA-R encephalitis is immunotherapy and tumor removal.

Case report

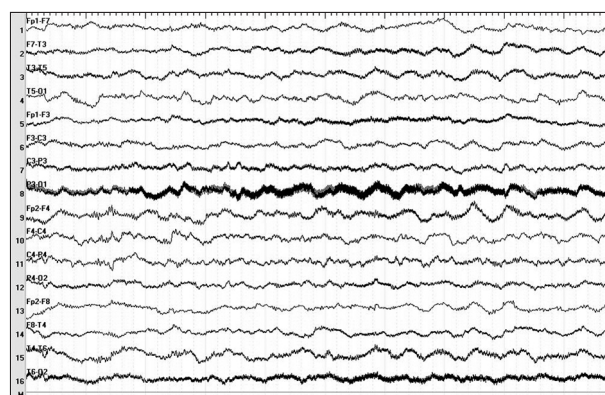
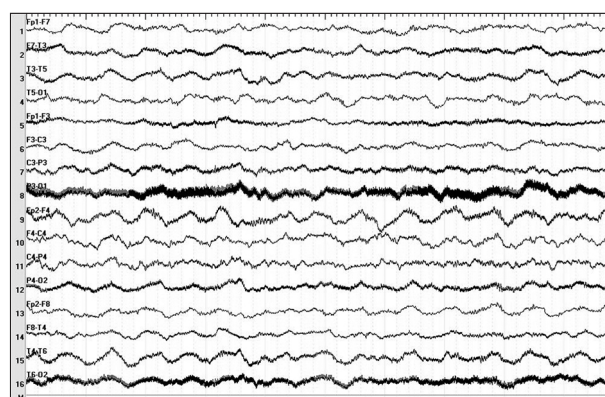
A 24-year-old woman was referred to our intensive care unit from another hospital. Previously healthy woman presented with acute behavioral changes one month ago. She had persecutory delusion and auditory hallucinations, followed by decreased responsiveness. With a diagnosis of acute psychosis she was given olanzapine. Over several days she became gradually confused, and she demonstrated left-sided focal motor seizures with secondary generalization. The patient was taken to the emergency unit of a psychiatry clinic. At her initial examination, her body temperature was 38.5 °C and her serum creatinine kinase level has raised to 1007 IU/L. A diagnosis of neuroleptic malign syndrome was considered, olanzapine was stopped and bromocriptine was started. Because of convulsive epileptic status she was transferred to a general hospital and treated with intravenous phenobarbital. After her status epilepticus had stopped, the patient was referred to our intensive care unit.

On examination she appeared alert, but there was no spontaneous speech or appropriate verbal response. She had no neck stiffness or focal neurological abnormality. She had autonomic dysfunction, including hypertension, tachycardia, sweating. *She was put on endotracheal intubation and mechanical ventilation.* Ten days later she also began to exhibit limb and oro-lingual-facial dyskinesias. Despite antiepileptic therapy, focal motor seizures over the left side of the body continued.

Hematologic and serum chemical tests yielded negative findings. Her computed tomography of the brain was also normal. Magnetic resonance imaging of the brain showed T2-FLAIR hiperintensities on the left precentral-and anterior cingulat gyri (**Figures 1., 2.**). The first and second EEG showed diffuse slowing of background activity without any epileptiform discharges; seven days later however, the third EEG showed generalized rhythmic delta frequency of 1-1.5 Hz with superimposed rhythmic beta frequency predominantly on the anterior regions of the hemispheres (**Figures 3., 4.**). Lumbar



Figures 1., 2. Magnetic resonance imaging of the brain showed T2-FLAIR hiperintensities on the left precentral- and anterior cingulat gyri



Figures 3., 4. Generalized rhythmic delta frequency of 1-1,5 Hz with superimposed rhythmic beta frequency predominantly on the anterior regions of the hemispheres

puncture was done and the CSF showed five white cells/mm; protein and glucose levels were within normal limits.

Oral sodium valproate 1000 mg/day and levetiracetam 1000 mg/day were administered for frequent seizures. Acyclovir was started empirically to treat possible HSV infection.

Bacterial cultures and viral studies by polymerase chain reaction and culture of CSF were found to be negative.

Thyroid peroxidase antibodies and anti thyroglobulin antibodies were not detected in serum. Anti-NMDA receptor encephalitis was suspected and serum was sent for anti-NMDA-R antibody and empiric treatment with methylprednisolone administered at 1 g/day for five days. Within days she became more alert, she was able to intermittently follow commands with her eyes and improvement in her clinical status allowed us to withdraw the ventilatory support.

Serum tumor markers were within normal limits. USG and CT scans of the chest, abdomen, and pelvis revealed no underlying tumor.

The diagnosis was established by the presence of NMDA-R antibodies in the serum. She was given IVIG 0.4 g/kg/day for five days. At fifth day of her therapy, urinary system infection was developed and fluconazole was added to her medication. At the second day of fluconazole, her liver enzymes increased. General edema and hypoventilation were observed. The patient progressed to a deep coma with unresponsiveness to verbal and painful stimuli. After two days she passed away.

Discussion

In this case report we presented a patient with anti-NMDA-R encephalitis, who had EDB in her EEG in addition to other characteristic clinical features.

Anti-NMDA-R encephalitis is a severe form of encephalitis associated with antibodies against NR1 and NR2 subunits of the NMDA-R. It is commonly seen in young women presented with psychiatric symptoms, usually preceded by fever, headache, or viral infection-like illness. Anxiety, insomnia, fear, grandiose delusions, mania, and paranoia are frequent manifestations. The disease may not be clinically distinguished from a primary psychotic illness; therefore the patients are often seen initially by psychiatrists and are given neuroleptic drugs. Our patient also had psychiatric symptoms and was initially misdiagnosed with a psychiatric disorder.

