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CASE REPORT

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Diagnostic and therapeutic aspects of Anti-NMDA-receptor antibody encephalitis in pediatrics

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ABSTRACT

Autoimmune / paraneoplastic encephalitis has common features with rapidly progressing clinical pictures combining behavioral or mood disturbances, seizures, memory impairment, cerebrospinal fluid (CSF) inflammatory reaction, and changes in brain imaging. Their early identification and treatment improve patient outcomes. They are secondary to the presence of an antibody directed most often against antigens of the central nervous system (CNS), which may be common to antigens expressed by tumor tissue. Among these, encephalitis with - anti-receptor antibodies-N-methyl-D-aspartate (R-NMDA), of recent description, seem particularly frequent. We present the case of a 13-year-old adolescent with convulsions and agitation.

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1. INTRODUCTION

Encephalitis is a severe central nervous system infection of the brain parenchyma leading to neurologic dysfunction, such as headaches and altered levels of consciousness. [1] Furthermore, because a large proportion of encephalitis cases have an unknown cause, it is possible that previously reported incidence numbers are underestimations. Furthermore, the large proportion of unknown causes makes it difficult to assess regional differences and the possible impact of specific etiologic causative pathogens. Autoimmune / paraneoplastic encephalitis [2,3] have common characteristics, associating various neurological and psychiatric symptoms of evolution rapid, such as behavioral or mood disturbances, seizures and memory impairment with cerebrospinal fluid (CSF) inflammatory reaction and changes in brain imaging. The diagnosis of these encephalitis is confirmed by the demonstration of an antibody directed against an antigen of the central nervous system (CNS), either against an intracellular antigen (group I encephalitis) , or against a membrane antigen. (group II encephalitis), in particular anti-receptor antibodies-N-methyl-D-aspartate (R-NMDA). [2] Anti-R-NMDA antibody encephalitis occurs predominantly in women (80% in the largest series of 419 patients. [4]

The clinical presentation is stereotyped associating quickly, over one to four weeks, symptoms psychiatric (100% of cases), the onset of seizures convulsive (76%), large abnormal movements choreic type or especially localized dyskinesias in the face and mouth (86%), dysautonomia (69%) and alveolar hypoventilation (66%) which may lead to hospitalization in intensive care. [3]

Prodromes In 70% of cases, the neuropsychiatric presentation is preceded, within 15 days, by prodromes that may suggest a viral episode with headache, nausea, vomiting, fever, diarrhea, or symptoms respiratory non-specific upper airways. [3,4,5]

In the paraneoplastic forms, these antibodies would be secondary to the immunization within the tumor which would

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express abnormally a common antigen with the CNS. However, a tumor is not always found. This disease preferentially affects young subjects and has a very evocative clinical presentation. The outcome is favorable in more than 75% of patients, provided adequate treatment is in place. Recognition of these encephalitis is therefore essential. [6]

Here, we describe a case of 13-year old teenager, who suffered from N MDA Encephalitis, and which caused us problems of care.

2. CASE REPORT

A 13-year-old teenager admitted for lateralization of the gaze, then 05 minutes after arriving at the hospital, the child presented with a generalized tonicoclonic convulsion.

the clinical examination found conscious teenager, cooperative, scored 15 / 15th according to Glasgow score, with good temporo-spatial orientation, responsive pupils and without motor or sensory deficit, he complained of Headache concept and was feverish at 39ºC. Blood pressure is high 130/89 mm/Hg. We also found a red angina.

The day after his hospitalization, the patient presented an hypertensive crisis at 150 / 12mm / Hg, and a fever at 40 ° c, with behavioral disturbances such as agitation, visual and auditory hallucinations.

Admission brain CT scan showed Occipital hypodense lesion, cortico-subcortical bilateral asymmetric not very expansive. Absence of cerebral meningeal hemorrhage. Lack of peri-cerebral collection and no detectable bone lesion (Figure 1). We completed by magnetic resonance imaging MRI which showed bilateral and asymmetric hyper signal under posterior parietal cortical, internal frontal and posterior temporal. Slight involvement of the deep gray matter. Presence of bilateral posterior parietal gyriform contrast enhancement in favor of encephalitis (Figure 2).

No abnormalities were found on the hemogram, the reactive C protein was negative. We also performed a lumbar puncture finding a clear fluid with cytology 02 cellular elements, a glycorachia at 0.52 g / l and a proteinorachia at 0.12 g / l.

