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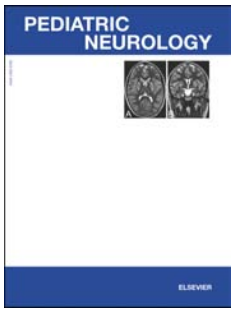

Three phenotypes of anti-NMDA receptor antibody encephalitis in children: prevalence of symptoms and prognosis

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Title: Three phenotypes of anti-NMDA receptor antibody encephalitis in children: prevalence of symptoms and prognosis

Short title: Subtypes of NMDA encephalitis

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ABSTRACT

BACKGROUND: Anti-N-methyl-D-aspartate (NMDA) receptor antibody encephalitis is becoming an increasingly recognized cause of encephalopathy in cases previously presumed to be viral encephalitis. Various manifestations of this disease include altered mental status, behavior changes, seizures, and movement disorders. We have noted three distinct subtypes of this disease which appear to have differential responses to immunotherapies as well as differences in prognosis.

METHODS AND PATIENTS: We report a case series of eight patients observed at our children's hospital from 2009 through 2013 that appear to clearly fall into one of our three clinical categories. To find comparable articles reflecting this classification, we then performed a Medline search of all articles involving the subject heading 'anti-NMDA receptor encephalitis' or just the keyword phrase 'NMDA encephalitis' and we found 162 articles to review. 22 articles were eliminated for being basic science in focus, and we were able to 105 of the remaining articles, most of which were case reports or case series, although a few were larger reviews. For the sake of our review, we defined type 1 or "classic" anti-NMDA receptor antibody encephalitis as having a duration less than 60 days and being characterized predominantly by a catatonic or stuporous state, type 2 or psychiatric-predominant anti-NMDA receptor antibody encephalitis as having no notable catatonic or stuporous state in addition to the presence of predominantly behavioral/psychiatric symptoms, and type 3 or catatonia-predominant anti-NMDA receptor antibody encephalitis as having a duration of 60 days or longer of being in a predominantly catatonic or stuporous state.

RESULTS: We note that the poorest responders, even to aggressive immunotherapies, are the catatonia persistent type anti-NMDA receptor antibody encephalitis, which has as its hallmark, prolonged periods of severe encephalopathy. Patients with predominantly psychiatric symptoms, which we call the psychiatric predominant NMDA receptor antibody encephalitis, have had excellent responses to plasma exchange or other immunotherapies and appear to have the least residual deficits at follow-up. Patients with fairly equal representations of periods of altered mental status, behavior problems, and movement disorders appear to have an intermediate prognosis and likely require early aggressive immunotherapy.

CONCLUSIONS: In our case series, we discuss representative examples of these clinical subtypes and their associated outcomes, and we suggest that tracking these subtypes in future cases of anti-NMDA receptor antibody encephalitis might lead to better understanding and better risk stratification with regards to immunotherapy decisions.

Keywords: NMDA, autoimmune, encephalitis, immunotherapy

INTRODUCTION

Anti-NMDA receptor antibody encephalitis has multiple presentations described in the literature. When initially discovered in adults, there was an association with ovarian tumors, specifically teratomas. Classically, the disease presents with seizures,

encephalopathy, and a movement disorder. However, there have been wide-ranging presentations involving various psychiatric symptoms – from mood disturbances to frank psychosis, various neurologic symptoms – speech changes and catatonia for example, and various degrees of seizure severity.[1-9] Typical treatments consist of a 3-5 day course of high-dose steroids followed by intravenous immunoglobulin or plasma exchange. In tumor-negative refractory cases, patients are typically treated with intravenous cyclophosphamide or rituximab.[2,4,7-9] As noted in an overview of several hundred patients, more mild symptom presentation and removal of a tumor, if present, are considered good prognostic signs.[2] We have noted in our cases that certain presentations lent themselves to better prognoses than others, and we go through these cases below with our classification scheme and comparison to historical cases in the literature.

CASE PRESENTATIONS

1) Type 1 - "Classic" anti-NMDA receptor antibody encephalitis

Case 1: The patient was a healthy 11 year-old Hispanic male who presented with seizures and irritability. He later developed dysarthria, periods of aphasia, facial twitching, and drooling, although he was able to follow commands. After another seizure, he deteriorated neurologically further, developing agitation, violent behaviors, and a depressed mental status, eventually requiring intubation. EEG monitoring showed no evidence of seizures. CSF testing showed 57 white blood cells/mm^3 and 2000 red blood cells/mm^3 and a normal protein. Testing for arboviruses, Bartonella henslae, enterovirus,

EBV, HSV, HIV, measles, mumps, Mycoplasma pneumoniae, rabies, syphilis, Toxoplasma gondii, and WNV was negative. CSF testing sent to ARUP for NMDA receptor antibodies was positive. CT and ultrasound imaging were negative. He was initially started on high-dose steroids followed by 7 rounds of plasma exchange. He had minimal improvement, and we gave him intravenous immunoglobulin and 2 doses of rituximab at 375 mg/m^2 over 3 weeks. After the rituximab, he only had slight improvement, and he was dosed with cyclophosphamide 1000 mg/m^2, to which had the best response and he was alert and ambulatory by discharge. 4 months later, he continued to have persistent behavioral problems, impacting his school and home life. He has continued to respond well to pulse doses of cyclophosphamide, but he has required multiple doses.

Case 2: The patient was a healthy 4 year-old Hispanic male who presented with progressive mental status changes and seizures over 4 weeks. He was started on anti-epileptics, but he had more staring spells followed by periods of violent behavior. EEG monitoring showed seizure activity, but escalation of his seizure medications did not result in improvement. His speech regressed, and he developed diffuse choreoathetosis. His CSF had 16 white blood cells/mm^3, 94 red blood cells/mm^3, and a markedly elevated protein to 634 mg/dL. Testing for arboviruses, Bartonella henslae, CMV, enterovirus, EBV, HHV-6, Lyme, Mycoplasma pneumoniae, VZV, and WNV was negative. His NMDA receptor antibody titer, sent to ARUP, in his serum was elevated to 1:160 and 1:80 on repeat testing. Imaging with CT and ultrasound was negative, and EEG monitoring showed no seizures. He had high-dose steroids with no improvement, and he

then received 7 rounds of plasma exchange, to which he responded well. 3 months later, he still had some residual speech problems, although his movement disorder, mental status changes, and agitation were much improved. 8 months later, his parents felt that he was back to his baseline with only mild behavior problems.

