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Nmdar Antibodies Encephalitis Think About It

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Abstract

Anti-NMDA-(Nmethyl D aspartate) antibody encephalitis is a common autoimmune encephalitis in children, often complicating herpes encephalitis. It is a progressive encephalitis with psychiatric expression that can err the diagnosis, it is associated with it. epilepsy, abnormal movements. There is a wide range of clinical spectrum that varies according to age. Diagnostic confirmation is based on the positivity of NMDA antibodies in the CSF. The prognosis is often good with Rituximab, rarely neurocognitive-behavioral sequelae. We report through 5 paediatric observations the gradual onset, an exceptional age of onset in an 8-month-old infant, the heterogeneity of the clinical picture according to the age of the child of psychiatric symptoms in an autistic adolescent, but also in a 3-year-old girl. The EEG is of great contribution by its slowed down aspect, fast rhythms and delta brush and has made it possible to guide the diagnosis, on the other hand the lumbar puncture and the brain MRI are not contributive. NMDA encephalitis was a postviral complication of herpes encephalitis due to the absence of testicular teratoma or germinoma on testicular and pelvic ultrasound, and the positivity of NMDA antibodies. Rituximab is often a saltatory treatment with recovery of a good neurocognitive score and physiological background tracing on EEG.

Keywords: NIL

Introduction

Anti-N-methyl-d-aspartate (a NMDAR) antibody encephalitis was first described in 2007 by Dalmau and colleagues, who identified 12 patients with significant neuropsychiatric symptoms [1,2]. Currently it is considered a severe autoimmune neurological disease with a specific clinical picture. The onset is gradual, after a prodromal phase simulating a virus, followed by a second phase of epileptic seizures and abnormal movements, followed by a phase of neurocognitive decline, motor deficit, orofacial dyskinesias, then secondary aphasia, and coma with dysautonomic symptoms [3].

The diagnosis of encephalitis is clinical, with specific electroencephalographic signs :d diffuse elta with rapid rhythms, confirmed by the detection of anti-NMDAr antibodies in the blood and urine[4]. We report 5 paediatric cases including infants, young children, school-aged children, and adolescents, with a variable clinical range according to age, but a good favourable clinical course on Rituximab. The particularity of our study is the reporting of the youngest case, a boy aged 8 months.

Objective of the study:

emphasize the variability of the clinical phenotype as a function of age, the diagnostic difficulty related to the predominance of non-specific psychiatric signs for the untrained eye demonstrate that its prognosis is favorable under treatment, except for special cases.

Patients and methods

It is a study of the clinical profile and prognosis of a series of five pediatric clinical cases of NMDA encephalitis over a period of 7 yearsfrom January 1, 2018 to June 30, 2024. This is a study of patients'

charts where we noted clinical signs, EEG, brain MRI, NMDA antibodies in the CSF, with precision of the evolution on rutiximab .

Results

We report a series of 5 cases treated in our department, 3 girls and 2 boys, the average age is 5 years with extremes of 8 months and 15 years (table 1)

We noted a gradual onset with a viral infection with fever over a month, asthenia, insomnia, anorexia. The aNMDAr encephalitis triad characterized by: epilepsy, abnormal movements, and psychomotor regression was found in all patients, but with a degree of severity varying according to age: psychiatric signs predominant in the oldest (15-year-old boy), but also found in a 4-year-old girl, neurocognitive regression, epilepsy, and abnormal movements: dyskinesia, dystonia in the youngest children :(8 months, 3 years, 5 years).

The EEG confirmed the diagnosis in all patients, especially in those whose picture was purely psychiatric showing a diffuse slowdown: diffuse delta and delta brush or rapid rhythm aspect specific to this encephalitis.

The brain MRI was normal except in the 15-year-old boy showing an atrophy of the hippocampus very characteristic of the pathology.

Cerebrospinal fluid analysis showed pleiocytosis and hyperproteinarachia in 2 patients (8 months and 3 years).

Confirmation of NMDAr encephalitis is the presence of aNMDAR antibodies in the CSF in all patients. Herpes encephalitis is evidenced by HSV1 IgM and IgG serology positivity, and the paraneoplastic origin was ruled out by negative abdominal-pelvic ultrasound in all patients. We report that two patients showed signs of severity: dysautonomic signs: hypoventilation and status epilepticus were transferred to intensive care with a short stay.

