ISSN No. 2394-3971

Case Report

NMDA ENCEFALITIS CASE REPORT AND LITERATURE REVIEW

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Submitted on: January 2018
Accepted on: May 2018
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Abstract:
Encephalitis has many causes, but for most patients, the cause still remains unknown. Worldwide, up to 85% of cases are of unknown cause, and there is concern about new and emerging triggers. N-methyl-D-aspartate receptor (anti-NMDA-R) encephalitis is an immune-mediated syndrome that remains under-recognized despite a growing body of literature.[1,2] This syndrome has been predominantly described in young females with a constellation of symptoms, including personality changes, autonomic dysfunction, and neurologic decompensation. It is commonly associated with mature ovarian teratomas.[3] We describe the classic presentation of anti-NMDA-R encephalitis in a young woman, with antecedents in psychiatric disorders which is hospitalized in the Infectious Disease Hospital, UHC Mother Theresa with the admission diagnosis: Acute Viral Encephalitis. We reviewed the literature summarizing the differential diagnosis, investigative approach and therapeutic options related to this disorder[4,5]. We succeed to give good supportive care and involve multiple health disciplines. This case highlights the need for increased awareness and high diagnostic suspicion when approaching the patient with suspected viral encephalitis.

Keywords: encephalitis, NMDA-receptor, psychiatric disorders, autoimmune

Background

Many cases of Autoimmune Encephalitis associated with antibodies against the N-methyl D -aspartate (NMDA) receptors have recently been reported. NMDA receptor is a protein in the brain that helps control the electrical activity of nerves and therefore antibodies against these receptors are likely to have an important role in directly causing the disease. The symptoms and signs seen in patients with NMDA Receptor Antibody associated Encephalitis can be distinctive and are prompting many clinicians to request the NMDA receptor antibody test to diagnose this condition. The disease mainly affects young people, with around 30% of

cases under 18 years of age. Women are affected more often than men. Recent reports suggest that between 20 and 57% of females may have an underlying tumor.[6,7] The most common tumor found in women is called an ovarian teratoma and is a non-cancerous tumor but is thought to stimulate the production of NMDA receptor antibody.[8] At the onset, the most distinctive features include prominent psychiatric symptoms, seizures, confusion and memory loss. Patients sometimes show bizarre and disturbing behaviors.[8,9] Typically 10 to 20 days later, patients develop a movement disorder, variations in blood pressure, heart rate and temperature and may become less conscious. If these symptoms and signs are recognized, another cause s excluded (particularly infections) and the antibody result is positive, treatments should be started.[10] Treatment consists of immune therapies and removal of a tumor if present. The immune therapies use medicines to dampen down the immune system.[11] These include steroids, immunoglobulin and plasma exchange. All drugs have known side-effects but their benefits are generally felt to outweigh possible side-effects.[12] Prompt therapies offer a good chance of substantial recovery in the majority of patients. As they improve there is often a reduction in the amount of NMDA receptor antibody in the person's blood when the test is repeated. Recovery is usually slow and many patients spend a few months in the hospital, including time in the intensive care unit. Those who return to work typically only do so after a year or two. In summary, NMDA Receptor Antibody Encephalitis is a recently identified autoimmune disease that causes psychiatric features, confusion, memory loss and seizures followed by a movement disorder, loss of consciousness and changes in blood pressure, heart rate and temperature.

The Case

Below we present the case of a 35 -year-old woman, previously recognized with psychotic disorders and for obesity, were brought to the Infectious Disease Hospital (emergency room) on March 21-st, 2014.

The admission diagnosis was Acute Encephalitis.

Because of the severe clinical situation and altered conscious state, the patient was immediately placed in the ICU.

She was febrile without focal neurologic deficits or meningeal signs. Familiars were questioned a very carefully anamnesis. They revealed the patient has first hospitalized to the Psychiatric Hospital three weeks ago. She manifested confusion, weird attitude, agitation, auditory hallucinations. She was treated for a week with sedatives and reacted with good therapy results. She was diagnosed with the psychotic disorder and discharged home with ambulatory therapy.

In a week, symptoms progressed requiring another admission to a psychiatric hospital. On the second admission, the patient manifested auditory hallucination, altered conscious and did not communicate. Except for these important psychiatric symptoms, this time she also manifested fever. The first imagery results,(chest X rays) revealed bilateral pneumonia.

For this, the patient was transferred to the Infectious Disease Hospital, for further diagnosis and treatment and was immediately placed in the ICU.

