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Co-Existence of NMDAR Encephalitis with Multiple Sclerosis: A Case Report

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1. Abstract

NMDAR (N-methyl-D-aspartate receptor) encephalitis is common auto-immune encephalitis. There are references with overlap with demyelinating diseases. NMDAR encephalitis happens in multiple sclerosis patients (MS). We describe a young female with NMDAR encephalitis, who after four months complained about disturbances on both her lower limbs and diagnosed with multiple sclerosis. Bearing in mind, that in the first place we found non-specific T2 lesions without enhancement in magnetic resonance imaging (MRI) of brain, we wonder if she also was a patient with multiple sclerosis.

2. Introduction

NMDAR encephalitis is the most common auto-immune encephalitis. It is characterized by the presence of antibodies targeting the GluN11 subunit of the NMDA receptor in the central nervous system. Most commonly affected are young females and children. The usual symptoms include prominent psychiatric manifestations (anxiety, irritability, irregular behavior, delusions, hallucinations, distorted thought, psychosis), insomnia, memory deficits, epileptic seizures, decreased level of consciousness, dyskinesias and autonomic dysregulation. This disorder may be associated with tumors, especially ovarian teratoma, herpes virus infection or an overlap with demyelinating diseases [1-2]. Some studies describe an overlap between NMDAR encephalitis and neuro-inflammatory diseases like neuromyelitis optica spectrum disorders (NMOSD), acute demyelinating encephalomyelitis, and myelin oligodendrocyte glycoprotein (MOG) inflammatory demyelinating disease [3-8]. However, an association between NMDAR encephalitis and multiple sclerosis is rare [3-5]. Herein we report a case of a female adolescent with a course from anti NMDAR encephalitis to multiple sclerosis.

3. Case Presentation

A 16-year-old female was hospitalized in the child and adolescent psychiatric clinic of our hospital due to progressively worsening bizarre behavior, visual hallucinations, aggression and fluctuating level of consciousness for about a month. Prior to these symptoms, she was complaining about new onset headache. She has been treated with anti-psychotic medication without any improvement. Thus, her treating psychiatrists sought for neurological assistance.

Her neurological evaluation was insignificant, revealing only a neutral plantar response to her right foot. Overall, she was displaying catatonic posture and from the evaluation of the other systems sinus tachycardia was recorded.

The brain MRI displayed a few non-specific T2 lesions without enhancement located in the juxtacortical region of the brain on both sides and the cervical spine MRI revealed several T2 lesions without enhancement. The electroencephalogram was normal. We proceeded with lumbar puncture where oligoclonal bands were detected in serum and in cerebrospinal fluid (CSF), as well as, anti NMDAR antibodies. The diagnosis of anti NMDAR encephalitis was reached, after excluding other possible demyelinating diseases and first line treatment with intravenous methylprednisolone, followed by intravenous immunoglobulin was administered. A whole-body positron emission tomography (PET) scan and a pelvis MRI in order to screen for tumors especially ovarian teratomas were performed with negative findings. The patient started slowly to recover and she was released from the hospital two weeks after the intravenous infusions with no neurologic semiology, apart from a neutral plantar response to her right foot. The

psychiatric symptoms had resolved. Monthly intravenous immunoglubilin infusions for 6 months were decided according to the International Consensus Recommendations for the Treatment of Pediatric NMDAR Antibody Encephalitis [15]. While on her third follow-up visit to our clinic for IVIG, the patient complained about experiencing new onset sensual disturbances on both her lower limbs. Her neurological evaluation revealed mild hemiparesis of her left upper and lower limbs, right lower limb hemi hypesthesia, paresthesia on both her lower limbs and flexor plantar responses on both sides.

A new set of brain- cervical and thoracic spine MRIs were performed. They revealed numerous T2 lesions periventicular, on both the cerebellar hemispheres, on the cervical and the thoracic spinal cord and one T2 lesion on the medulla oblongata with enhancement. The 2017 Mc Donald criteria for diagnosing multiple sclerosis were fulfilled [9]. She was treated with a 3-day course of intravenous methylprednisolone as a rescue therapy and her main immunotherapy was up-scaled to rituximab. At the time of her re-evaluation, a month later, the hemiparesis and the hemi hypesthesia had recovered and she has not suffered any new clinical relapse or radiological worsening, a year later.