In the following term of the disease, rigidity, elevation of creatine kinase levels and autonomic instability are usually interpreted as neuroleptic malignant syndrome, although these are in fact the expected findings in anti-NMDA-R encephalitis^{1,2}. The association of psychiatric features together with seizures and oro-lingual-facial dyskinesias lead to suspicion of anti-NMDA-R encephalitis. Autonomic instability and hypoventilation is described as a significant feature of this illness.

EEGs are abnormal in most patients and usually show diffuse slowing of background activity. Schmidt et al reported polymorphic diffuse slowing of the background activity in the majority (91.3%) of 23 patients with anti-NMDA receptor encephalitis. The slowing was severe in nine (39.1%) patients. Seven patients also had a unique electrographic pattern characterized by rhythmic delta activity at 1-3 Hz with superimposed bursts of rhythmic 20-30 Hz beta frequency activity "riding" on each delta wave. The authors named this pattern this pattern EDB brush because of its resemblance to the delta brush EEG pattern seen in premature infants. And the patients having EDB have more severe disease with a tendency toward a worse outcome⁴.

Wickström et al reported, an 11-month-old girl with relapsing of acute herpes simplex encephalitis, who after an initial response to antiviral treatment, deteriorated with seizures, abnormal movements, focal neurologic deficits and psychiatric symptoms. The patient has the NMDA-R antibodies in the serum and her EEG showed EDB⁵.

In our patient, there was no sign of EDB in the first two EEGs, but the third EEG recorded EDB two weeks after.

Initially described as a paraneoplastic syndrome affecting young women with ovarian teratomas, anti-NMDA-R encephalitis is associated with mediastinal teratomas, sex-cord stromal tumors, small-cell lung cancer and testicular teratomas. We searched for a malignancy in our patient but did not determine one.

About 75% of patients with NMDA-R antibodies recover or have mild sequel; rest of the patients remain severely disabled or die. The prognosis depends on early diagnosis along with treatment as soon as possible. Anti-NMDA-R encephalitis should be treated with tumor resection and immunotherapy (corticosteroids, IVIG, or plasma exchange)^{1, 2, 6-8}. Our patient was given IVIG and methylprednisolone, but died due to hepatic failure. Also, her having EDB was one of the signs of worse outcome.

Conclusion

Anti-NMDA-R encephalitis, if diagnosed and treated early, shows a good prognosis and the chances of relapses are diminished. Many young patients exhibiting psychiatric features due to anti-NMDA-R encephalitis are likely to be admitted to psychiatrists

rather than neurologists and are often misdiagnosed. The other remarkable point is a unique EEG finding, which is called EDB. Its presence in the correct clinical context should raise a strong suspicion of the aforementioned diagnosis. The identification of this pattern, as in our case, enables early diagnosis and treatment of anti-NMDA-R encephalitis.

REFERENCES

1. Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, et al. Anti-NMDA receptor encephalitis: Case series and analysis of the effects of antibodies. *Lancet Neurol* 2008;7(12):1091-8. [http://dx.doi.org/10.1016/S1474-4422\(08\)70224-2](http://dx.doi.org/10.1016/S1474-4422(08)70224-2).
2. Dalmau J, Lancaster E, Hernandez EM, Rosenfeld MR, Gordon RB. Clinical experience and laboratory investigations in patients with Anti-NMDA receptor encephalitis. *Lancet Neurol* 2011;10(1):63-74. [http://dx.doi.org/10.1016/S1474-4422\(10\)70253-2](http://dx.doi.org/10.1016/S1474-4422(10)70253-2).
3. Vitaliani R, Mason W, Ances B, Zwerdling T, Jiang Z, Dalmau J. Paraneoplastic encephalitis, psychiatric symptoms and hypoventilation in ovarian teratoma. *Ann Neurology* 2005;58(4):594-604. <http://dx.doi.org/10.1002/ana.20614>.
4. Schmitt SE, Pargeon K, Frechette ES, Hirsch JL, Dalmau J, Friedman D. Extreme delta brush; A unique EEG pattern in adults with anti-NMDA receptor encephalitis. *Neurology* 2012;79(11):1094-100. <http://dx.doi.org/10.1212/WNL.0b013e3182698cd8>.
5. Wickström R, Fowler A, Cooray G, Karlsson-Parra A, Grillner P. Viral triggering of anti-NMDA receptor encephalitis in a child - an important cause for disease relapse. *Eur J Paediatr Neurol* 2014;18(4):543-6. <http://dx.doi.org/10.1016/j.ejpn.2014.03.011>.
6. Tüzün E, Zhou L, Baehring JM, Bannykh S, Rosenfeld MR, Dalmau J. Evidence for antibody-mediated pathogenesis in anti-NMDA receptor encephalitis associated with ovarian teratoma. *Acta Neuropathol* 2009;118(6):737-43. <http://dx.doi.org/10.1007/s00401-009-0582-4>.
7. Dalmau J, Tuzun E, Wu H. Paraneoplastic anti-N-Methyl-D-Aspartate receptor encephalitis associated with ovarian teratoma. *Ann Neurol* 2007;61(1):25-36. <http://dx.doi.org/10.1002/ana.21050>.
8. Padma S, Sundaram PS, Marmattom BV. PET/CT in the evaluation of anti-NMDA receptor encephalitis: what we need to know as a NM physician. *Indian J Nucl Med* 2011;26(2):99-101. <http://dx.doi.org/10.4103/0972-3919.90262>.