2) Type 2 - Psychiatric predominant anti-NMDA receptor antibody encephalitis

Case 3: The patient was a healthy 17 year-old African-American male who presented with a generalized tonic-clonic seizure. After a brief hospitalization, he was discharged on valproic acid. About 3-4 weeks later, he became extremely emotionally labile, easily crying while watching television. He then engaged in more bizarre behaviors, such as rearranging the furniture in the home, saying he needed to save the world, cursing and pacing, and expressing sexual desires verbally and physically. He alternated between aggression and disinhibited behaviors. The patient had 4 total lumbar punctures, and all the CSF results had a normal white blood cell count/mm^3 and a normal protein. Testing for drugs of abuse, enterovirus, EBV, HSV, HHV-6, syphilis, Chlamydia, and WNV was negative. Despite his history of seizures, repeat EEG testing showed no seizures. His NMDA receptor antibody titers were negative in the serum twice, sent to Mayo Medical Laboratories and ARUP, but his CSF NMDA receptor antibody titer was positive at 1:1, which was noted at ARUP and verified as positive at Mayo. CT and ultrasound imaging was negative. Intravenous steroids had no impact. With plasma exchange, he recovered quickly with near complete resolution of his behavioral abnormalities after 5 exchanges. 3 months later, his mother felt he was normal. However, he relapsed 10 months after his

initial hospitalization. His symptoms with his relapse were nearly identical, and, although he required plasma exchange, intravenous immunoglobulin, rituximab, cyclophosphamide, and intravenous methotrexate, he had a nearly complete recovery.

Case 4: The patient was a healthy 4 year-old African-American female who presented with several seizures and severe agitation. After initially started on anti-epileptics, she deteriorated and developed severe agitation, frank hallucinations, severe persistent insomnia, and severe violent and bizarre behavioral outbursts. She had periods of intermittently depressed mental status, although her behavioral changes were most prominent. She also had a movement disorder consistent with tardive dyskinesia, although this resolved when her quetiapine was discontinued. Her CSF had a normal protein and 12 white blood cells/mm^3. Testing for arboviruses, enterovirus, EBV, HSV, influenza, rabies, VZV, and WNV was negative. EEGs did not show evidence of seizures. NDMA receptor antibody testing in her serum was positive, verified on repeat testing, both of which were sent to Athena Diagnostics. CT and ultrasound imaging were negative. She was started on high-dose steroids with minimal improvement. Following 5 rounds of plasma exchange, she had slight improvements, and she was dosed with 1000 mg/m^2 of IV cyclophosphamide. She was markedly improved by 6 months and her mother only noted some mild emotional lability at 9 months. She was otherwise back to her baseline.

Case 5: The patient was a healthy 2 year-old African-American female who presented with a precipitous behavioral decline over 2 weeks. Her mother initially noticed that the

patient was sitting in her bed at night talking to herself incessantly. She developed severe insomnia followed by agitation and violent behaviors, such as throwing things and biting. She had some brief staring spells and mild intermittent oromotor twitching. Following admission, she had severe, refractory periods of extreme agitation and aggression. Her CSF testing showed only 2 white blood cells/mm^3 and a normal protein. Testing for EBV, HSV, and WNV was negative. Her serum titer, sent to ARUP, of NMDA receptor antibodies was 1:160. CT and ultrasound imaging was negative for tumors. EEG monitoring did not show evidence of seizures. Given the severity of her symptoms, she was started concurrently on high-dose steroids and plasma exchange, for which she had 7 exchanges. By the completion of her 7^{th} exchange, she was markedly improved. She was dosed with rituximab because of persistent speech regression. We are continuing to follow her progress.

3) Type 3 - Persistent Catatonia anti-NMDA receptor antibody encephalitis

Case 6: The patient was a healthy 2 year-old Hispanic male who presented with several seizures over a few weeks, prompting initiation of levetiracetam. Following this, he had a progressive neurologic decline over several months, including the evolution of diffuse choreoathetosis, mood lability, inappropriate laughter, deterioration in his mental status, and autonomic changes. Eventually, he required gastrostomy tube placement for nutrition. His cerebrospinal fluid (CSF) white blood cell count was slightly elevated at 7/mm^3 but a repeat a month later had 0 white blood cells/mm^3; CSF protein was also normal on both lumbar punctures. Testing for adenovirus, an arbovirus panel,

cytomegalovirus (CMV), Epstein-Barr virus (EBV), fungal blood, CSF, urine and routine blood cultures, herpes simplex virus (HSV), rhinovirus, parainfluenza viruses 1-3, influenza virus, Mycoplasma pneumoniae, respiratory syncytial virus (RSV), and West Nile virus (WNV) was all negative. 10 weeks later, the patient remained persistently encephalopathic with waxing and waning dystonic movements and choreoathetosis. Multiple electroencephalograms (EEGs) showed no evidence of seizures. At this time, his serum, sent to Athena Diagnostics, tested positive for NMDA receptor antibodies, and this was later confirmed on repeat serum testing on two separate occasions, both of which were also sent to Athena. Imaging with CT (computed tomography) and ultrasound was negative for tumors. He was started empirically prior to the test results on plasma exchange and he received 7 exchanges. He had clear improvement in his movement disorder and agitation, although he remained persistently and severely encephalopathic. He was later re-admitted for intravenous high-dose steroids, without clear benefit, and another 5 rounds of plasma exchange. He again had some improvement with his movement disorders and agitation, although he remained severely encephalopathic. By 12 months, his mental status had improved, although he remained nonverbal and required gastrostomy tube supplementation for his feeding. Two years after onset, he remained severely speech delayed with slow developmental progress. Upon routine yearly tumor screening approximately four years after his onset, he had a noted testicular tumor that was removed. We continue to track his progress following this procedure in regards to his speech delay.

