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Case Report

Unilateral predominance of abnormal movements: A characteristic feature of the pediatric anti-NMDA receptor encephalitis?

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ABSTRACT

Anti-NMDA receptor encephalitis is a treatable autoimmune disease characterized by cognitive, motor and psychiatric features that primarily affects young adults and children. We present a case of a 7-year-old boy with asymmetrical (mainly right hemibody) and abnormal polymorphic movements without concomitant scalpictal EEG changes but had background slowing predominating over the left hemisphere. This report illustrates previous descriptions of asymmetric presentation of abnormal movements in pediatric anti-NMDA receptor encephalitis and emphasizes the importance of video-EEG interpreted within the overall clinical context, to differentiate epileptic from non-epileptic abnormal movements in patients with autoimmune encephalitis.

1. Case report

A 7-year-old boy with normal development and an unremarkable past medical history presented fever and seizures with upward eye deviation, right facial and upper limb paresthesias followed by clonic movements, vomiting, secondary generalization and postictal aphasia. The further clinical course was marked by rapid deterioration with aphasia, behavioral abnormalities with involuntary laughter, fluctuation of consciousness and development of facio-buccal dyskinesias, chewing, and tongue thrusting movements. One week after the onset, he could not walk anymore and developed almost continuous, bilateral, non-stimulus induced, abnormal limb movements, predominating on the right hemibody during wakefulness, characterized. The movements were by a polymorphous phenomenology combining dystonia, choreoathetosis, myorhythmia and tremor intermixed with low amplitude and fast frequency clonic-like movements predominately involving the right hand. These movements disappeared during sleep. Antiseizure drugs (Valproic acid, Clonazepam) were initially administrated without success. The EEG did not show any ictal change during the abnormal movements during video-EEG monitoring.

Head CT scan and brain MRI were unremarkable. EEG in the awake state showed abnormal activity with diffuse, sometimes rhythmic, slow waves (0.5–3 Hz) predominates over the left hemisphere, contralateral to the abnormal movements (Fig. 1A). During non-REM sleep, the EEG showed bursts of atypical fronto-central theta rhythms also predominating over the left hemisphere (Fig. 1B/Video-EEG). CSF analysis showed a lymphocytic pleocytosis (33 white cells/mm^3) with CSF-specific oligoclonal bands and normal glucose, protein and lactate levels.

Anti-NMDA receptor antibodies were identified in the CSF and treatment with intravenous (IV) methylprednisolone was initiated (30 mg/kg daily for 3 days). Then treatment with immunoglobulin, rituxamab and immunoadsorption plasmatherapy was required to observe gradual clinical improvement. Ancillary tests comprising thoraco-abdominal-pelvic CT scan and immunological tests were unremarkable. Six months after the onset of the illness, he had complete behavioral and motor recovery with cessation of abnormal movements. However some cognitive disabilities remained including reading problems associated with orientation and memory difficulties.

Abbreviations: NMDA, N-Methyl-D-aspartate; IV, intravenous; CSF, cerebrospinal fluid; EEG, electroencephalogram; CT, computed tomography; MRI, magnetic resonance imaging.

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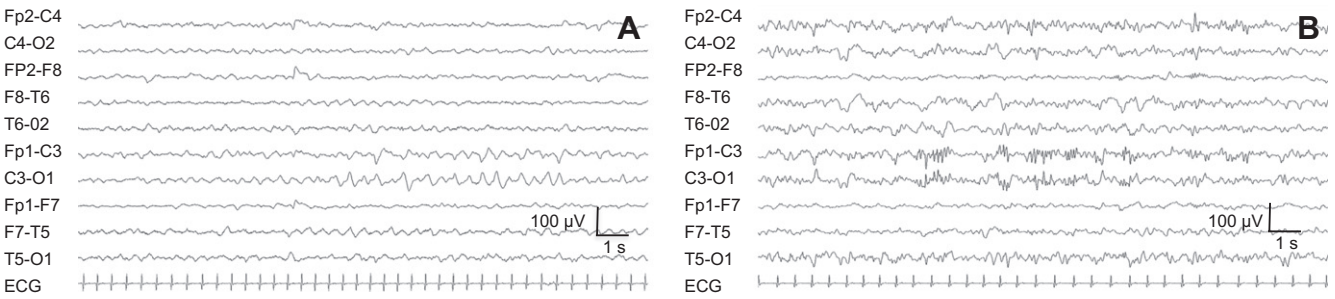

Fig. 1. A: Awake state. B: Sleep.

