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Case Report

A 19-Month-Old Spanish Boy with Anti-NMDAR Encephalitis: Case Report and Review of Literature

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Abstract

Background and Aim: The classic definition of acute encephalitis consists of altered consciousness associated with fever, seizures or focal neurological alterations on neuroimaging or electroencephalography. However, there are particularities that may provide a glimpse of the probably autoimmune versus infectious etiology of the same neurological picture.

Case presentation: A 19-month-old male starts with motor clumsiness and refusal to ambulation and leg claudication in the context of febrile pharyngotonsillitis. Simultaneously, first episode of forced gaze's lateralization and cephalic deviation with right tonic movements and sucking. On examination: intense irritability with no contact, denial-type stereotypies, hemiparetic gait, pronation and adduction of the right arm and foot with frequent stumbling.

Results: Neuroimaging tests, electroencephalogram, laboratory tests and antistreptolysin-O were normal, no pathological clinical exome and detection of antibodies in cerebrospinal fluid paired with serum. Such as diagnosis: acute autoimmune encephalitis due to anti-NMDA-R (N-methyl-D-aspartate Receptor) antibodies and movement disorder (choreoathetosis, hemidystonia). We initiate treatment with intramuscular penicillin and oral clobazam with erratic response. Fortunately, high doses of intravenous (iv) corticosteroids and immunoglobulins, oral corticotherapy and iv rituximab on our patient were used. Months later, clear improvement with autonomous ambulation without assistance, adequate manual opening and entire disappearance of dystonic-myoclonic movements.

Conclusions: Choreoathetoid movements accompanied by irritability in an infectious context should lead us to think of Sydenham's chorea. However, new developments in the analysis of biological samples and a high index of suspicion may lead us to autoimmune pathology and the consequent early use of immunotherapy with optimal results.

***Keywords:** Choreoathetosis, Pediatric Encephalopathy, Anti-NMDA-Receptor.*

Introduction

Anti-NMDA (anti-N-methyl-D-aspartate) receptor encephalitis, such as an autoimmune disease was first described in 2007 by Dalmau et al. as a paraneoplastic syndrome associated with ovarian and testicular neoplasms [1,2]. However, subsequent studies revealed a different pattern in younger patients and men, where neoplastic changes are less common. In children under six, neoplastic changes are typically absent. The exact incidence remains uncertain due to limited epidemiological studies [2,3]. While hypotheses about viral infection links have been explored, none have been substantiated. Recent data include some cases in increasingly younger patients, with a study who cited a patient as young as 23-months-old by Wandiger et al. [3].

Prior reviews distinct pediatric course of the disease with neurological symptoms prevailing over psychiatric ones [4,5].

The case report's objective is to detail a case of anti-NMDAR encephalitis in a young child, covering clinical presentation, imaging findings, and management. The intention is to raise awareness of this rare but severe condition and contribute to the expanding knowledge on anti-NMDAR encephalitis in the pediatric population.

Case Presentation

A 19-month-old boy with acute febrile pharyngotonsillitis who started treatment with oral amoxicillin. The following day, sudden onset of motor clumsiness, refusal to stand upright and gait claudication. While he was staying on the car seat, a first episode consisting of lateralization of the gaze and cephalic deviation to the left with a sensation of rigidity of the right arm and sucking movements was evidenced. Subsequently, generalized weakness and tendency to sleep with little response were observed when he was stimulated. On arrival at the emergency department, he showed a partial recovery, so admitting him to the hospital for monitoring was decided. Family history: healthy and no consanguineous parents. Healthy 4-year-old brother. No history of neurological or tumor pathology. Personal history: pregnancy controlled, delivery at 41 weeks. Immediate neonatal period without incidents. Immunization schedule up to date and normal psychomotor development.

