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Life-Threatening Bradycardia in Anti-NMDA-Receptor Encephalitis and a Novel Use for Permanent Pacing

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ABSTRACT

Background: Pediatric anti-NMDA receptor encephalitis (pNMDARE) is an autoantibody-mediated disorder that can cause severe autonomic dysfunction, including symptomatic bradycardia and asystole. Dysautonomia can last for years, making it very challenging to manage.

Objective: To describe outcomes of 5 pNMDARE patients with life-threatening bradycardic and/or asystolic events who were managed with permanent or semi-permanent pacemaker implantation.

Methods: We performed a retrospective chart review of 5 patients from multiple institutions. We included patients with a diagnosis of pNMDARE (confirmed by positive cerebrospinal fluid and/or serum anti-NMDAR antibodies) who had a permanent or semi-permanent pacemaker placed due to symptomatic bradycardia, sinus pauses, and/or asystole. Assessed outcomes included mortality, the presence of additional bradycardic/asystolic events after pacemaker implantation, pacemaker complications (lead/device infection, device malfunction), and the ongoing need for ventricular pacing.

Results: Four patients had permanent pacing systems placed, and one patient had a semi-permanent pacemaker placed. Three patients required continued intermittent ventricular pacing months to years after disease onset. None of the patients had further episodes of symptomatic bradycardia or asystole after pacemaker implantation. One patient, who had a severe, intractable form of pNMDARE, died after discontinuing immunotherapies; she had multiple pacemaker interrogations that demonstrated no sign of pacemaker dysfunction.

Conclusion: Permanent and semi-permanent pacemakers are a safe, effective management strategy for cases of pNMDARE with prolonged courses of severe bradycardia and/or asystole.

1 | Introduction

Anti-NMDA receptor encephalitis (NMDARE) is an autoantibody-mediated disorder classically characterized by seizures, movement disorders such as dystonia and chorea, psychosis with auditory and/or visual hallucinations and delusions, and autonomic instability [1]. Pediatric NMDARE (pNMDARE) often requires a long recovery period lasting months to years [2, 3]. pNMDARE represents the most common form of autoimmune encephalitis in the pediatric population, leaving many children with long-term neurodevelopmental sequelae even following recovery [3]. It is

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triggered by various known and unknown etiologies including ovarian teratoma and herpes simplex virus meningoencephalitis (HSV ME) [1, 4]. Treatment consists of symptomatic therapies (e.g., anti-seizure medications) as well as immune modulator therapy, typically starting with high-dose intravenous (IV) corticosteroids like methylprednisolone (IVMP) followed by IV immunoglobulin (IVIG) and rituximab to reduce the risk of potential relapse [5, 6], while plasma exchange (PLEX) is often initiated if symptoms are particularly severe or medically refractory [7]. Early diagnosis and treatment are generally regarded as protective against long-term negative neurocognitive sequelae.

A cardinal feature of pNMDARE is autonomic dysfunction. Prior reports suggest the onset of autonomic dysfunction may be days to months after initial symptom onset [8, 9]. Additionally, severe autonomic dysfunction is usually associated with poorer outcomes and longer recoveries [9, 10]. Patients may develop severe, symptomatic bradycardia, in some cases resulting in asystole. The etiology of bradycardia in pNMDARE is thought to be multifactorial. These patients often have high vagal tone from parasympathetic overstimulation, which can cause bradycardia [11, 12]. In some instances, the bradycardia in pNMDARE can be attributed to seizure activity: seizures can activate regions of the telencephalon involved in the regulation of the sympathetic and parasympathetic neurons of the heart. This can result in a "lockstep" phenomenon in which the cardiac autonomic discharges synchronize with epileptogenic activity, resulting in profound bradycardia or asystole [11, 13, 14]. Several studies have also described episodes of profound sinus bradycardia in pNMDARE that were not triggered by vagal stimuli or seizures, indicating the etiology of bradycardia is multifactorial and not fully understood [11, 13].