The evolution was favorable in 4/5 of patients on rituximab with normalization of the clinic and a theta rhythm then alpha on EEG. It was unfavorable in an 8-month-old infant with underlying mitochandriopathy. The long-term evolution with a follow-up ranging from one year to 7 years shows a normal neurocognitive assessment, and normal schooling.

Our 1stcase, hospitalized in 2016, 3-year-old girl, with normal psychomotor development until 1 month before hospitalization when the mother reported the notion of a flu-like syndrome with asthenia, insomnia, withdrawal, with a generalized toncicoclonic crisis. Faced with fever and psychomotor regression, she was referred to us from a peripheral hospital. On clinical examination, we found: fever, lethargy, focal and generalized epileptic seizures, hypotonia, faciobrachial dyskinesias, dystonia, cognitive decline, with loss of psychomotor acquisitions. Progression to akinetic mutism, dehydration due to swallowing disorders, and dysautonomic signs. The EEG was pathological with diffuse slow waves, and delta brush appearance contrasting with two normal brain MRIs 15 days apart, a lumbar puncture: hyperproteinopia at 1g/L. AntiNMDA antibodies in the blood and CSF confirmed the diagnosis of NMDA encephalitis, requested after failure of treatment with aciclovir and corticosteroid of inflammatory encephalitis.put on rutiximab Rahaf, currently 7 years old, has recovered, neurosensory, neuromotor, as well as neurocognitive, and is conducting normal schooling.

The second particular case is a 15-year-old boy known for autism spectrum disorder presented to our consultation for generalized tonic-clonic epileptic seizures, the mother reports that for a few weeks he has shown school regression and dystonic seizures, then the child has withdrawn into himself with mutism

In view of this clinical picture, NMDAR encephalitis is suspected, the EEG showed slow, diffuse, overloaded waves of rapid rhythm

The MRI showed damage to the hippocampus

put under rutiximab we noted a neurocognitive improvement with disappearance of seizures and EEG abnormalities, schooling is resumed afterwards

Discussion

NMDA encephalitis was described for thefirst time by Dalmau, in 2007, in adult women with neuropsychiatric signs with ovarian teratoma[2,5]

Hughes' team was able to show that autoantibodies caused reversible loss of RN1 receptors proportional to the levels of circulating IgG anti-NMDA antibodies. This loss of receptors would in turn impact the functioning of the dopaminergic, adrenergic, and

Volume 7, Issue 4; July-August 2024; Page No 389-394

cholinergic pathways and would be the cause of Dyautonomia[6,7].

In the Dalmau series, patients with NMDA encephalitis are often transferred from the psychiatric ward (they initially suffered from psychotic signs of bipolar mood disorder with inhibition and agitation and aggressiveness) and referred to neurology in the face of the appearance of neurological signs: fever, epileptic seizures, abnormalities of the CSF, EEG and brain MRI. The etiological agent: teratoma expressing NMDA receptors, is the trigger of the disease, and constitutes a good prognosis, given the benignity of the tumor [2,6,7].

The viral origin of NMDA encephalitis predominates in children with a viral prodrommal like phase, implying an early immune reaction [8,9]

Some argue for a predominant immune response at the level of the central nervous system, as evidenced by: pleocytosis, oliguoclonal peak, and intrathecal synthesis of NR1 antibodies[10,11].

The clinical presentation goes through a prodromal phase, then a psychotic phase, then a neurological phase [5,12] (Figure 1).

Psychiatric clinical symptoms inaugurate the clinical picture [5] after a flu-like phase, and precede neurological signs associating epileptic seizures, abnormal movements oral and facial dyskinesias, and cognitive decline with memory and language disorders. In our series all the signs are found in a mixed infectious, psychiatric and neurological way with a predominance of psychiatric signs in adolescents, and in the 4-year-old girl, infants present a psychomotor regression with convulsive seizures and abnormal movements in the first place. Our series describes the same symptoms reported by [3,13,14]

A recent study showed that anti-NMDAR encephalitis attacks were predominant in a group of prepubertal children, suggesting that the change in hormonal activity related to puberty may represent a key factor in the progression of the clinical presentation of anti-NMDAR encephalitis in different ages [1,21].