Case 7: The patient was a healthy 11 year-old African-American female who presented with back-to-back generalized tonic-clonic seizures, and she was started empirically on carbamazepine and discharged. However, her mental status declined rapidly over the several weeks. She eventually became severely encephalopathic to the point where she required gastrostomy tube and tracheostomy tube placement for nutrition and airway management/protection, respectively. The patient's CSF testing showed no increase in white blood cells or protein. Testing for Lyme, HSV, an arbovirus panel, rickettsial titers, enterovirus, WNV, and a CSF and acid-fast bacilli (AFB) culture was negative. Shortly following her admission, her CSF results for NMDA receptor antibodies came back positive at 1:40, sent to Associated Regional and University Pathologists Laboratory (ARUP). Imaging for tumors with CT, ultrasound, and a positron-emission tomography (PET) scan was negative. The patient received high-dose steroids, intravenous immunoglobulin, 2 doses of rituximab at 375 mg/m^2, one dose of cyclophosphamide at 1000 mg/m^2, one dose of intravenous methotrexate at 1000 mg/m^2, and 4 doses of intravenous methotrexate at 2500 mg/m^2. Her agitation improved slightly after the methotrexate, but overall improvement was minimal. Multiple EEGs showed no evidence of seizures. In addition, her serum NMDA titers were tested, confirmed at both Athena and ARUP, and were elevated at 1:2560, even 12 months following presentation. Because of the severity of her symptoms, we worked with the gynecologists at our institution to remove her ovaries empirically, due to concerns about the possibility of microscopic tumor foci. This did not lead to significant clinical or serologic improvement.

Case 8: The patient was a healthy 5 year-old Hispanic female who presented initially with lethargy. Over the next several days, she regressed to a completely unresponsive state, and she had diffuse choreoathetosis, seizures, and spasticity. Her CSF had 0 white and 0 red blood cells/mm^3 and the protein was normal. Testing for adenovirus, arbovirus, CMV, EBV, human herpes virus-6 (HHV-6), HSV, varicella-zoster virus (VZV) and WNV was negative. Initial serum testing sent to Mayo Medical Laboratories for NMDA receptor antibodies was negative, although CSF and serum testing, sent to ARUP and Athena, repeated 3 months later was positive. Imaging with CT, ultrasound, and PET scans was negative. Despite the initial negative test, the patient was treated with high-dose steroids, 7 rounds of plasma exchange, and 5 days of intravenous immunoglobulin. She had no response and was given rituximab 375 mg/m^2 twice and cyclophosphamide 500 mg for 3 months. She still had no response. She was noted to have persistent electrographic seizures early in her course, although later EEGs showed resolution. She was treated intermittently over 6 months with intravenous immunoglobulin and plasma exchange. Over this period, she had slight improvement and was somewhat more alert. At a 20 month follow-up visit, despite good seizure control, she remains nonverbal but is slowly improving.

DEFINING CLINICAL SUBTYPES

As reflected in the cases above, we note that there appears to be a clear difference between certain phenotypes in anti-NMDA receptor antibody encephalitis (see Table 1 for classification scheme). We define type 1, or the "classic," anti-NMDA receptor antibody encephalitis as having slight to moderate degrees of severity of seizures,

movement disorders, catatonia/stupor, agitation/aggression, and bizarre behaviors and/or mood disturbances AND having the duration of time spent in a predominantly catatonic or stuporous state less than 60 days. Type 2, or the psychiatric-predominant, anti-NMDA receptor antibody encephalitis is defined as having predominantly behavioral/psychiatric and/or mood disturbances along with minimal to zero time periods where the patient is in a predominantly catatonic or stuporous state. Type 3, or the catatonia/stupor-predominant, anti-NMDA receptor antibody encephalitis is defined as having minimal to only slight behavioral/psychiatric symptoms AND time spent in a predominantly catatonic or stuporous state of greater than 60 days. In addition, we found that the movement disorders of the type 3 patients were often very severe, although this was less evident in our literature review.

LITERATURE REVIEW

To test our hypothesis against existing case reports of anti-NMDA receptor antibody encephalitis, we searched as a subject name or keyword in Medline for 'anti-NMDA receptor antibody encephalitis' or simply 'NMDA encephalitis.' We identified 162 articles for review, of which 22 were basic science articles or translational research, and we were able to review 105 of the remaining 140 articles. Large case series and cross-sectional studies had little information with respect to individual patient clinical courses and, therefore, patients in these articles could not be classified. We were able to review 75% of the case reports and small case series. We assessed these articles for the number of patients, ages, existence of a teratoma or other neoplasm (which were nearly universally removed), estimation of duration of psychiatric symptoms, severity (if

present) of a movement disorder, requirement (or not) of mechanical ventilation, estimation of duration spent in a catatonic/stuporous state, time until discharge, and reported outcomes. According to our classification scheme above, we classified only those case reports in which number of days until discharge was stated or could easily be inferred, in order to have some marker for response to treatments. We classified 26 articles representing 28 total patients (see Table 2). 17 articles with 19 patients we classified as type 1 anti-NMDA receptor antibody encephalitis, 2 articles with 2 patients we defined as type 2 anti-NMDA receptor antibody encephalitis, and 7 articles with 7 patients we defined as type 3 anti-NMDA receptor antibody encephalitis.[5,7,10-33] In terms of the time until discharge, the average time until discharge for the type 1 patients for these articles was 2.6 months, the type 2 was 0.47 months, and the type 3 was 10.3 months (not including two patients that died). Of the remainder of the articles, 50 articles had patients either in part or totality that we could not classify based on limited information according to our scheme above. 19 articles had 1 or more patients that we suspected were type 1, 8 articles had 1 or more patients that were suspected type 2, and 5 articles had 1 or more patients that were suspected type 3.[2,6,8,9,34-108] However, none of these patients could be classified because of limited data despite aspects of the clinical description that we felt were more suggestive of one type or another. In addition, 7 of the 19 patients that were Type 1 had a teratoma or other neoplasm at presentation or noted later in the course, neither of the Type 2 patients had a neoplasm, and 4 of the 7 Type 3 patients had a teratoma or other neoplasm at presentation or later in the course.

In comparison to our patients, the time to discharge of the two Type 1 patients was 1.4 months and 0.5 months for patients 1 and 2, respectively. The three Type 2

patients were 0.7 months, 1.8 months, and 0.6 months for patients 3-5, respectively. The three Type 3 patients time to discharges for patients 6-8 were 1.5 months, 3.9 months, and 1.8 months, respectively. Although outcomes were difficult to compare for our literature review, upon discharge, Type 2 patients clearly had the least remaining neurologic deficits, and the Type 3 patients all had profound deficits at initial discharge. The Type 1 patients appeared to have an intermediate recovery by the time of discharge. It should be noted that in patients 4 and 6, the diagnosis was delayed moreso than with the other patients. None of our patients had a tumor at initial presentation, although patient 6 had a testicular tumor noted approximately 4 years after diagnosis, and we are still following his progress after its resection.