In the ICU, a severe clinical situation was observed. The patient continued febrile with altered conscious (didn`t communicate and reacted to dolorous stimulus only).Psychiatry was consulted in the first place. Monoclinic seizures were observed, so brain computerized tomography (CT) and MRI were immediately requested. They resulted normal, while CSF showed 30 cells and mildly elevated lymphocytes and

protein. The culture of CSF resulted in sterile.

In 5 days we noticed a progressive worsening of conscience (According to GCS she was admitted with 9 -10 points and she rapidly goes to 7-8). At this point, the patient became apneic, with a decreased level of consciousness (had a witnessed generalized tonic-clonic seizure).

She was immediately intubated in the ICU (A/C, VT 650 ml, Fr14, FiO2 100%, PEEP 6 mmH2O)

The patient at this point undergoes to a general consultant, which considered the case as a probable meningoencephalitis, of unknown origin, in which dominated the psychotic syndrome.

Presuming the case as severe acute encephalitis of unknown origin, the patient was tracheostomized 10 days after intubation.

Treatment first started with antipsychotics and in a second moment was completed with antibiotics, antivirals, anti-inflammatory drugs and supportive intensive care therapy was started for this presumed acute encephalitis.

FB and BAL were added to routine conventional methods for airway clearance and also provided samples for cultures. Cultures from the BAL confirmed Acinetobacter baumani as a cause of VAP.

Meantime, the protocol of neuroinfections and related differential diagnosis had started. The CSF culture resulted steril, but it was also examined for Borrelia, Enteroviruses, coronas, TB and WNE, which also resulted negative.

Serological tests for TB, HIV, Varicella, Borreliosis, and Syphilis resulted negative.

Ceruloplasmin and Cupruria ranged between normal values.

BhCG and CA 19-9 also resulted in normal values.

Laboratory monitoration was performed every day with hemogram, biologic balances, prothrombin index, and gasometry.

Hemocultures and agriculture were dynamically taken according to their protocols and they resulted negative. Imagery examination consisted in continuous Chest X rays (showed bilateral pneumonia which had a progressive improvement from one examination to other)

Abdominal ultrasound resulted in normal parameters. Continuous EEG demonstrated non-convulsive status epilepticus, requiring high doses of anticonvulsants and general anesthesia.

Being in front of an Acute Encephalitis which reflected a rich clinical presentation but with no objective laboratory or imagery data, required a continuous neurologic consult which, concluded the case as a probable NMDA Encephalitis

The patient was followed up for 46 days in the ICU.

She stayed in mechanical ventilation support for 28 days.The patients underwent a complex therapy which changed dynamically.

Our therapeutic protocols consisted in the management of infections, airways (by avoiding barotrauma during generalized seizures), and autonomic dysfunction which most of the time were life-threatening, parenteral and enteral therapy, early fisiotherapy which resulted successfully in the end with lack of sechelae.

Discussion

Anti-NMDA-R encephalitis is a complex syndrome with characteristic symptomatology, variable response to treatment and a broad differential diagnosis. [13]

The identification of NMDA-receptor antibodies has established a laboratory diagnosis for the characteristic clinical syndrome of "encephalitis of unknown origin" and compatible clinical features.

[14,15]This diagnosis must be considered in the differential of all patients presenting with findings of "viral encephalitis", regardless of age or sex (previous reports have emphasized the classic presentation in the "young female"), especially when findings out with presumed diagnosis are detected, as noted in our patient in which fever is incompatible with diagnosis of brief psychotic disorder. Similarly, the presence of seizures early in the illness course should raise diagnostic suspicion. [16]Complex and generalized seizures are reported in the majority of cases (76%) in the largest case series, distinguishing anti-NMDA-R encephalitis from most causes of viral encephalitis and suggesting that seizures are part of the natural history of this syndrome. Investigations should be requested with the intent of confirming the diagnosis while excluding mimics and confirmatory testing should be requested in all patients presenting with psychiatric, neurologic and autonomic symptoms/signs that are not better explained by an infectious disease process.

Regarding our case, we reviewed the literature highlighting the differential diagnosis, investigative approach and therapeutic options related to this disorder. We couldn`t realize the laboratory diagnosis, but we managed to get through all the possible differential diagnoses, excluding in this way all other possible causes of encephalitis. Diagnosis and management necessitate and communication between various medical professionals including infectologists, internists, neurologists, psychiatrists, intensivists, cardiologists, radiologists, gynecologic and urologic surgeons, and pathologists. With care as described, prognosis remains good with 75% of cases recovering with minimal deficits.

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