In some cohorts, most pediatric patients presented with partial motor or complex seizures, while generalized tonic-clonic seizures or status epilepticus were rarely presented. Cases of continuous partial epilepsy in antiNMDAR pediatric encephalitis have been reported rarely [3,13,14]

-Our study is in agreement with all the studies described reproducing all the clinical signs with their variability according to age: predominance of psychiatric signs in older children, a noisy neurological picture in infants: Our study found that there is a range of clinical signs ranging from the complete picture associating epilepsy, abnormal movements, and neurocognitive decline in infants to psychomotor regression with dystonia in 5-year-old school-aged boys, to a predominant psychiatric picture in a 15-year-old adolescent.

-Our study also reported the diagnostic contribution of lumbar puncture, and EEG, and non-contributory MRI for diagnosis. The viral origin following herpes encephalitis, and the normality of the radiological assessment: thoraco-abdominal CT, testicular ultrasound supported the viral origin in the child.

- The favorable evolution under antiCD20 also comforted the immunological origin of this encephalitis.

- The particularity of our study, apart from the clinical spectrum as a function of age, is that it occurs on an underlying terrain suggesting a genetic predisposition to this NMDA encephalitis, as described in herpes encephalitis.

Our paediatric cases of non-paraneoplastic anti-NMDAR encephalitis were treated with rituximab with no apparent side effects. The results were good [17,18].

Conclusion

NMDAR encephalitis is an autoimmune limbal encephalitis that is often postviral in children. The contrast between the richness of clinical signs and the poverty of brain MRI The predominance of psychiatric symptoms that can delay the diagnosis, requires a rigorous approach based on the anamnesis (virus, behavioral modification) the associated clinical signs: dystonia, dyskinesia, epileptic seizures, anorexia, insomnia, dysautonomic signs and on the appearance of delta brush on EEG. of NMDA antibodies in CSF and blood. The prognosis remains favourable with rituximab. The prevention of encephalitis 0 NMDA involves corticosteroid treatment combined with aciclovir for herpes encephalitis.

Volume 7, Issue 4; July-August 2024; Page No 389-394

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Volume 7, Issue 4; July-August 2024; Page No 389-394

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Table 1 Clinical features, radiological EEG and patient evolution

Patient	**Symptoms**	**EEG**	**Mri**	**Lcr**	**Evolution**
Farid Boy 15 years old, **TSA**	TCG Crisis Dystonic seizures Academic regression Akinetic mutism, withdrawal into oneself	Diffuse slow waves overloaded with fast rhythms	Hippocampal Involvement	Hproteinorachia RNMDA+ antibodies	Clinical Improvement+ EEG Autistic but back to school
Samir Boy 8 months **Cytopathy** **Mitochandrial**	Herpes encephalitis Improvement with Acilovir Then secondary degradation: Convulsive state Dystonia ,dyskinesia BF Dysautonomia PLlymphocytosis	Slow waves Diffuse	Hypersignal Fronto-temporo-occipital	Hproteinorachia RNMDA+ antibodies	Clinical Improvement +EEG Partial
Rahaf, daughter 3 years old	Crisis ETCG, asthenia, insomnia Dystonia, dyskinesia BF Motor regression, neuro cognitive: language, memory. Akinetic mutism, withdrawal into oneself Signs of dysautonomia	Diffuse slow waves overloaded with fast rhythms	Normal	Hproteinorachia RNMDA+ antibodies	Clinical Improvement+ EEG Autistic but back to school

Volume 7, Issue 4; July-August 2024; Page No 389-394

Sami Boy5 years old ATCD-free	CTCG, Partial Crisis Dystonia ,dyskinesia BF Motor regression. Neurocognitive regression :p language era, memory	Slow waves Diffuse	Hypersignal Fronto-temporo-occipital	Lymphocytosis RNMDA+ antibodies	Clinical Improvement +EEG Recovery Engine Cognitive Behavioural
4-year-old girl	Start 1 month, CTCG Psychiatric signs Agitation Aggressiveness Insomnia	Slow motion Delta Brush	Normal	protein 1g/L RNMDA+ antibodies LCR	Clinical Improvement +EEG Recovery Cognitive Behavioural

Atcd, history, MRI, magnetic resonance imaging, NMDAr n methyl dehydrogenaseacid, antibody acid, receprors, Tsa, autism spectrum disorders, Tcg, generalized tonic-clonic seizures, EEG, electroencephalogram, CSF, cerebrospinal fluid

Volume 7, Issue 4; July-August 2024; Page No 389-394