DISCUSSION

The heterogeneity of anti-NMDA receptor antibody encephalitis has been well described, although we feel these cases suggest distinct clinical subtypes.[1-9] Certainly, the symptoms of anti-NMDA receptor antibody encephalitis follow a fairly predictable temporal pattern in most patients, however, it is unclear why certain patients have a protracted phase of psychiatric symptoms whereas others have a near-complete or complete absence of these symptoms and rapidly descend into a stuporous state. In our clinical experience, the Type 3 patients stand in sharp contrast to the Type 2 patients, who appear to respond quite favorably to aggressive immunotherapies and who clearly have the least residual deficits in the first 3-6 months after onset. The “classic” or Type 1 anti-NMDA receptor antibody encephalitis, in which the movement disorder, duration of

encephalopathy, and psychiatric symptoms seem to be of intermediate prevalence as compared to Types 2 and 3, appears to have an intermediate prognosis between the two, at least initially (see Table 1). When comparing these phenotypes across the literature, outcomes are more difficult to track and compare across articles, however, the amount of time until discharge generally agrees with our hypothesis. We postulate that differences in immune system activation or antigenic target are possibly responsible for these different phenotypes. Although it can be argued that different temporal variations explains the apparent different phenotypes, we would note there are inexplicably obvious cases in which, despite several months of symptoms, the progression of the syndrome "arrests" at the "psychiatric stage," and, on the opposite end of the spectrum, there are those that have a refractory dense catatonia/stupor. In addition, recent cases that have very unusual phenotypes, such as the patient with episodic paroxysmal weakness by Labate et al suggests that there are phenotypic differences that are not easily explained within the heterogeneity of the disorder.[58] We would argue that future studies of this disorder should consider tracking these differences, as more rigorous studies might help to uncover the differences on a molecular level between these distinct subtypes.

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payment for or given lectures for the MSAA and Medilogix, and has stock/stock options with DioGenix and Amplimmune. Dr. Donna Graves has consulted for Teva Pharmaceuticals and Bayer and has received payment for or given lectures for Teva, Bayer, Novartis, and Pfizer.

REFERENCES

[1] Dalmau J, Lancaster E, Martinez-Hernandez E, Rosenfeld MR, Balice-Gordon R. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. Lancet Neurol. 2011; 10(1): 63–74.

[2] Titulaer MJ, McCracken L, Gabilondo I et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis:an observational cohort study. Lancet Neurol. 2013;12(2): 157–165.

[3] Armangue T, Titulaer MJ, Alaga IM et al. Pediatric Anti-N-methyl-D-Aspartate Receptor Encephalitis—Clinical Analysis and Novel Findings in a Series of 20 Patients. J Pediatr. 2013;162(4):850-856.

[4] Breese EH, Dalmau J, Lennon VA, Apiwattanakul M, Sokol DK. Anti-N-Methyl-D-Aspartate Receptor Encephalitis: Early Treatment is Beneficial. Pediatr Neurol. 2010;42(3):213-214.

[5] Cantarín-Extremera V, Duat-Rodríguez A, González-Gutiérrez-Solana L, López-Marín L, Armangue T. Clinical Case of Anti-N-methyl-D-aspartate Receptor Encephalitis in an 8-Month-Old Patient With Hyperkinetic Movement Disorder. Pediatr Neurol. 2013;48(5):400-402.

[6] Raha S, Gadgil P, Sankhla C, Udani V. Nonparaneoplastic Anti-N-Methyl-D-Aspartate Receptor Encephalitis: A Case Series of Four Children. Pediatr Neurol. 2012;46(4):246-249.

[7] Ikeguchi R, Shibuya K, Akiyama S, et al. Rituximab Used Successfully in the Treatment of Anti-NMDA Receptor Encephalitis. Intern Med. 2012;51(12):1585-1589.

[8] Kashyape P, Taylor E, Ngb J, Krishnakumar D, Kirkham F, Whitney A. Successful treatment of two paediatric cases of anti-NMDA receptor encephalitis with Cyclophosphamide: The need for early aggressive immunotherapy in tumour negative paediatric patients. Eur J Paediatr Neurol. 2012;16(1):74-78.

[9] Mirza MK, Pogoriler J, Paral K, et al. Adjunct Therapeutic Plasma Exchange For Anti-N-methyl-D-aspartate Receptor Antibody Encephalitis: A Case Report and Review of Literature. J Clin Apher. 2011;26(6):362–365.

[10] Lesher AP, Myers TJ, Tecklenburg F, Streck CJ. Anti-N-methyl-D-aspartate receptor encephalitis associated with an ovarian teratoma in an adolescent female. J Pediatr Surg. 2010;45(7):1550-1553.

[11] Maqbool M, Oleske DA, Huq AH, Salman BA, Khodabakhsh K, Chugani HT. Novel FDG-PET findings in anti-NMDA receptor encephalitis: a case based report. J Child Neurol. 2011;26(10):1325-1328.

[12] Bseikri MR, Barton JR, Kulhanjian JA, et al. Anti-N-methyl D-aspartate receptor encephalitis mimics viral encephalitis. Pediatr Infect Dis J. 2012;31(2):202-204.

[13] Ishiura H, Matsuda S, Higashihara M, et al. Response of anti-NMDA receptor encephalitis without tumor to immunotherapy including rituximab. Neurology. 2008;71(23):1921-1923.

[14] Tan A, Shuey N, Bladin C. A modern perspective on the differential diagnosis between encephalitis lethargica or anti-NMDA-receptor encephalitis. J Clin Neurosci. 2010;17(9):1204-1206.

[15] Schmiedeskamp M, Cariga P, Ranta A. Anti-NMDA-receptor autoimmune encephalitis without neoplasm: a rare condition? N Z Med J. 2010;123(1322):67-71.

[16] Mesquita J, Siva L. Anti-NMDA receptor encephalitis suspected as cause of drug-induced psychosis. J Neuropsychiatry Clin Neurosci. 2011;23(4):E2.

[17] Kung DH, Qiu C, Kass JS. Psychiatric manifestations of anti-NMDA receptor encephalitis in a man without tumor. Psychosomatics. 2011;52(1):82-85.

[18] Uchino A, Iizuka T, Urano Y, et al. Pseudo-piano playing motions and nocturnal hypoventilation in anti-NMDA receptor encephalitis: response to prompt tumor removal and immunotherapy. Intern Med. 2011;50(6):627-630.

[19] Yu AY, Moore FG. Paraneoplastic encephalitis presenting as postpartum psychosis. Psychosomatics. 2011;52(6):568-570.