The dysautonomia in pNMDARE may last anywhere from weeks to years, making it even more challenging to manage [11, 15]. The first line therapy for managing symptomatic bradycardia is pharmacological management with medications such as atropine, isoproterenol, or epinephrine [16]. These agents are typically limited to the intensive care unit and are therefore an inadequate solution for long-lasting bradycardia. A study conducted by Nazif et al. described 6 cases of NMDARE with symptomatic sinus bradycardia, 3 of whom were treated with temporary pacing [12]. The patients were all eventually able to wean from pacing, leading the authors to conclude that permanent pacing is unnecessary in this population [12]. In contrast, we present 5 cases of pNMDARE with prolonged courses of severe dysautonomia resulting in life-threatening bradycardic and/or asystolic events requiring semi-permanent or permanent pacemaker placement.

2 | Methods

This is a multicenter retrospective case series of 5 patients with pNMDARE who required permanent or temporary-permanent pacemaker placement due to severe bradycardia. Diagnosis was based on the combination of clinical criteria and the presence of positive cerebrospinal fluid (CSF) anti-NMDAR antibodies. We collected demographic data including patient age at presentation and sex. Clinical data included relevant past medical history, serum and CSF labs including anti-NMDAR antibody results, all imaging and electrodiagnostic workups, and hospital course. Assessed outcomes included mortality, the presence of additional bradycardic/asystolic events after pacemaker implantation, pacemaker complications (lead/device infection, device malfunction), and ongoing need for ventricular pacing.

Symptomatic bradycardia was defined as a heart rate below the lower limit of normal for age with signs of hemodynamic instability or symptoms of poor cardiac output (presyncope, syncope). Sinus pause was defined as >3 s between QRS complexes. Asystole was defined as absence of electrical activity for >6 s.

3 | Results

3.1 | Patient 1

A previously healthy 18-year-old male presented with altered mental status, twitching movements of the mouth, and manic behavior. His CSF and serum studies returned positive for anti-NMDAR antibodies (CSF titer 1:320, serum titer 1:640), confirming the diagnosis of pNMDARE. He was treated with IVMP, IVIG, PLEX, and rituximab, followed later by tocilizumab due to lack of clinical improvement with first- and second-line agents. His clinical course was complicated by seizures and several bacterial infections.

He developed severe autonomic dysfunction with paroxysmal sympathetic hyperactivity and was intubated for airway protection due to altered mentation. He developed sinus bradycardia and had several episodes of sinus pauses/asystolic events lasting up to 6 s, until several weeks into his admission he experienced asystole lasting 30 s and requiring CPR with return of spontaneous circulation (ROSC).

Due to his prolonged hospital course with severe bradycardia and asystole, the decision was made to proceed with pacemaker placement. However, in the setting of recent treatment of MSSA bacteremia, concern persisted regarding transvenous pacemaker placement due to the risk of lead infection. Based on its lower infectious risk profile, a permanent Medtronic Micra VR Leadless Pacemaker (LPM) was placed to prevent further episodes of bradycardic arrest. After 48 h of negative blood cultures, the LPM was placed in his right ventricular septum without complication.

Four days after pacemaker placement, he developed bacteremia with *Staphylococcus hemolyticus*. There was initial concern that the LPM was the source of infection. However, an F-fluorodeoxyglucose positron emission tomography–CT scan showed no sign of infection around the pacemaker and identified a popliteal thrombophlebitis as the source of infection. After treatment with appropriate antibiotics, his blood cultures cleared and his LPM was never infected. He was ultimately discharged from the hospital and has been recovering steadily. His pacemaker checks showed stable parameters: 7.3% ventricular pacing 3 months after placement, and 5.1% ventricular pacing 2 years after placement at a lower rate limit of 50 beats per minute (BPM). He made considerable neurological recovery, although he continues to have language and cognitive deficits.

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3.2 | Patient 2

A 15-year-old previously healthy female presented with altered mental status, disinhibited behavior, and gait instability. Her CSF and serum studies were positive for anti-NMDAR antibodies (CSF titer 1:320, serum titer 1:2560), confirming the diagnosis of pNMDARE. Pelvic imaging revealed an ovarian teratoma as the etiology of pNMDARE. She was treated with resection of the teratoma, IVMP, IVIG, PLEX, intrathecal dexamethasone, and rituximab.

Three weeks into her hospital course, she developed autonomic instability with labile blood pressures, shallow breathing that required intubation, and bradycardia. Review of her telemetry revealed episodes of profound bradycardia with sinus pauses and junctional escape rhythms, including an episode of asystole lasting 45s (Figure 1) for which she received chest compressions resulting in ROSC. To prevent further episodes of bradycardia, she was treated with norepinephrine and isoproterenol for 2 weeks; though, following discontinuation of these medications, she experienced a second episode of asystole requiring chest compressions resulting in ROSC.