In physical examination, he was irritable, refused contact with strangers, oscillating behavior, calmed down over his mother's arms. Coordinated oculomotor movements. No facial asymmetries. Normal axial and peripheral tones. No spasticity. Preserved strength. Normal symmetrical osteotendinous reflexes. No clonus. Gait with hemiparetic-hemidystonic attitude, maintained pronation and adduction of the right arm and foot and dropping it, with frequent stumbles and falls (bilateral, more accentuated on the right). He always looked for a point of support, preferably on the left. Erratic manipulation with both hands, especially right one was worse when he attempted to hold objects bimanually to improve stability. He managed to separate the index finger to point, although if he wanted to press, he rectified the final movement (dysmetria). He constantly presented abnormal movements of cephalic "denial" type (stereotypies), lingual contouring (oral dyskinesias) as well as brief, disordered rotation of upper and lower extremities (chorea). No swallowing difficulties or sialorrhea. No auditory clonus or fasciculations (Figure 1).

Figure 1: Constant findings on neurological examination. *Right hemidystonia (elbow flexion and intra-rotation), the patient is forced to hold an object with his right hand to improve stability during he is crawling.*

As additional tests:

Venous blood gases, blood tests (hemogram, biochemistry and coagulation including normal CK (creatine kinase), ammonium and lactate with ASLO (antistreptolysin-O) of 2 IU/ml, lumbar puncture with normal cytochemistry and viral PCR detection were negative, infectious screening as respiratory viruses and CSF (cerebrospinal fluid) culture were negatives, urine catecholamines were normal; chest X-ray, abdominal ultrasound, scrotal ultrasound, CT, and brain MRI were normal. Video EEG with sleep deprivation: within normality (image 2). Viral serology with normal lymphocytes and complement profile. Antibodies in CSF paired with serum with positive result of Anti-NMDA antibodies. Rest of autoantibodies (antiMOG, antiGLyR, AntiGFAP, Anti AQP4 negative). IMEGEN exome: no alterations related to the patient's clinic.

As discharge diagnoses:

Acute autoimmune encephalitis due to anti-NMDA-R antibodies, behavioral alteration, gait disturbance, movement disorder (choreoathetosis, right hemidystonia, stereotypies, oral dyskinesias), sleep disorder, secondarily generalized focal motor seizures and streptococcal pharyngotonsillitis' suspicion (without microbiological confirmation).

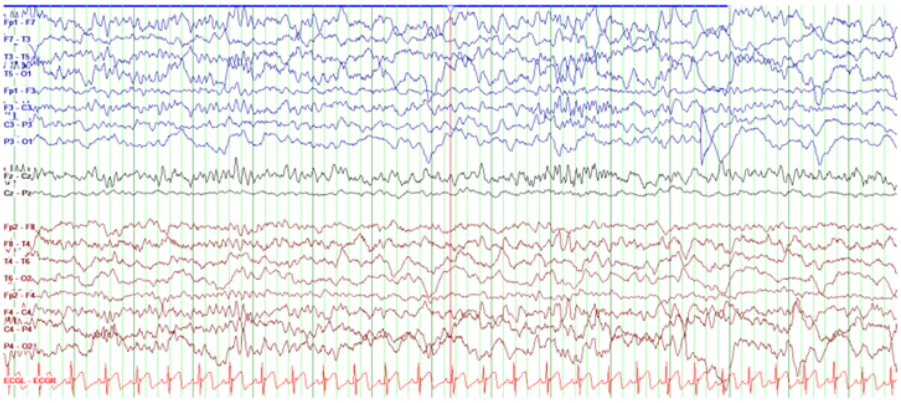

Figure 2. Electroencephalogram. *20-minute tracing with wake/sleep background activity within the normal range for the patient's age and recording conditions. No epileptiform activity, asymmetries, or other significant abnormalities. No paroxysmal episodes were recorded.*

After the first study, in the presence of focal seizures in sleep, treatment was started with oral clobazam, with worsening for 48 hours: absence of autonomous ambulation and more marked abnormal movements, so it was withdrawn. Given the clinical suspicion in the differential diagnosis of Sydenham's chorea versus autoimmune encephalitis, treatment was started with intramuscular Penicillin G 1.2 MU and 2nd dose at 21 days and the study was extended with lumbar puncture with extraction of auto.antibodies in cerebrospinal fluid; subsequent hospital treatment with iv methylprednisolone at 30mg/kg for 5 days followed by iv immunoglobulins for 48 hours. At discharge, oral prednisolone at 2 mg/kg/day for 6 weeks with a descending regimen.