[20] Dean Z, Vincent A, Farrugia ME. End of the bed (end of the video) diagnosis. Pract Neurol. 2012;12(2):135-138.

21 Perogamvros L, Schnider A, Leemann B. The role of NMDA receptors in human eating behavior: evidence from a case of anti-NMDA receptor encephalitis. Cogn Behav Neurol. 2012;25(2):93-97.

22 Shaaban HS, Choo HF, Sensakovic JW. Anti-NMDA-receptor encephalitis presenting as postpartum psychosis in a young woman, treated with rituximab. Ann Saudi Med. 2012;32(4):421-423.

23 See AT, Woo YL, Crawford R. Acute encephalitis secondary to an ovarian teratoma. J Obstet Gynaecol. 2012;32(6):604-606.

24 McCarthy A, Dineen J, McKenna P, et al. Anti-NMDA receptor encephalitis with associated catatonia during pregnancy. J Neurol. 2012;259(12):2632-2635.

25 Sorita A, Mathew JP, Factor P. A 35-year-old woman with unusual behavior and prolonged respiratory failure. Chest. 2013;143(5):1504-1507.

26 Hegarty CP, Mikli JE. Behavioural disturbance requiring medical referral: A case of anti-N-methyl-D-aspartate receptor encephalitis in the emergency department. Emerg Med Australas. 2013;25(1):87-89.

27 Leypoldt F, Titulaer MJ, Aguilar E, et al. Herpes simplex virus-1 encephalitis can trigger anti-NMDA receptor encephalitis: case report. Neurology. 2013;81(18):1637-1639.

28 Sonn TS, Merritt DF. Anti-NMDA-receptor encephalitis: an adolescent with an ovarian teratoma. J Pediatr Adolesc Gynecol. 2010;23(5):e141-144.

29 Frechette ES, Zhou L, Galetta SL, Chen L, Dalmau J. Prolonged follow-up and CSF antibody titers in a patient with anti-NMDA receptor encephalitis. Neurology. 2011;76(7 Suppl 2):S64-S66.

30 Day GS, High SM, Cot B, Tang-Wai DF. Anti-NMDA-receptor encephalitis: case report and literature review of an under-recognized condition. J Gen Intern Med. 2011;26(7):811-816.

31 Alexopoulos H, Kosmidis ML, Dalmau J, Dalakas MC. Paraneoplastic anti-NMDAR encephalitis: long term follow-up reveals persistent serum antibodies. J Neurol. 2011;258(8):1568-1570.

32 Dabner M, McCluggage WG, Bundell C, et al. Ovarian teratoma associated with anti-N-methyl D-aspartate receptor encephalitis: a report of 5 cases documenting prominent intratumoral lymphoid infiltrates. Int J Gynecol Pathol. 2012;31(5):429-437.

[33] Thomas A, Rauschkolb P, Gresa-Arribas N, Schned A, Dalmau JO, Fadul CE. Anti-N-methyl-D-aspartate receptor encephalitis: a patient with refractory illness after 25 months of intensive immunotherapy. JAMA Neurol. 2013;70(12):1566-1568.

[34] Splinter WM, Eipe N. Anti-NMDA receptor antibodies encephalitis. Paediatr Anaesth. 2009;19(9):911-913.

[35] Wong-Kisiel LC, Ji T, Renaud DL, et al. Response to immunotherapy in a 20-month-old boy with anti-NMDA receptor encephalitis. Neurology. 2010;74(19):1550-1551.

[36] Llorens V, Gabilondo I, Gómez-Esteban JC, et al. Abnormal multifocal cerebral blood flow on Tc-99m HMPAO SPECT in a patient with anti-NMDA-receptor encephalitis. J Neurol. 2010;257(9):1568-1569.

[37] Maramattom BV, Philip C, Sundaram PS. Idiopathic anti-NMDA-receptor encephalitis in a young Indian girl. Neurol India. 2010;58(4):671-672.

[38] Chan SH, Wong VC, Fung CW, Dale RC, Vincent A. Anti-NMDA receptor encephalitis with atypical brain changes on MRI. Pediatr Neurol. 2010;43(4):274-278.

[39] Hung TY, Foo NH, Lai MC. Anti-N-methyl-d-aspartate receptor encephalitis. Pediatr Neonatol. 2011;52(6):361-364.

[40] Hofmann C, Baur MO, Schroten H. Anti-NMDA receptor encephalitis after TdaP-IPV booster vaccination: cause or coincidence? J Neurol. 2011;258(3):500-501.

[41] Chapman MR, Vause HE. Anti-NMDA receptor encephalitis: diagnosis, psychiatric presentation, and treatment. Am J Psychiatry. 2011;168(3):245-251.

[42] Greiner H, Leach JL, Lee KH, Krueger DA. Anti-NMDA receptor encephalitis presenting with imaging findings and clinical features mimicking Rasmussen syndrome. Seizure. 2011;20(3):266-270.

[43] Verhelst H, Verloo P, Dhondt K, et al. Anti-NMDA-receptor encephalitis in a 3 year old patient with chromosome 6p21.32 microdeletion including the HLA cluster. Eur J Paediatr Neurol. 2011;15(2):163-166.

[44] Creten C, van der Zwaan S, Blankespoor RJ, et al. Late onset autism and anti-NMDA-receptor encephalitis. Lancet. 2011;378(9785):98.

45 Tamma PD, Agwu AL, Hartman AL. Behavior outbursts, orofacial dyskinesias, and CSF pleocytosis in a healthy child. Pediatrics. 2011;128(1):e242-e245.

46 Taguchi Y, Takashima S, Nukui T, Tanaka K. Reversible "brain atrophy" in anti-NMDA receptor encephalitis. Intern Med. 2011;50(21):2697.

47 Goldberg EM, Taub KS, Kessler SK, Abend NS. Anti-NMDA receptor encephalitis presenting with focal non-convulsive status epilepticus in a child. Neuropediatrics. 2011;42(5):188-190.

48 Bushman ET, Mellion SA, King MA. Nine-year-old girl with altered mental status. Clin Pediatr. 2011;50(12):1161-1163.

49 Sameshima A, Hidaka T, Shima T, Nakashima A, Hasegawa T, Saito S. Anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian immature teratoma. J Obstet Gynaecol Res. 2011;37(12):1883-1886.

50 Iadisernia E, Battaglia FM, Vanadia E, Trapolino E, Vincent A, Biancheri R. Anti-N-methyl-D-aspartate-receptor encephalitis: cognitive profile in two children. Eur J Paediatr Neurol. 2012;16(1):79-82.

