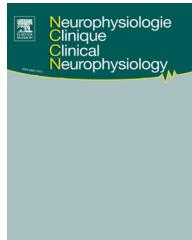




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ORIGINAL ARTICLE/ARTICLE ORIGINAL

Anti-NMDA-R encephalitis: Should we consider extreme delta brush as electrical status epilepticus?

Encéphalite à anticorps anti-NMDA-R : l'extreme delta brush est-il une forme d'état de mal épileptique ?

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Summary Seizures are common clinical manifestations in anti-*N*-methyl-d-aspartate receptor (anti-NMDA-R) encephalitis, among other neurological and psychiatric symptoms. During the course of the disease, some specific EEG patterns have been described: generalized rhythmic delta activity (GRDA) and extreme delta brush (EDB). In comatose patients, the association of these EEG abnormalities with subtle motor manifestations can suggest ongoing non-convulsive status epilepticus (NCSE). We report the case of a 28-year-old woman admitted for a clinical presentation typical of anti-NMDA-R encephalitis, which was confirmed by CSF analysis. She was rapidly intubated because of severe dysautonomia and disturbed consciousness. Clinical examination revealed subtle paroxysmal and intermittent myoclonic and tonic movements,

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correlated on video-EEG with GRDA and/or EDB. NCSE was then suspected, but electroclinical manifestations persisted despite many anti-epileptic drugs combinations, or reappeared when barbiturate anesthesia was decreased. In order to confirm or dismiss the diagnosis, intracranial pressure (ICP) and surface video-EEG monitoring were performed simultaneously and revealed no ICP increase, thus being strongly against a diagnosis of seizures. Sedation was progressively weaned, and clinical condition as well as EEG appearance progressively improved. Literature review revealed 11 similar cases, including 2 with focal NCSE. Of the nine other cases, NCSE diagnosis was finally excluded in 5 cases. NCSE diagnosis in association with anti-NMDA-R encephalitis is sometimes very difficult and its occurrence might be overestimated. Video-EEG is highly recommended and more invasive techniques may sometimes be necessary.

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MOTS CLÉS

Activité delta ;
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Résumé Les encéphalites auto-immunes à anticorps anti-récepteurs-NMDA (Ac anti-NMDA-R) se manifestent typiquement par des troubles neurologiques, psychiatriques, et des crises d'épilepsie. À l'EEG, des patterns particuliers ont été décrits : activités lentes delta rythmiques (OLDR) diffuses et *extreme delta brush* (EDB). La présence chez des patients comateux de ces anomalies EEG rythmiques, associées à des manifestations motrices erratiques, fait suspecter un état de mal épileptique non convulsivant (EMENC). Nous rapportons le cas d'une patiente de 28 ans adressée pour un tableau typique d'encéphalite à Ac anti-NMDA-R, confirmé par l'analyse du LCR. Devant la dysautonomie sévère et les troubles de conscience, la patiente est rapidement intubée. L'examen clinique objectif des mouvements myocloniques et toniques intermittents. L'EEG retrouve des OLDR, puis un aspect d'EDB typique. Ces éléments électro-cliniques, temporellement corrélés sur la vidéo-EEG, conduisent à une escalade de la thérapeutique anti-épileptique, en plus du traitement spécifique. Devant le caractère réfractaire et prolongé de l'EMENC, une mesure de la pression intracrânienne est réalisée, venant remettre en cause le diagnostic initial. La levée de la sédation, à 2 mois du diagnostic, est suivie d'une amélioration clinique et électro-encéphalographique. Après analyse de la littérature, nous avons retrouvé 11 cas similaires, dont 2 sont des états de mal partiel. Le diagnostic d'EMENC fut finalement réfuté dans 5 cas sur les 9 restants. Diagnostiquer un EMENC dans un contexte d'encéphalite à Ac anti-NMDA-R s'avère délicat. L'usage de la vidéo-EEG est fortement recommandé, et des techniques plus invasives peuvent parfois être nécessaires.

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Introduction

Anti-*N*-methyl-*D*-aspartate receptor encephalitis is a recently described autoimmune and paraneoplastic encephalitis [5]. It is the second most common immune-mediated encephalitis, after acute disseminated encephalomyelitis, and represents 4% of all encephalitis. Women are more frequently affected than men, and an underlying tumor (mostly ovarian teratoma) is observed in 60% of cases. The clinical picture is stereotyped [5], usually starting with psychiatric and neurological symptoms: acute psychosis episode, hallucinations, seizures, dyskinesia, vegetative (hemodynamic and respiratory instability), and/or cognitive impairment. Brain MRI shows non-specific abnormalities in 50% of the cases, in various locations: hippocampus, cerebellum, fronto-basal cortex, insula and/or basal ganglia. Cerebrospinal fluid (CSF) is abnormal in 80% of patients [5]. Diagnosis is based on detection of Ig G antibody against the NR1 sub-unit of NMDA receptor [5].

Specific treatment of any underlying tumor (surgical resection) and immunotherapy are associated with a slow recovery without sequelae in about 75% of cases [5]. Decrease of antibody level against NMDA-R seems to be a

good indicator of treatment efficacy and favorable outcome [5]. In order to rapidly initiate the treatment, tests other than antibody detection are necessary.

EEG abnormalities are observed almost constantly in NMDA-R encephalitis [5], but they are usually non-specific (focal or diffuse polymorphic slow-waves). However, some particular patterns that could help to suggest the diagnosis have been recently described: generalized rhythmic delta activity (GRDA); excessive beta frequency activity; and their co-occurrence that gives rises to, a peculiar pattern named *extreme delta brush*, which is considered highly specific of the disease [14].

Epileptic seizures are very common in NMDA-R encephalitis, occurring in 76% of the patients. Initially considered quite rare [5], a growing number of non-convulsive status epilepticus (NCSE) cases have been published over the last few years [1,2,6–11,13]. They are usually diagnosed electrically, because of rhythmic EEG abnormalities more or less associated with erratic motor manifestations in a comatose patient.

We report the case of a female patient with a typical clinical presentation. EEG showed prolonged rhythmic slow-waves associated with intermittent motor symptoms during

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