Given her ongoing autonomic instability with multiple episodes of asystole, failed attempt at weaning chronotropic medications, and prolonged hospital course, the decision was made to proceed with pacemaker placement. Due to her recent administration of steroids and rituximab, there was hesitation to place a transvenous pacing system for fear of developing lead infection. Thus, she underwent successful LPM implantation in the right ventricular septum, which was set at a lower rate limit of 60 BPM. Shortly thereafter, she was weaned off norepinephrine and isoproterenol, which allowed her care to progress so she could participate in physical therapy and transfer out of the ICU. Her pacemaker interrogations showed stable settings and 5.2% ventricular pacing 6 weeks after placement, and 5.4% ventricular pacing 6 months after placement at an adjusted lower rate limit of 50 BPM. Since LPM implantation, she has not had any more episodes of asystole. She has had reasonable neurological recovery over 12 months of follow-up appointments, although she continues to have language, neurocognitive, and motor deficits.

3.3 | Patient 3

A previously healthy 8-year-old female presented with 1 week of headaches, malaise, difficulty ambulating, dystonia, and chorea, and subsequently developed refractory status epilepticus requiring multiple anti-seizure medications. Serum and CSF studies were positive for anti-NMDAR antibodies, confirming the diagnosis of pNMDARE. She was admitted to intensive care for escalating seizure management and received immunotherapy with IVMP, IVIG, and PLEX. She initially exhibited labile blood pressures, and on hospital day 18, she developed symptomatic bradycardia to heart rates of 30 BPM with associated hypotension requiring epinephrine. Within minutes, she developed asystole, requiring chest compressions for 5 s while another dose of epinephrine was administered, after which her pulse and blood pressure improved. Three days later, she experienced another asystolic event. CPR was initiated, and she received 1 round of epinephrine with ROSC after 5 min. She continued to have multiple clinically significant episodes of bradycardia and hypotension.

Given her ongoing clinically significant episodes of bradycardia and asystole, she underwent transvenous single-chamber permanent pacemaker implantation into the right ventricle on hospital day 38, which was set to a lower rate limit of 50 BPM. She had no further clinically significant bradycardic episodes following implantation. Pacemaker interrogation 2 months after placement revealed 1.4% ventricular pacing at a lower rate limit of 50 BPM.

Unfortunately, she continued to exhibit debilitating movement disorders and seizures that were refractory to aggressive immunotherapy and antiepileptic treatments. She was ultimately discharged after 6 months of hospitalization with tracheostomy and gastrostomy tube dependence. Her pre-discharge pacemaker interrogation revealed a well-functioning implant with 3.1% ventricular pacing and no evidence of problems with pacemaker sensing or capture. At her last outpatient visit, the patient's family declined further immunotherapies and did not continue to refill her antiepileptic medications. They moved to another country where the patient died about 1 year after discharge of unknown mechanism.

3.4 | Patient 4

A previously healthy 16-year-old female presented with progressive headaches, confusion, memory impairment, dysarthria, emotional lability, and seizures. Both her serum and CSF were positive for anti-NMDAR antibodies, confirming the diagnosis of pNMDARE, which was associated with a left-sided ovarian

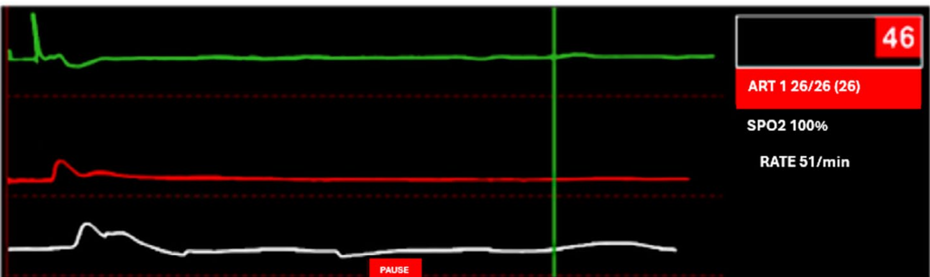

FIGURE 1 | Telemetry demonstrates asystole with resultant hypotension. The top tracing is the ECG tracing demonstrating a junctional escape beat at the start, followed by asystole; the middle tracing is the arterial line which shows no pulsatility and demonstrates a mean arterial pressure of 26; the bottom tracing is pulse oximetry, showing a flat waveform.