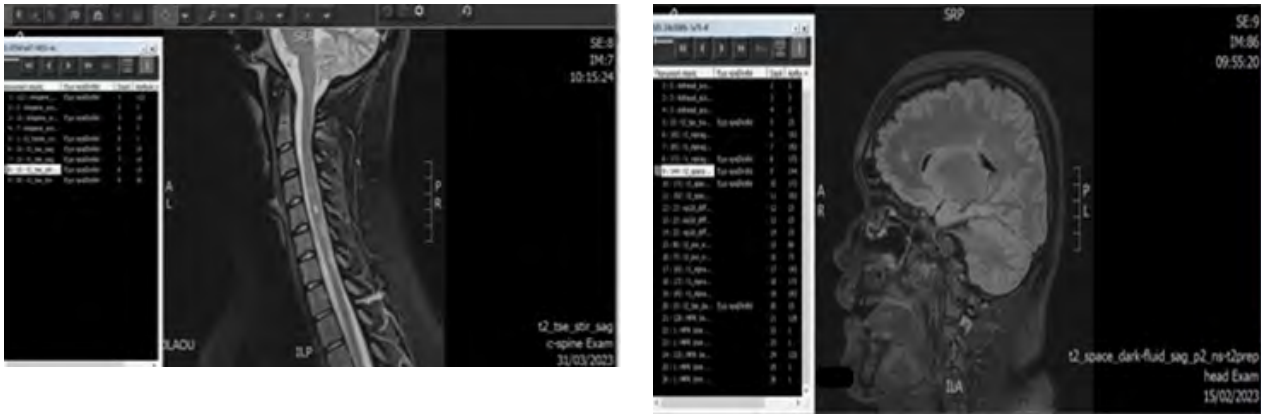

Figure 1: MRI findings from the first admission.

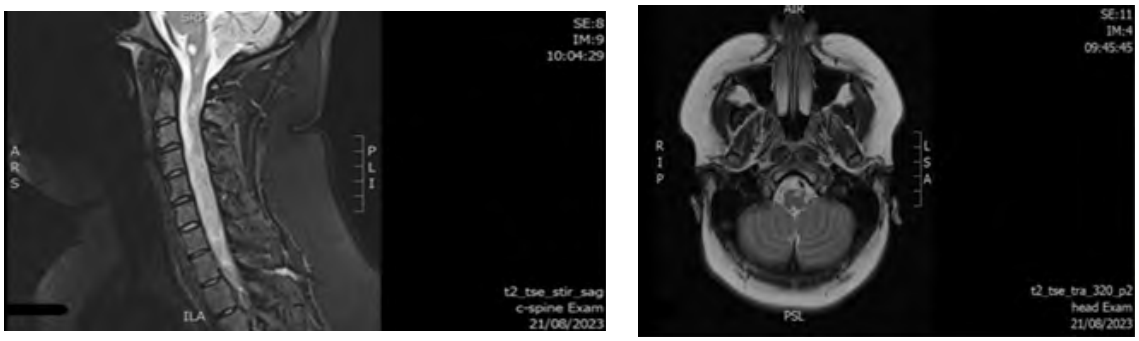

Figure 2: MRI findings after four months.

4. Discussion

Less than half of patients with NMDAR encephalitis show abnormalities in brain MRI, such as T2-weighted and fluid-attenuated inversion recovery (FLAIR) hyperintense lesions [10-11]. The detected lesions are usually small, do not enhance and most of the time do not explain the clinical symptoms. Half of these patients have lesion in temporal lobes and hippocampus [1]. There is only one report [12], for two patients who presented with anti-NMDAR encephalitis and in the follow-up diagnosed with multiple sclerosis. Both of them had non-enhancing contrast lesions in the brain (one of them also in spine) and had episodes of relapsing-remitting form of MS with new demyelinating lesions, after one year. Our patient had oligoclonal bands both in serum and the CSF and a relapse after a short time (4 months). There are also reports of multiple sclerosis patients experiencing NMDAR-encephalitis [7]. Can we consider that pre-existing demyelinating lesions to the central nervous system (CNS) can provoke NMDAR encephalitis or that there is reciprocal association of these two diseases?. It is crucial to make the appropriate diagnosis, because the treatment of each disease is different. In our case there was a short time of appearance of these two distinct diseases and therefore we chose as a prophylactic treatment rituximab, a drug that can benefit both [2,13-15].

5. Conclusion

There are references with co-existence of NMDAR encephalitis and MS. More often the diagnosis of MS preexist, but like our case the diagnosis of MS can follow NMDAR encephalitis, in cases that have from the first time non-specific T2 lesions without enhancement in MRI of brain.

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