The echocardiography as well as the abdominal echography do not show objective abnormalities which could explain this arterial hypertension, notably a stenosis of the renal artery. The electroencephalogram had shown numerous slow paroxysmal puffs predominantly anterior and medium, slowed down and widely diffused in the hyperpnea with the occurrence of irritative elements in the fronto-central areas, especially on the right, little modified by intermittent light stimulation.

in conclusion: Trace very compatible with an encephalitic attack with also irritating elements in anterior and middle right regions, on a relatively preserved waking rhythm

In view of its signs of dysautonomia, in the radiological absence of a bulabire involvement, as well as the radiological and electrical abnormalities, the diagnosis of autoimmune encephalitis seemed to us the most probable despite the negativity of the N-methyl-D-aspartate receptor antibodies in the blood and the impossibility of making them in the cerebrospinal fluid.

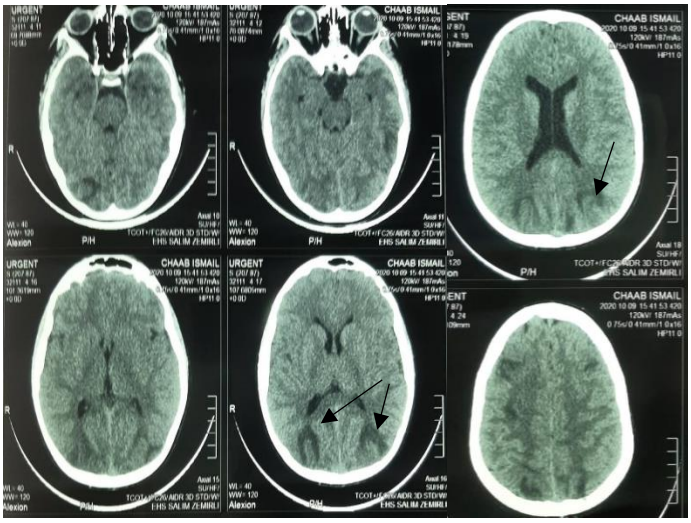

Figure 1. Occipital hypodense lesion, cortico-subcortical bilateral asymmetric in CT sacn.

Our teenager benefited from during bolus of glucocoricoids at a rate of 1g / kg for 3 days associated with immunoglobulin cures D1 and D4, as well as an antihypertensor type loxen in syringe shoot and a neuroleptic type risperidone for the psychotic disorders which our teenager has presented and difficult to control clinically considering the extreme agitation.

As soon as the threatening tentional figures decreased, we reduced the doses of loxen and then switched to an inhibitor of the conversion enzyme type captopril at raion of 1.5 mg / kg / day, and relayed by oral corticosteroid therapy for 10 days at a dose of 01 mg / kg / day.

The outcome was good with improvement in fever and psychotic disorders. arterial hypertension was stage 1.

We decided to release our patient on the 11th day of hospitalization with captopril which we had kept for a month. The anti-hypertensive therapy was therefore stopped after the measurements recorded during ambulatory blood pressure monitoring remained normal.

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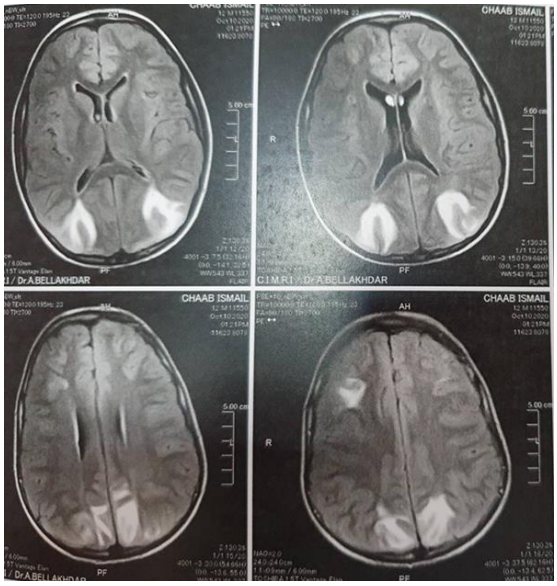

Figure 2. Bilateral and asymmetric hyper signal under posterior parietal cortical, internal frontal and posterior temporal.

we have a follow-up of a year, the teenager is doing well the electroencephalogram objective the existence of electrical anomalies and worries about schooling linked to concentration disorders. No neoplasia was detected in our patient.