2. Discussion

Recognition of pediatric anti-NMDA receptor encephalitis based on the clinical, immunological and electrical features is essential to avoid misdiagnosis and treatment delay [1–5]. In patients with paroxysmal events, there are different scenarios trying to address the key question of how to differentiate between seizures and non-epileptic abnormal movements based on semiological features and EEG findings. The clinical presentation in our patient with almost continuous unilateral movements predominating in the upper limb may resemble that of epilepsia partialis continua (EPC), however the polymorphous phenomenology combining dystonia, choreoathetosis, myorhythmia and fast frequency and low amplitude clonic-like movements is not a usual feature in the latter. EPC is rather characterized by repetitive, monomorphic, simple and brief myoclonic jerks with regular or irregular occurrence [6,7]. In our patient, some additional key features supported the diagnosis of movement disorder instead of seizures the including non-stereotyped clinical presentation, the fact that movements systematically disappeared during sleep, and persistence of both, clinical and electrophysiological findings despite antiseizure drugs but with a response to immunotherapy [8–10]. The EEG abnormalities found in our patient were highly characteristic. Different interictal EEG patterns have been described in anti-NMDA receptor encephalitis including a non-specific and polymorphic generalized or focal slowing, mainly frontotemporal, polymorphic slowing, excessive beta frequency activity, and their co-occurrence, known as "extreme delta brush", which is considered highly specific of the disease [5,11–21]. On the other hand, focal seizures with a characteristic ictal electroclinical pattern have been reported in children with anti-NMDA receptor encephalitis. In focal seizures, the EEG features have consisted of a time-limited, focal rhythmic sharply contoured 6 to 12 Hz activity, that subsequently spread to one or both hemispheres associated or not with clinical manifestations such as limb posturing [22].

The unilateral predominance of the abnormal movements observed in our patient has been previously reported in anti-NMDA receptor encephalitis, mainly in series of pediatric patients [5,12–14,23–29]. The unilateral predominance of the abnormal movements or seizures is a classical feature in other systemic antibody-mediated diseases including *Rasmussen* syndrome, systemic lupus erythematosus involving the central nervous system, *Hashimoto* encephalitis and *Sydenham* chorea, however the underlying pathophysiology of unilateral or bilateral asymmetric symptoms in autoimmune diseases remains poorly understood [12,30–34]. The role of anti-NMDA receptor antibodies in the generation of the abnormal rhythmic activity during EEG seems to be clear, but the mechanisms underlying the changes are unknown [11,12,35]. We speculate a thalamocortical origin of the slow oscillations occurs in the context of a thalamic deafferentation secondary to disruption of glutamatergic neurotransmission, such as the EEG slowing observed during anesthesia with Ketamine, an anti-NMDA receptor antagonist [12,36].

Finally, although the diagnosis of epileptic seizures is based on the presence of an electroclinical correlation between the abnormal paroxysmal phenomenon and a corresponding ictal EEG discharge, some patients can be misdiagnosed as having a non-epileptic event when the absence of ictal discharges occurs during the paroxysmal motor activity. However this is not uncommonly observed during scalp EEG monitoring in patients of patients with mesial or basal cortical seizures, mainly extratemporal, remote from the recording electrodes of EEG. Some cases of epilepsia partialis continua, notably in Rasmussen syndrome, have no scalp ictal EEG changes due to low amplitude or deep intrasulcal origin of the spikes or a tangential orientation of the dipole [8–11,37–42].

3. Conclusion

With the present case report, we want to illustrate the clinical presentation of movement disorders, manifestation increasingly characterized and recognized as part of the spectrum in autoimmune encephalitis, support previous descriptions of unilateral or bilateral asymmetrical presentation of the abnormal movements in pediatric population with anti-NMDA receptor encephalitis and finally highlight the importance of the video-EEG to assess the electroclinical correlation of the paroxysmal events in order to differentiate between epileptic seizures and abnormal movements. The lack of electroclinical correlation must be interpreted carefully within the overall clinical context and is not always secondary to non-epileptic paroxysmal manifestations because of the well-known limitations of the scalp video-EEG recordings in some cases such as patients with deep or small generators of seizures.

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Conflict of interest

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- Dr. Vanessa Benjumea-Cuartas: Dr. Benjumea-Cuartas drafted the initial manuscript and approved the final manuscript as submitted.
- Dr. Monika Eisermann: Dr. Eisermann reviewed and revised the manuscript, created the video and approved the final manuscript as submitted.
- Dr. Hina Simonnet was involved in the care of the patient, revised the manuscript and approved the final manuscript as submitted.

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- Pr. Isabelle Desguerre was involved in the care of the patient and revised the manuscript and approved the final manuscript as submitted.
- Dr. Anna Kaminska revised the manuscript and approved the final manuscript as submitted.

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