51 Frawley KJ, Calvo-Garcia MA, Krueger DA, McMasters RL. 'Benign' ovarian teratoma and N-methyl-D-aspartate receptor (NMDAR) encephalitis in a child. Pediatr Radiol. 2012;42(1):120-123.

52 Houtrow AJ, Bhandal M, Pratini NR, Davidson L, Neufeld JA. The rehabilitation of children with anti-N-methyl-D-aspartate-receptor encephalitis: a case series. Am J Phys Med Rehabil. 2012;91(5):435-441.

53 Kuo YL, Tsai HF, Lai MC, Lin CH, Yang YK. Anti-NMDA receptor encephalitis with the initial presentation of psychotic mania. J Clin Neurosci. 2012;19(6):896-898.

54 Borlot F, Santos ML, Bandeira M, et al. Anti-N-methyl D-aspartate receptor encephalitis in childhood. J Pediatr (Rio J). 2012;88(3):275-278.

55 Mann A, Machado NM, Liu N, Mazin AH, Silver K, Afzal KI. A multidisciplinary approach to the treatment of anti-NMDA-receptor antibody encephalitis: a case and review of the literature. J Neuropsychiatry Clin Neurosci. 2012;24(2):247-254.

56 Finné Lenoir X, Sindic C, van Pesch V, et al. Anti-N-methyl-D-aspartate receptor encephalitis with favorable outcome despite prolonged status epilepticus. Neurocrit Care. 2013;18(1):89-92.

[57] Hachiya Y, Uruha A, Kasai-Yoshida E, et al. Rituximab ameliorates anti-N-methyl-D-aspartate receptor encephalitis by removal of short-lived plasmablasts. J Neuroimmunol. 2013;265(1-2):128-130.

[58] Labate A, Quattrone A, Dalmau J, Gambardella A. Anti-N-methyl-D-aspartate-glutamic-receptor encephalitis presenting as paroxysmal exercise-induced foot weakness. Mov Disord. 2013;28(6):820-822.

[59] Grillo E, da Silva RJ. Anti-N-methyl-D-aspartate receptor encephalitis and parvovirus B19: A possible link? J Pediatr. 2013;163(4):1233-1234.

[60] Chia PL, Tan K, Foo D. Profound sinus node dysfunction in anti-N-methyl-d-aspartate receptor limbic encephalitis. Pacing Clin Electrophysiol. 2013;36(3):e90-e92.

[61] Ryan SA, Costello DJ, Cassidy EM, Brown G, Harrington HJ, Markx S. Anti-NMDA receptor encephalitis: a cause of acute psychosis and catatonia. J Psychiatr Pract. 2013;19(2):157-161.

[62] Iizuka T, Sakai F, Ide T, et al. Anti-NMDA receptor encephalitis in Japan: long-term outcome without tumor removal. Neurology. 2008;70(7):504-511.

[63] Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol. 2008;7(12):1091-1098.

[64] Parratt KL, Allan M, Lewis SJ, Dalmau J, Halmagyi GM, Spies JM. Acute psychiatric illness in a young woman: an unusual form of encephalitis. Med J Aust. 2009;191(5):284-286.

[65] Gable MS, Gavali S, Radner A, et al. Anti-NMDA receptor encephalitis: report of ten cases and comparison with viral encephalitis. Eur J Clin Microbiol Infect Dis. 2009;28(12):1421-1429.

[66] Fawcett RG. Acute psychosis associated with anti-NMDA-receptor antibodies and bilateral ovarian teratomas: a case report. J Clin Psychiatry. 2010;71(4):504.

[67] Mohr BC, Minoshima S. F-18 fluorodeoxyglucose PET/CT findings in a case of anti-NMDA receptor encephalitis. Clin Nucl Med. 2010;35(6):461-463.

[68] Varvat J, Lafond P, Page Y, Coudrot M, Reynaud-Salard M, Tardy B. Acute psychiatric syndrome leading young patients to ICU: consider anti-NMDA-receptor antibodies. Anaesth Intensive Care. 2010;38(4):748-750.

69 Braakman HM, Moers-Hornikx VM, Arts BM, Hupperts RM, Nicolai J. Pearls & Oy-sters: electroconvulsive therapy in anti-NMDA receptor encephalitis. Neurology. 2010;75(10):e44-e46.

70 Johnson N, Henry C, Fessler AJ, Dalmau J. Anti-NMDA receptor encephalitis causing prolonged nonconvulsive status epilepticus. Neurology. 2010;75(16):1480-1482.

71 Prüss H, Dalmau J, Harms L, et al. Retrospective analysis of NMDA receptor antibodies in encephalitis of unknown origin. Neurology. 2010;75(19):1735-1739.

72 Pryzbylkowski PG, Dunkman WJ, Liu R, Chen L. Case report: Anti-N-methyl-D-aspartate receptor encephalitis and its anesthetic implications. Anesth Analg. 2011;113(5):1188-1191.

73 Kirkpatrick MP, Clarke CD, Sonmezturk HH, Abou-Khalil B. Rhythmic delta activity represents a form of nonconvulsive status epilepticus in anti-NMDA receptor antibody encephalitis. Epilepsy Behav. 2011;20(2):392-394.

74 Camdessanché JP, Streichenberger N, Cavillon G, et al. Brain immunohistopathological study in a patient with anti-NMDAR encephalitis. Eur J Neurol. 2011;18(6):929-931.

75 Gabilondo I, Saiz A, Galán L, et al. Analysis of relapses in anti-NMDAR encephalitis. Neurology. 2011;77(10):996-999.

76 Torgovnick J, Izzo P, Arsura E, Sethi NK, Amrami B, Martone L. An unusual case of anti-NMDA-receptor encephalitis in the Psychiatry Inpatient Unit. J Neuropsychiatry Clin Neurosci. 2011;23(3):E8-E9.

77 Suzuki H, Samukawa M, Kitada M, et al. A case of anti-N-methyl-D-aspartate receptor encephalitis with systemic sclerosis. Eur J Neurol. 2011;18(11):e145-e146.

78 Caplan JP, Binius T, Lennon VA, Pittock SJ, Rao MS. Pseudopseudoseizures: conditions that may mimic psychogenic non-epileptic seizures. Psychosomatics. 2011;52(6):501-506.