3. DISCUSSION

This report demonstrates the difficulty in identifying behavioral aberration, often a first sign of anti-NMDA-receptor antibody encephalitis,in infants. Seizures or seizure mimics with psychiatric symptoms should raise suspicion. Prompt aggressive empiric treatment was initiated priorto CSF confirmation and was based on symptomatology and absence of common etiologies. Immune therapies rapidly arrested further evolution and were followed by full clinical recovery.

Furthermore, the contribution of recently described immune-mediated forms of encephalitis, such as those associated with voltage-gated potassium channels and the N-methyl-D-aspartate (NMDA) receptor antibodies, is unclear [7,8]. Anti-NMDAR encephalitis is the most common antibody-associated encephalitis [7]. Anti-R-NMDA antibody encephalitis predominantly occurs in women (80% in the largest series of 419 patients. [2] against our clinical observation or it was a boy.

In about 70% of patients, the clinical course of anti-NMDA-receptor antibody encephalitis is preceded by a nonspecific prodromal stage with fever, headache, nausea, or upper respiratory symptoms.[4] Psychiatric symptoms are diverse, manifesting by a change in behavior and by the appearance anxiety disorders, deficit symptoms with anxiety, insomnia, withdrawal, social withdrawal, loss of memory and symptoms productive with visual or auditory hallucinations and delusions, [4,5] Our teenager suffered from headache for 5 days after the mother and the day after his hospitalization he presented significant psychaitric disorders. he also had seizures witch are extremely frequent, present in almost 80% of cases. [5]

They are most often generalized, tonicoclonic (45% of cases) and more rarely partial. Severe status epilepticus, convulsive or not, are possible. The dysautonomic picture is rarely in the foreground and should always be discussed first, in front of a patient in intensive care, a state of shock. Our patient had presented threatening hypertension led us to give intravenous treatments. This table, however frequent during illness (about two thirds of cases) [3,4] may include hypertension or hypotension, rhythmic disturbances with tachycardia or bradycardia sometimes requiring the placement of a pacemaker, fever, hypersalivation, erectile dysfunction or urinary incontinence. Cerebrospinal fluid is abnormal in 80% of patients at diagnosis. He finds moderate hyperlymphocytosis (9–219 elements / µl; median value: 24 elements / µl), hyperproteinorachia (56–129 mg / dl; median: 67 mg / dl) with normal glycorachia. [3]

When they are sought, specific oligoclonal bands are found in the CSF in 60% of patients. [5] The analysis of the CSF was without abnormalities in our patient at the beginning. The Electroencephalogram is abnormal in almost all cases. [1] It mainly shows slowed, diffuse and disorganized activity, like the case of our patient.

Brain MRI is abnormal in only 50% of patients. [5] In addition, the anomalies found are often discrete and non-specific. The most frequently found abnormalities are T2-weighted sequence hypersignals or fluid low attenuation inversion recovery (FLAIR) in the hippocampi and cerebral cortex. Anomalies of the frontobasal and insular region, basal ganglia, cerebellar cortex, brainstem or spinal cord are less common [5]. The key to diagnosis is the detection of antibodies anti-R-NMDA in CSF. [7,10]

These antibodies can also be measured in the blood, but it is their presence in the CSF which signs the diagnosis. Their detection in the CSF was impossible in our patient for technical problems. In tumor-negative patients, treatment with high dose steroids and intravenous immunoglobulin or plasma exchange is the first line therapy. Relapses occur in 20–25%; the rate may be higher in patients without an associated tumor. [10] For second-line treatment, in patients without diagnosed tumor or with delayed diagnosis, second-line treatment combining rituximab (375 mg /m^2 every week for four weeks) and cyclophosphamide (750 mg /m^2 together time after the first dose of rituximab,

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followed by one dose per month) has been proposed with clinical benefit in 65% of patients [4,10]. Due to the risk of relapse, some teams offer maintain mycophenolate immunosuppression mofetil or azathioprine for at least one year. [4]

Approximately 75% of patients have a favorable outcome without sequelae or with persistence of moderate disturbances in attention, impulsivity, disinhibition, sleep disturbances with hypersomnia or modification of the nycthemeral rhythm. [4] Our patient kept abnormalities on the electroencephalogram as sequelae and worries about schooling linked to concentration disorders.

4. CONCLUSION

Anti-R-NMDA antibody encephalitis should be discussed in front of any encephalitis table, in the same way than viral encephalitis. The clinical course is one of progressive clinical deterioration that can be halted and often reversed by early diagnosis and treatment

CONFLICTS OF INTEREST

none relevant to this article.

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