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teratoma seen on pelvic CT. She was treated with IVMP, IVIG, PLEX, rituximab, and teratoma resection.

Despite aggressive therapy, she had profound persistent dysautonomia. Cardiac monitoring demonstrated fluctuations between sinus tachycardia and sinus bradycardia with junctional escape beats, and asystole lasting 6.1 s (Figure 2). Given the ongoing clinical instability and persistent symptomatic bradyarrhythmias despite aggressive therapy, a single lead permanent transvenous pacemaker was placed in the right ventricle on day 49 of illness and set to a lower rate limit of 40 BPM. After pacemaker placement, she had no further episodes of sinus pause or symptomatic bradycardia. She exhibited nearly full recovery within 6 months of her diagnosis, though she continued to have persistent mild memory impairment. Her pacemaker interrogations 8 months and 2 years after placement revealed no pacing required.

3.5 | Patient 5

A previously healthy 16-year-old female presented with headaches, visual hallucinations, psychosis, and facial dyskinesias. CSF studies confirmed the diagnosis of pNMDARE. Pelvic ultrasound showed no teratoma. She was treated with IVMP, IVIG, PLEX, and rituximab. Her clinical course was complicated by prolonged intubation requiring tracheostomy, aspiration pneumonia, and UTI.

Throughout her admission, she had persistent autonomic dysfunction with labile temperatures, blood pressure, and heart rate. She had multiple episodes of bradycardia to around 30 BPM and an episode of asystole lasting 10 s. On day 37 of illness, she developed asystole requiring 20 s of chest compression resulting in ROSC. The next day, she had another asystolic event lasting 2 min requiring chest compressions and epinephrine which again resulted in ROSC. To prevent further sinus pauses, a single-lead temporary-permanent transvenous pacemaker was placed in the right ventricle with the lead externalized from the neck and attached to an external pacemaker generator with a lower rate limit of 60 BPM. Six weeks after the pacemaker was placed, her pacemaker interrogation revealed no additional pacing required, and the temporary-permanent pacemaker was removed. She did not have any additional bradycardic arrests, and on follow-up had full neurologic recovery. See Table 1 for a summary of the cases.

4 | Discussion

One of the most challenging clinical features of pNMDARE to manage is autonomic dysfunction. The duration of dysautonomia is highly variable, lasting anywhere from weeks to years [8, 10]. It is difficult to predict how long it will last, and it can result in serious morbidity and mortality if inadequately treated. While the reported incidence of dysautonomia varies greatly from 27%–69% in the literature, studies generally arrive at the same conclusion regarding the multitude of autonomic phenomena by which it manifests [17–21]. A retrospective case series including 119 patients with NMDARE in China reported sinus tachycardia as the most common manifestation of dysautonomia [18] while another described general "cardiac autonomic dysfunction" as the most common type of autonomic dysfunction among their 132 cases of children and adults with NMDARE [19]. Corroborating other sympathomimetic findings in pNMDARE, our group leveraged the idea that autonomic dysfunction may be an early cardinal sign of pNMDARE to differentiate it from non-pNMDARE mimickers by using elevated relative systolic and diastolic blood pressure early in the disease course [20].

Higher CSF anti-NMDAR antibody titer and the presence of an ovarian teratoma are potential risk factors for the development of autonomic dysfunction [19], and indeed 2/5 cases we presented were associated with an ovarian teratoma. However, it is notable that bradycardia is a less frequent manifestation of autonomic dysfunction in NMDARE, with a recent study reporting 7.1% of their children with pNMDARE experienced sinus bradycardia [21]. Our study highlights the need for neurologists to be prepared for the possibility of their patients with NMDARE requiring escalating cardiac care due to bradycardia and sinus pauses in collaboration with their cardiology colleagues.