79 Pascual-Ramírez J, Muñoz-Torrero JJ, Bacci L, Trujillo SG, García-Serrano N. Anesthetic management of ovarian teratoma excision associated with anti-N-methyl-D-aspartate receptor encephalitis. Int J Gynaecol Obstet. 2011;115(3):291-292.

80 Naoura I, Didelot A, Walker F, Luton D, Koskas M. Anti-N-methyl-D-aspartate receptor encephalitis complicating ovarian teratomas: a case report. Am J Obstet Gynecol. 2011;205(4):e6-e8.

81 Lee M, Lawn N, Prentice D, Chan J. Anti-NMDA receptor encephalitis associated with ictal asystole. J Clin Neurosci. 2011;18(12):1716-1718.

82 Barry H, Hardiman O, Healy DG, et al. Anti-NMDA receptor encephalitis: an important differential diagnosis in psychosis. Br J Psychiatry. 2011;199(6):508-509.

83 Pham HP, Daniel-Johnson JA, Stotler BA, Stephens H, Schwartz J. Therapeutic plasma exchange for the treatment of anti-NMDA receptor encephalitis. J Clin Apher. 2011;26(6):320-325.

84 Wali SM, Cai A, Rossor AM, Clough C. Appearance of anti-NMDAR antibodies after plasma exchange and total removal of malignant ovarian teratoma in a patient with paraneoplastic limbic encephalopathy. BMJ Case Rep. 2011;2011.

85 Finke C, Kopp UA, Prüss H, Dalmau J, Wandinger KP, Ploner CJ. Cognitive deficits following anti-NMDA receptor encephalitis. J Neurol Neurosurg Psychiatry. 2012;83(2):195-198.

86 Lekoubou A, Viaccoz A, Didelot A, et al. Anti-N-methyl-D-aspartate receptor encephalitis with acute disseminated encephalomyelitis-like MRI features. Eur J Neurol. 2012;19(2):e16-e17.

87 Pinho J, Rocha J, Rodrigues M, et al. Diversity in anti-N-methyl-D-aspartate receptor encephalitis: case-based evidence. Psychiatry Clin Neurosci. 2012;66(2):153-156.

88 Uruha A, Kitazawa Y, Kuroda M, Tanaka K, Koide R. Anti-NMDAR encephalitis in small-cell lung cancer: a case report. Clin Neurol Neurosurg. 2012;114(3):260-261.

89 Matsumoto T, Matsumoto K, Kobayashi T, Kato S. Electroconvulsive therapy can improve psychotic symptoms in anti-NMDA-receptor encephalitis. Psychiatry Clin Neurosci. 2012;66(3):242-243.

90 Leypoldt F, Buchert R, Kleiter I, et al. Fluorodeoxyglucose positron emission tomography in anti-N-methyl-D-aspartate receptor encephalitis: distinct pattern of disease. J Neurol Neurosurg Psychiatry. 2012;83(7):681-686.

91 Salazar R, James E, Elsayed M, et al. Profuse sialorrhea in a case of anti N-methyl-D-aspartate receptor (NMDAR) encephalitis. Clin Neurol Neurosurg. 2012;114(7):1066-1069.

92 Magley J, Towner D, Taché V, Apperson ML. Pregnancy outcome in anti-N-methyl-D-aspartate receptor encephalitis. Obstet Gynecol. 2012;120(2 Pt 2):480-483.

93 Dulcey I, Céspedes MU, Ballesteros JL, et al. Necrotic mature ovarian teratoma associated with anti-N-methyl-D-aspartate receptor encephalitis. Pathol Res Pract. 2012;208(8):497-500.

94 Nazif TM, Vázquez J, Honig LS, Dizon JM. Anti-N-methyl-D-aspartate receptor encephalitis: an emerging cause of centrally mediated sinus node dysfunction. Europace. 2012;14(8):1188-1194.

95 Batra R, Pang Y, Friedman MT. Therapeutic plasma exchange in anti-N-methyl-D-aspartate-receptor (anti-NMDA-R) encephalitis associated with benign ovarian teratoma. J Clin Apher. 2012;27(4):227-228.

96 Günther A, Brodoehl S, Witte OW, Freesmeyer M, Dalmau JO, Redecker C. Atypical posthypoxic MRI changes in hypermetabolic regions in anti-NMDA-receptor encephalitis. Neurology. 2012;79(7):720-721.

97 Evoli A, Spinelli P, Frisullo G, Alboini PE, Servidei S, Marra C. Spontaneous recovery from anti-NMDAR encephalitis. J Neurol. 2012;259(9):1964-1966.

98 Tsutsui K, Kanbayashi T, Tanaka K, et al. Anti-NMDA-receptor antibody detected in encephalitis, schizophrenia, and narcolepsy with psychotic features. BMC Psychiatry. 2012;12:37.

99 Vural A, Arsava EM, Dericioglu N, Topcuoglu MA. Central neurogenic hyperventilation in anti-NMDA receptor encephalitis. Intern Med. 2012;51(19):2789-2792.

100 Hansen HC, Klingbeil C, Dalmau J, Li W, Weissbrich B, Wandinger KP. Persistent intrathecal antibody synthesis 15 years after recovering from anti-N-methyl-D-aspartate receptor encephalitis. JAMA Neurol. 2013;70(1):117-119.

101 Reid DK, Clardy SL. Neurological picture. Anti-NMDA-receptor encephalitis: unusual presentation of an uncommon condition. J Neurol Neurosurg Psychiatry. 2013;84(1):69-70.

102 Sanmaneechai O, Song JL, Nevadunsky N, Moshé SL, Overby PJ. Anti-N-methyl-d-aspartate encephalitis with ovarian cystadenofibroma. Pediatr Neurol. 2013;48(3):232-235.

103 Gumbinger C, Hametner C, Wildemann B, Veltkamp R, Bösel J. Administration of isoflurane-controlled dyskinetic movements caused by anti-NMDAR encephalitis. Neurology. 2013;80(21):1997-1998.

104 Lim SY, Panikkath R, Mankongpaisarnrung C, Islam E, Mulkey Z, Nugent K. Anti-N-methyl-D-aspartate receptor encephalitis. Am J Med Sci. 2013;345(6):491-493.

105 Titulaer MJ, McCracken L, Gabilondo I, et al. Late-onset anti-NMDA receptor encephalitis. Neurology. 2013;81(12):1058-1063.

106 Kayser MS, Titulaer MJ, Gresa-Arribas N, Dalmau J. Frequency and characteristics of isolated psychiatric episodes in anti–N-methyl-d-aspartate receptor encephalitis. JAMA Neurol. 2013;70(9):1133-1139.

