

SLE and Anti-NMDA Receptor Encephalitis in an 18 Year-Old Presenting with a Skin Rash

Abstract

Encephalitides such as anti-NMDA receptor encephalitis have been on the rise in recent years. Anti-NMDA receptor encephalitis most commonly presents as psychosis, delusions, and other neurological deficits. As with most autoimmune disorders, anti-NMDA receptor encephalitis has a higher incidence in females and the average age of onset is 23 years. An 18 year old male presented with a rash and agitation that was diagnosed as HSV, and suffered TEN after beginning acyclovir treatment. After the patient deteriorated and was unsuccessful in responding to multiple sedatives for agitation, the proper autoimmune pathology was narrowed down to anti-NMDA receptor encephalitis. In previous cases of anti-NMDA receptor encephalitis – patients responded to some sedative agents like dexmedetomidine. The patient responded well to IVIG, methylprednisone, and hydroxychloroquine treatment. 80% of people show full recovery from the condition if treated properly, this patient passed away from cardiac arrest 8 months after recovering. The unique case presented discusses the challenges of diagnosing and managing anti-NMDA receptor encephalitis, and warrants the need for further investigation of the pathophysiology and differing responses to sedative agents in patients.

Keywords: NMDA receptor encephalitis; Anti-RN1 antibody; NMDA; Precedex; Etomidate; Propofol; Critical care; Rash; TEN

Case Report

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Abbreviations: SLE: Systemic Lupus Erythematosus; ICU: Intensive Care Unit; ED: Emergency Department; CNS: Central Nervous System; IV: Intravenous; CT: Computed Tomography; ARDS: Acute Respiratory Distress Syndrome; IVIG: Intravenous Immunoglobulin

Introduction

Autoimmune conditions like SLE have their common presentations and populations. There is evidence of autoimmune conditions playing a role in neuropsychiatric conditions like Anti-NMDA receptor encephalitis which can present as psychosis, delusions, catatonia, seizures, and hypoventilation requiring intubation [1]. It accounts for 1 – 4 % of all encephalitides [1]. One study showed that out of 100 patients that had NMDA receptor encephalitis the median age was 23, 91 were women, and all 100 presented with psychiatric symptoms – particularly psychosis [1]. This condition has higher incidences in Asian and African American populations. This points in the direction that uncommon autoimmune conditions like Anti-NMDA receptor encephalitis, Anti-AMPA receptor encephalitis, Anti-GABA receptor encephalitis, Susac's syndrome, Whipple disease, and CNS vasculitis should be considered as potential etiologies when patients present with psychotic symptoms in their 20s. Anti-NMDA receptor encephalitis is associated with ovarian teratoma 59% of the time in women [1,2]. The presence of an ovarian teratoma is a good prognostic indicator of recovery from anti-NMDA receptor encephalitis. Twelve case reports in men that showed no underlying malignancies. Approximately 80% of

individuals achieve full recovery, while the others remain severely distressed or die [3].

The pathogenesis of Anti-NMDA receptor encephalitis is not well understood; however, there are some proposed theories. One study examines the reversibility of psychosis induced by NMDA receptor encephalitis, and proposes that anti-NR1 antibodies attack the GluN1 subunit on the NMDA receptor resulting in internalization of the receptor [4]. This causes NMDA receptor hypofunction resulting in psychosis and agitation [4].

This case report discusses the potential obstacles in sedating a patient with anti-NMDA receptor encephalitis, and suggests that further research is implicated in identifying the pathophysiology behind this condition to better target pharmacotherapy and management. The case was unique in that the patient was a young male who presented to the ED for a skin rash, then deteriorated rapidly and was agitated in the ICU despite intubation and sedation with max doses of Versed, Propofol, Precedex and frequent doses of Etomidate.

Case Presentation

Presentation

An 18-year-old Hispanic male presented to the ED for IV antivirals because of a 3 week history of a skin rash and positive Tzanck smear. He had a diffuse, desquamating maculopapular rash with a positive Nikolsky's sign that involved his upper chest, face, neck and palms. Skin biopsy later showed toxic epidermal necrosis.

Initial workup

Soon after admission CT scan showed ARDS, he had 2 episodes of seizure, was intubated and transferred to ICU.

ICU Course

Patient was diagnosed with septic shock secondary with pneumonia. He developed multiorgan failure with severe anasarca- encephalopathy, elevated liver enzymes, acute kidney injury, and respiratory failure.