One month later, evaluated in multidisciplinary orthopediatric consultation with clear improvement: autonomous ambulation without help, some increase of base for balance control persists, but he was able to carry his weight without help, getting up from the floor without difficulty, right manual opening, supination of the forearm and brachiation in walking, he achieved direct grip with the right limb. Sleep was more restful and without constant movements or awakenings. Simultaneously, positive result for anti-NMDA antibodies in CSF was found, confirming the clinical diagnosis. Residual symptomatology with motor clumsiness was still presented, so treatment with two doses of intravenous Rituximab 500mg/m2 (one dose each two weeks) was completed with favorable evolution, with continued outpatient follow-up. One-month later, he had showed up a complete recovery to his baseline condition.

Discussion

We define encephalitis as the alteration of mental status for more than 24 hours, associated with 2 or more findings related to brain parenchymal inflammation: fever, seizures or focal neurological disorders, cerebrospinal fluid pleocytosis and abnormalities in neuroimaging and electroencephalography. The growing interest in autoimmune etiology, highlighting the anti-NMDA receptor, should lead the clinician to consider immunomodulatory treatments, optimizing results and avoiding serious sequelae [6].

The particularity of our case is described by the clinical debut in the form of a movement disorder: focal seizure with secondary involvement of the level of consciousness and irritability of the infant child, as well as the anodyne tests (e.g., EEG) versus Psychiatric pathology of the adolescent patient [7]. Autoimmune encephalitis is a devastating disease that can cause neurodevelopmental delay or regression. However, its pathogenesis is unclear, with immune system disorders following infection likely to play an important role. It is essential to recognize the distinctive clinical symptoms of infectious forms because of their good response to immunotherapies [8].

Similarly, despite the low incidence of rheumatic fever which has decreased in recent decades due to socioeconomic improvements and the treatment of pharyngotonsillitis, let us not forget that Sydenham's chorea remains the most frequent cause of acquired chorea in childhood, and it is now believed that both clinical entities may be overlapping within the same spectrum of post-streptococcal pathology [9].

In recent years, the diagnostic frequency of autoimmune encephalitis has increased considerably. This fact is undoubtedly related to the dynamic development of new diagnostic methods in blood and cerebrospinal fluid, as well as therapeutic progress. Proof of this, the reviews carried out by the Alliance against Autoimmune Encephalitis who already advocate first line treatments with corticosteroids in combination with intravenous immunoglobulins and emphasize the role played by rituximab, a pathway reflecting the script of our case.

In conclusion, it is observed that the clinical response improves with early initiation of immunomodulatory treatment, which should be repeated periodically until the patient is completely asymptomatic. Not forgetting that behavioral alterations are usually the last item to be normalized [10].

Conclusion

The particularity of our case is described by the clinical debut in the form of a movement disorder: focal seizure with secondary involvement of the level of consciousness and irritability, as well as the anodyne electroencephalogram. Even though the incidence of rheumatic fever is low, Sydenham's chorea remains the most common cause of acquired chorea in infancy, so we have to think about it in our differential diagnosis versus autoimmune etiology. An important review by the Autoimmune Encephalitis Alliance was found, it already agrees to immunosuppressive treatment as first-line as our study reveals. Furthermore, Rituximab plays a good role with a complete disappearance of the symptoms.

Conflict of Interest

The authors declare no conflict of interest.

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