The bradycardia seen in these patients can be very challenging to manage. While chronotropic agents such as atropine, epinephrine, and isoproterenol are a useful first step in managing symptomatic bradycardia, they typically require central access and ICU status for administration and are therefore not an ideal solution for many pNMDARE patients with prolonged symptomatology [16]. Temporary pacing is an alternative therapy for hemodynamically unstable bradycardic events in those who fail medical management and has been utilized in some cases of NMDARE, as reported by Nazif et al. However, it is also a temporizing measure limited by similar constraints as medications, often requiring ICU status and limiting mobility [12]. Temporary pacing devices are designed to be used for 1–6 weeks, limiting their usefulness in patients with

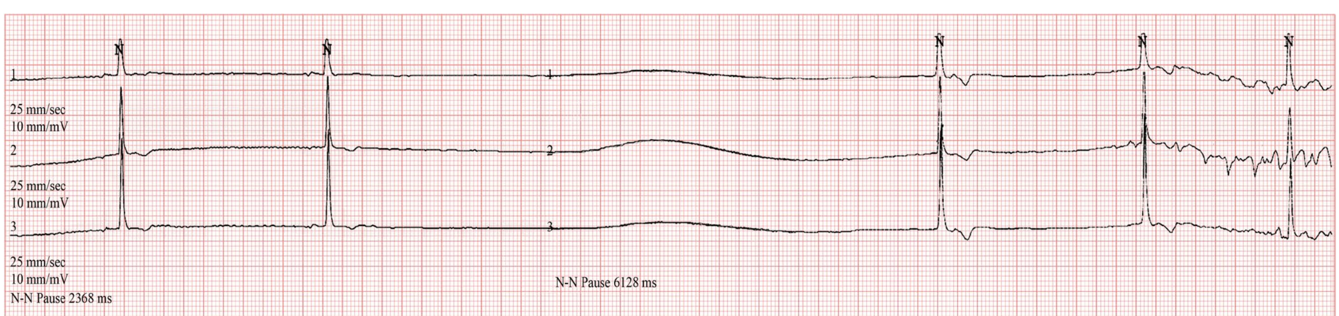

FIGURE 2 | Holter monitor demonstrates two beats of bradycardia followed by a 6.1 s pause followed by a junctional escape rhythm.

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TABLE 1 | Summary of Patients.

Patient	Age (yrs)/ Sex/Etiology	pNMDARE treatment	Indication for pacing	Type of pacemaker	Duration of pacing requirement	Pacemaker complications
1	18/M/idiopathic	IVMP, IVIG, rituximab, tocilizumab	Symptomatic bradycardia, 30-s asystole requiring compressions	Leadless pacemaker (permanent)	5.1% ventricular pacing for 2 years at a lower rate limit of 50 BPM	None. LPM did not become infected despite *S. hemolyticus* thrombophlebitis with bacteremia
2	15/F/teratoma	IVMP, IVIG, PLEX, IT dexamethasone, rituximab, teratoma resection	Symptomatic bradycardia, 45-s asystole requiring compressions	Leadless pacemaker (permanent)	5.4% ventricular pacing for 6 months at a lower rate limit of 50 BPM	None
3	8/F/idiopathic	IVMP, IVIG, PLEX, rituximab, cyclophosphamide, tocilizumab	Symptomatic bradycardia, two asystolic episodes requiring compressions and epinephrine	Transvenous RV permanent pacemaker	3.1% ventricular pacing at 6-month interrogation at lower rate limit of 50 BPM	None. Patient died in the outpatient setting of unknown cause without evidence of pacemaker dysfunction.
4	16/F/teratoma	IVMP, IVIG, PLEX, rituximab, teratoma resection	Symptomatic bradycardia, sinus pause of 6 s	Transvenous RV permanent pacemaker	No ventricular pacing required after 8 months	None
5	16/F/idiopathic	IVMP, IVIG, PLEX, rituximab, ECT	Symptomatic bradycardia, 20-s asystole requiring compressions	Transvenous RV temporary-permanent pacemaker	Pacemaker removed after 6 weeks, no further episodes of asystole	None

Abbreviations: BPM, beats per minute; ECT, electroconvulsive therapy; IT, intrathecal; IVIG, intravenous immunoglobulin; IVMP, intravenous methylprednisolone; LPM, leadless pacemaker; PLEX, plasma exchange; RV, right ventricle.