He had to be placed on mechanical ventilation, and was severely agitated while on maximum doses of Versed, Propofol, Precedex and was still requiring frequent doses of Etomidate. The encephalopathy and multiorgan failure was not clear, an autoimmune panel was strongly positive for ANA 1:640, anti-Smith and RNP antibody. SLE with macrophage activation syndrome was considered due to the clinical course, high titer ANA, elevated ferritin level, and persisting hypocomplementemia. Pulse methylprednisolone was started, and showed some improvement. Bone marrow biopsy showed positive myelodysplasia.

His respiratory status improved, but he was still agitated. He was empirically treated for autoimmune encephalitis with IVIG and responded well. He was positive for GAD-receptor and the NMDA-receptor antibodies, but stiff man syndrome was not seen. In the meantime, he was extubated 2 times but required reintubation both times, bedside tracheostomy was done on Day 24. After receiving the 4 doses of IVIG, methylprednisolone and hydroxychloroquine – he clinically improved and was switched to and tolerated a trach collar on Day 26. His agitation resolved, and was communicate and follow commands. The tracheostomy tube was removed on Day 28. The patient was discharged home on Day 29 with outpatient physical therapy.

Prognosis

The patient died due to a cardiac arrest 8 months after discharge.

Discussion

Studies show that patients usually women and children present with delusional and psychotic features, this patients presentation was unique in that he did not initially present with these features. The patient was agitated, but a rash was the primary reason why he decided to come to the hospital. The link between various autoimmune diseases an emerging topic in medicine that can be highlighted in this case. This patient's anti-NMDA receptor encephalitis could have been a secondary manifestation caused by an existing viral process, possibly HSV-1 due to the positive Tzank smear. Although the patient did not present with HSV-1 encephalitis, a study demonstrated 30% of 44 HSV-1 encephalitis cases were associated with concurrent anti-NMDA receptor encephalitis [5]. IgA and IgG anti-NMDA receptor antibodies were detected at the time of presentation or a week after presentation [5]. Some studies have shown that approximately 30% of patients with Anti-Smith antibodies have anti-NMDA receptor antibodies [6]. (It is a long sentence, I prefer to be writing as follow: (Although

the patient did not present with HSV-1 encephalitis [5]. IgA and IgG anti-NMDA receptor antibodies were detecting at the time of presentation or a week after presentation [5]. Some studies have shown that approximately 30% of patients with Anti-Smith antibodies have anti-NMDA receptor antibodies [6].

Excluding autoimmune encephalitides is extremely important in a patient's first psychotic episode even if they have a strong psychiatric family history. There are several cases where patients have a strong psychiatric family history, and a delayed diagnosis resulted in long-term impairments in memory and cognitive function. Potential genetic and environmental mechanisms behind anti-NMDA receptor encephalitis could be an avenue of further exploration.

Responses to pharmacotherapy for sedation and initial treatment of anti-NDMA receptor encephalitis have varied tremendously in the literature. One case report showed that Precedex was able to achieve an appropriate level of sedation post-operatively in a patient that underwent surgery for laproscopic ovariectomy for an ovarian teratoma [7]. The favorable response to Precedex was possibly due to the removal of the paraneoplastic teratoma. A concurrent animal study showed that ketamine exaggerated neuropsychiatric symptoms in rats [7]. However, another case report demonstrated that neuropsychiatric symptoms in a 21 year old female patient improved with ketamine infusion, after plasmapheresis, IVIG, and corticosteroids failed to improve her symptoms [8]. The proposed hypothesis behind ketamine improving her symptoms was framed around a study which demonstrated that low-dose ketamine had partial agonist effects enhancing potentiation of a subgroup of hippocampal NMDA receptors alleviating her agitation.^[3]There is no clear rational behind these different responses, and further investigation needs to be done in order to determine these varied responses. More investigation needs to be done to differentiate appropriate therapy for the various presentations, stages, and settings of anti-NDMA receptor encephalitis.

Patients have long hospital stays and are usually treated with IVIG, corticosteroids, cyclophosphamide, or rituximab. Long term (Long-term) management of the patients include hydroxychloroquine and corticosteroid treatment.

The differing responses to various treatments and presentations open the door to exploration for better understanding of the pathogenesis. Differences in the sex of the patient may also play a role in the prognosis of the patient. Since females with this condition may have underlying paraneoplastic tumors, the early identification and treatment could make their prognosis more favorable than males. However, no studies have been done to show this. This case report highlights the issues in identifying, treating, and sedating patients with anti-NDMA receptor encephalitis.

Conflict of Interest

There are no conflicts of interest.

Patient Consent Form

Patient consented permission to publish a case report.

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