107 Baizabal-Carvallo JF, Stocco A, Muscal E, Jankovic J. The spectrum of movement disorders in children with anti-NMDA receptor encephalitis. Mov Disord. 2013;28(4):543-547.

108 Cassa RS, Rosengart AJ. A young man with altered mental status and new-onset seizures. JAAPA. 2013;26(10):34-37.

Table 1: Proposed classification of phenotypes in anti-NMDA receptor antibody encephalitis according to symptom severity[1]

	Seizures	Movement Disorder	Catatonia	Agitation/ Aggression	Bizarre Behaviors
Type 1: "Classic" (Patients 1,2)	Moderate	Moderate	Slight-Moderate	Moderate	Slight-Moderate
Type 2: "Psych" (Patients 3-5)	Slight	Slight-Moderate	Slight or Not present	**Severe**	**Severe**
Type 3: "Catatonic" (Patients 6-8)	Slight-Moderate	**Severe**	**Severe and/or Prolonged**	Slight-Mod	Slight or Not present

[1] Slight symptom severity defined as minimally present. Moderate symptom severity defined as present either some of the time and/or approximately 50% of the time. Severe symptom severity defined as present for most of the time. Prolonged symptom severity as referring to catatonia is defined as lasting for longer than 60 days.

Table 2: Cases of anti-NMDA receptor antibody encephalitis according to subtype with therapy, time to discharge, and outcomes

Lead Author	Journal,Year	No. patients[a]	Ages[b]	Therapies[c]	Days until discharge[d]	Outcome[e]
Lesher AP	*J Pediatr Surg*, 2010	1[f]	15	I	0.67 months	Asymptomatic 20 days after onset
Maqbool M	*J Child Neurol*, 2011	1	15	S,I	2.5 months	Unknown
Bseikri MR[g]	*Pediatr Infect Dis J*, 2012	1[f]	11	S,I	1.8 months	Asymptomatic at 1 year
Ishiura H	*Neurology*, 2008	1	42	S,P,R	5.3 months	Described as "recovered nearly fully"
Tan A	*J Clin Neurosci*, 2010	2	32,22	1) S,I; 2) S	1) 2 months; 2)1.25 months	1) Able to work at 9 months; 2) Asymptomatic at 5 months
Schmiedeskamp M	*N Z Med J*, 2010	2	17, 23	1)S,I,P,Pr; 2)S,I,P,Pr	1)1.75 months; 2)3.1 months	1) Asymptomatic at 6 months; 2)Mild residual deficits at 4 months

Mesquita J	*J Neuropsychiatr Clin Neurosci*, 2011	1	21	1)S,I	1.7 months	"Mild psychomotor retardation and memory deficits" at discharge
Kung DH	*Psychosomatics*, 2011	1	24	S,I,R	4 months	Unknown
Uchino A	*Intern Med*, 2011	1[f]	21	S,I,P,Pr	2.6 months	Normal mental status exam and neurologic exam at 4 months
Yu AY	*Psychosomatics*, 2011	1[f]	29	E,S,P,R	6 months	Poor short-term memory and minimal abnormal movements at 3 months
Dean Z	*Pract Neurol*, 2012	1	23	S,P,Pr	2 months	Mild memory loss at 2 months
Perogamvros L	*Cogn Behav Neurol*, 2012	1[f]	22	P,I,Pr,A	5 months	Unknown
Shaaban HS	*Ann Saudi Med*, 2012	1	25	S,P	<2 months	Asymptomatic at 2 months

See AT	*J Obstet Gynaecol*, 2012	1[f]	31	S,P	2 months	"Capable of independent living" at 1 month
McCarthy A	*J Neurol*, 2012	1	32	S,P	3 months	"Much improved" at discharge, no other follow-up noted
Cantarin-Extremera V	*Pediatr Neurol*, 2013	1	8 months	S,I,Pr	0.7 months	"Stable" but requiring speech therapy for apraxia at 20 months
Sorita A	*Chest*, 2013	1[f]	35	S	2 months	"Nearly" asymptomatic at 1 year but unable to work because of memory issues
Hegarty CP	*Emerg Med Australas*, 2013	1	17	S, I	0.27 months	At 6 months, described as "functional," has some obsessive behaviors and insomnia
Leypoldt F	*Neurology*, 2013	1	24	S,Pr	0.67 months	At 4 months, symptoms "had improved," no other information given
Sonn TS	*J Pediatr Adolesc Gynecol*, 2010	1[f]	14	S,I,P,R	5 months	At 9 months, speaking in 3 word phrases and has notable chorea
Frechette ES	*Neurology*, 2011	1	18	S,I,R,C	12 months	At 21 months, able to speak but significant motor and psychiatric deficits

Day GS[h]	*J Gen Intern Med*, 2011	1	84	I,P	Patient died	Patient died
Alexopoulos H	*J Neurol*, 2011	1[f]	42	S,I	24 months	Patient had MI (thought to be unrelated) and died at a later date
Ikeguchi R	*Intern Med*, 2012	1	19	S,I,P,R,A	7.23 months	Unknown
Dabner M[i]	*Int J Gynecol Pathol*, 2012	1[f]	37	S,I,P	3.3 months	"Partial neurologic deficit" at discharge, no other information
Thomas A	*JAMA Neurol*, 2013	1[f]	30s[j]	S,I,P,R,C	Died after 25 months	Died after 25 months

[a] Only patients that fit the criteria were included for analysis, patients without enough information were not included in final count.
[b] Age in years unless otherwise stated.
[c] Please note that therapies are not given in order of administration and some patients had multiple courses. S-steroids, I-intravenous immunoglobulin, P-plasma exchange, Pr-oral prednisone, R-rituximab, C-cyclophosphamide, E-electroconvulsive therapy, A-azathioprine.
[d] Time to discharge given in months assuming a 30-day month and either extracted from reported time to discharge, estimated/extrapolated (if possible) based on reported timing and duration of symptoms and/or therapies, and rounded up to the nearest possible month if reported as "approximately" in the article or estimated to be approximate.
[e] Unless otherwise stated, duration is the amount of time following discharge.

[f] Denotes patient had a teratoma or other tumor that was removed.
[g] In this paper, only the second patient had sufficient enough information to classify.
[h] In this paper, only the second patient had sufficient enough information to classify.
[i] In this paper, only the second patient had sufficient enough information to classify.
[j] Specific age not given.