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months or years of symptomatic bradycardia. Permanent pacemakers are indicated in patients with symptomatic bradycardia without a reversible cause [22]. The decision of whether to use a temporary or permanent pacing system can be difficult, especially in pNMDARE, as there is little data on pacing in this population, so decisions are based on clinicians' judgment of individual cases. In many of the cases presented in this paper, patients exhibited symptomatic bradycardia for weeks to months prior to pacemaker placement, so it was felt that temporary pacing systems would not provide long enough durability to support these patients through their illness. Additionally, in some cases, the bradycardia was the only thing keeping patients in the ICU, so permanent pacemakers were placed to allow for progression of patient care and promote participation in therapies and transferring to floor status. On follow-up, several of the patients presented continued to require intermittent pacing for years, meaning their heart rates dropped below the pacemaker's programmed backup rate, which could be due to ongoing sinus pauses or resting bradycardia.

Several types of permanent pacemakers exist, each with unique risks and benefits. Transvenous pacemakers are the most commonly used, in which the leads travel through systemic veins and are actively fixed to the myocardium and connect to a pacemaker implanted in the chest wall. These systems provide a long-lasting source of pacing and can be a useful option in pNMDARE. However, they are associated with the risk of thromboembolism and infection. This was a particular concern in Patient 1, who recently had MSSA bacteremia and was thought to be high risk for lead or pocket infection, and Patient 2, in whom the immunosuppression was felt to raise the risk of pacemaker infection. For this reason, LPMs were elected in these cases. LPMs are small devices implanted directly into the right ventricular wall to provide pacing and do not rely on leads. They have a very low incidence of device-related infection due to their small surface area, absence of subcutaneous pocket, tendency for encapsulation by the myocardium, and parylene coating [23, 24]. There are only rare reports of bacteremia or endocarditis after LPM implantation, which resolved after antibiotic treatment [25]. Transvenous pacemakers can be removed relatively safely within 1 year of deployment, though it requires an additional procedure to do so. It is possible to extract permanent systems after 1 year, but the procedure becomes more complex due to increased adhesions around the leads. The evidence surrounding LPM extraction is evolving. A recent study showed an 88% success rate in extracting LPMs with a complication rate of 4%, and there were devices extracted up to 7 years after implantation [26]. Nonetheless, patients and their families should be informed that they may be permanent fixtures within the heart.

Another type of pacing system is a “semipermanent” or temporary-permanent (“temp-perm”) pacemaker. In this system, the transvenous leads have an active fixation mechanism to attach to the myocardium (unlike in temporary transvenous pacing in which leads have a passive fixation mechanism) and connect to an external pacing source [27]. This setup provides a more stable source of pacing than traditional temporary passive transvenous pacing leads with a lower rate of dislodgement, and they provide a longer duration of pacing (in some cases, they have been used for up to 11 months) [28]. Patients receiving temporary-permanent pacing do not always require ICU admission, but institutional protocols vary. This can be a helpful tool for pNMDARE patients due to the longer duration of pacing provided compared to temporary pacing, but practitioners should be mindful of the coexistent infection risk that comes with this form of pacing.

TABLE 2 | Summary of Pacing Systems.

Pacing system	Duration of use	Considerations	Extraction
Temporary transvenous	1–6 weeks	• Often requires ICU status • Increased infection risk	Easily extracted
Temporary-permanent (“semi-permanent”)	Several months (up to 11 months has been reported)	• More stable pacing system than temporary transvenous • Increased infection risk	Easily extracted
Transvenous permanent	Indefinite	• More stable pacing system than temporary or temporary-permanent • Cannot be used in infants due to size • Increased infection risk, including device pocket infections • Placement is often deferred if central lines are present	Relatively easily extracted within 1 year of deployment, though requires an extra procedure. May be extracted later on though involves greater risk due to increased adhesions.
Leadless (permanent)	Indefinite	• Can be used in infants • Decreased infection risk compared to other pacing systems • Can be placed in patients who have a central line present	Evolving evidence around extractability. There are reported successful extractions though families should be counseled that they may become permanent fixtures.

Note: Table 2 summarizes the types of pacing systems discussed in this paper and important considerations regarding each. It is important to note that this is not an exhaustive list of the types of pacing systems available or all factors taken into consideration when selecting devices. Decisions regarding pacemaker placement are nuanced and require the expertise of electrophysiologists in keeping with their own specific procedural skill set.

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To our knowledge, this is the first case series reporting the use of permanent pacing in pNMDARE. Table 2 provides a summary of the different pacing systems discussed in this paper and important considerations regarding each type. It is important to note that this is not an exhaustive list of the types of pacing systems available or all factors taken into consideration when selecting devices. Decisions regarding pacemaker placement are nuanced and require the expertise of electrophysiologists in keeping with their own specific procedural skill set.

5 | Limitations

The main limitation of this case series is the small sample size and lack of a control group, which limits the generalizability of our results. Another limitation is that in the presence of a pacemaker, we cannot determine how long these patients continued to have dysautonomia resulting in sinus pauses or asystole. These patients continued to require pacing for low heart rates, but this could be due to sinus pauses that the pacemaker is supporting them through versus normal resting bradycardia.

6 | Conclusion

pNMDARE can cause dysautonomia resulting in life-threatening bradycardic and/or asystolic events that require intervention. Dysautonomia can last anywhere from weeks to years, making it very difficult to treat. A previous study described the use of temporary pacing in NMDARE and concluded that permanent pacing is not indicated [12]. This is the first study that describes the need for permanent and semi-permanent pacing in pNMDARE due to persistent dysautonomia lasting longer than temporary pacing can provide. Transvenous permanent pacemakers are a useful tool in this population. LPMs, with their lower risk of infection, should also be considered in this population due to their immunosuppressed state. Temporary-permanent pacemakers can also be considered due to their improved longevity compared to temporary transvenous pacing.

Author Contributions

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. J. Dalmau, A. J. Gleichman, E. G. Hughes, et al., "Anti-NMDA-Receptor Encephalitis: Case Series and Analysis of the Effects of Antibodies," *Lancet Neurology* 7 (2008): 1091–1098.

2. G. Gombolay, J. N. Brenton, J. H. Yang, et al., "Isolated Psychiatric Symptoms in Children With Anti-N-Methyl-d Aspartate Receptor Encephalitis," *Pediatric Neurology* 159 (2024): 12–15.

3. L. B. Loerinc, L. Blackwell, R. Howarth, and G. Gombolay, "Evaluation of the Anti-N-Methyl-D-Aspartate Receptor Encephalitis One-Year Functional Status Score in Predicting Functional Outcomes in Pediatric Patients With Anti-N-Methyl-D-Aspartate Receptor Encephalitis," *Pediatric Neurology* 124 (2021): 21–23.

4. T. Armangue, M. Spatola, A. Vlagea, et al., "Frequency, Symptoms, Risk Factors, and Outcomes of Autoimmune Encephalitis After Herpes Simplex Encephalitis: A Prospective Observational Study and Retrospective Analysis," *Lancet Neurology* 17 (2018): 760–772.

5. N. Seery, R. Wesselingh, P. Beech, et al., "Rituximab Use for Relapse Prevention in Anti-NMDAR Antibody-Mediated Encephalitis: A Multicenter Cohort Study," *Neurol Neuroimmunol Neuroinflamm* 12 (2025): e200395.

6. M. Nosadini, M. Eyre, E. Molteni, et al., "Use and Safety of Immunotherapeutic Management of N-Methyl-d-Aspartate Receptor Antibody Encephalitis: A Meta-Analysis," *JAMA Neurology* 78 (2021): 1333–1344.

7. M. Ellul and T. Solomon, "Acute Encephalitis - Diagnosis and Management," *Clinical Medicine (London, England)* 18 (2018): 155–159.

8. S. R. Irani, K. Bera, P. Waters, et al., "N-Methyl-D-Aspartate Antibody Encephalitis: Temporal Progression of Clinical and Paraclinical Observations in a Predominantly Non-Paraneoplastic Disorder of Both Sexes," *Brain* 133 (2010): 1655–1667.

9. J. Dalmau, T. Armangue, J. Planaguma, et al., "An Update on Anti-NMDA Receptor Encephalitis for Neurologists and Psychiatrists: Mechanisms and Models," *Lancet Neurology* 18 (2019): 1045–1057.

10. S. Syamlal, K. Patel, and S. Haridas, "NMDA Receptor Encephalitis With Significant Autonomic Instability and PRES Like MR Images," *Annals of Indian Academy of Neurology* 25 (2022): 1244–1245.

11. S. R. Mehr, R. C. Neeley, M. Wiley, and A. B. Kumar, "Profound Autonomic Instability Complicated by Multiple Episodes of Cardiac Asystole and Refractory Bradycardia in a Patient With Anti-NMDA Encephalitis," *Case Reports in Neurological Medicine* 2016 (2016): 7967526.

12. T. M. Nazif, J. Vazquez, L. S. Honig, and J. M. Dizon, "Anti-N-Methyl-D-Aspartate Receptor Encephalitis: An Emerging Cause of Centrally Mediated Sinus Node Dysfunction," *Europace* 14 (2012): 1188–1194.

13. B. Ziaeian and K. Shamsa, "Dazed, Confused, and Asystolic: Possible Signs of Anti-N-Methyl-D-Aspartate Receptor Encephalitis," *Texas Heart Institute Journal* 42 (2015): 175–177.

14. J. W. Britton and E. Benarroch, "Seizures and Syncope: Anatomic Basis and Diagnostic Considerations," *Clinical Autonomic Research* 16 (2006): 18–28.

15. M. J. Titulaer, L. McCracken, I. Gabilondo, et al., "Treatment and Prognostic Factors for Long-Term Outcome in Patients With Anti-NMDA Receptor Encephalitis: An Observational Cohort Study," *Lancet Neurology* 12 (2013): 157–165.

16. F. M. Kusumoto, M. H. Schoenfeld, C. Barrett, et al., "2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society," *Circulation* 140 (2019): e382–e482.

23289503, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/acn3.70280 by Duke University Libraries, Wiley Online Library on [05/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

17. J. I. Byun, S. T. Lee, J. Moon, et al., "Cardiac Sympathetic Dysfunction in Anti-NMDA Receptor Encephalitis," *Autonomic Neuroscience* 193 (2015): 142–146.

18. L. Yan, S. Zhang, X. Huang, Y. Tang, and J. Wu, "Clinical Study of Autonomic Dysfunction in Patients With Anti-NMDA Receptor Encephalitis," *Frontiers in Neurology* 12 (2021): 609750.

19. Z. Chen, Y. Zhang, X. Wu, H. Huang, W. Chen, and Y. Su, "Characteristics and Outcomes of Paroxysmal Sympathetic Hyperactivity in Anti-NMDAR Encephalitis," *Frontiers in Immunology* 13 (2022): 858450.

20. N. R. Kass, E. Ledbetter, T. A. Erickson, et al., "Pediatric N-Methyl-d-Aspartate Receptor Encephalitis Is Differentiated From Encephalitis Mimickers by Early Elevated Blood Pressure," *Pediatric Neurology* 172 (2025): 71–77.

21. D. Li, J. Sun, G. Li, S. Miao, J. Yang, and J. Zhang, "Clinical Features of Autonomic Dysfunction in Children With Anti-N-Methyl-D Aspartic Receptor Encephalitis," *Italian Journal of Pediatrics* 51 (2025): 5.

22. Writing Committee M, M. J. Silka, M. J. Shah, et al., "2021 PACES Expert Consensus Statement on the Indications and Management of Cardiovascular Implantable Electronic Devices in Pediatric Patients: Executive Summary," *Annals of Pediatric Cardiology* 15 (2022): 323–346.

23. P. Palmisano, S. Iacopino, S. De Vivo, et al., "Leadless Transcatheter Pacemaker: Indications, Implantation Technique and Peri-Procedural Patient Management in the Italian Clinical Practice," *International Journal of Cardiology* 365 (2022): 49–56.

24. M. F. El-Chami, M. Bonner, R. Holbrook, et al., "Leadless Pacemakers Reduce Risk of Device-Related Infection: Review of the Potential Mechanisms," *Heart Rhythm* 17 (2020): 1393–1397.

25. M. F. El-Chami, K. Soejima, J. P. Piccini, et al., "Incidence and Outcomes of Systemic Infections in Patients With Leadless Pacemakers: Data From the Micra IDE Study," *Pacing and Clinical Electrophysiology* 42 (2019): 1105–1110.

26. P. Neuzil, D. V. Exner, R. E. Knops, et al., "Worldwide Chronic Retrieval Experience of Helix-Fixation Leadless Cardiac Pacemakers," *Journal of the American College of Cardiology* 85 (2025): 1111–1120.

27. A. A. Sovari, P. Zarghamravanbakhsh, and M. Shehata, "Temporary Cardiac Pacing," *Cardiac Intensive Care* (2019): 456–460.

28. K. Suarez and J. E. Banchs, "A Review of Temporary Permanent Pacemakers and a Comparison With Conventional Temporary Pacemakers," *Journal of Innovations in Cardiac Rhythm Management* 10 (2019): 3652–3661.

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