CASE REPORT

Adjunctive vagus nerve stimulation for treatment-resistant bipolar disorder: managing device failure or the end of battery life

José V Pardo^{1,2}

¹Department of Psychiatry, University of Minnesota, Minneapolis, Minnesota, USA
²Minneapolis Veterans Health Care System, Minneapolis, Minnesota, USA

Correspondence to
 Professor José V Pardo,
 jvpardo@umn.edu

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SUMMARY

The vagus nerve stimulation (VNS) device is used not only to treat refractory seizure disorders but also mood disorders; the latter indication received CE Mark approval in 2001 and Food and Drug Administration approval in 2005. Original estimates for the end of battery life (EOBL) were approximately 6–10 years. Many neuropsychiatric patients have or will soon face EOBL. A patient with severe, life-threatening, treatment-resistant bipolar disorder underwent 9 years of stable remission following 20 months of adjunctive VNS. The device ceased operation at EOBL. Because of logistical issues, re-initiation of VNS was delayed over several months. The patient relapsed with depression, mania and mixed states, and regained remission 17 months after device replacement. This case dictates prudence in managing stable patients in remission with VNS. If the device malfunctions, urgent surgical replacement is warranted with subsequent rapid titration to previous parameters as tolerated. Several months' delay may trigger relapse and prove difficult to re-establish remission.

BACKGROUND

Various estimates indicate that treatment-resistant mood disorders are relatively common, occurring in 20–30% of neuropsychiatric practices. A critical need is the development of treatment approaches for this group of patients that are frequently disabled—not to mention the high rates of suicide and high healthcare costs. Adjunctive vagus nerve stimulation (VNS) is indicated for treatment-resistant major depression or bipolar disorder, when either the patient cannot tolerate conventional treatments, or when unresponsive to medications or convulsive seizure therapy. It has become clear that VNS can take a long time to improve mood (eg, 1 year or more^{1–2}). However, little is known about what happens to mood-disordered patients in remission who stop VNS treatment. No general guidelines exist on the clinical management when treatment with VNS stops, such as in end of battery life (EOBL).

CASE PRESENTATION

A middle-aged woman was followed in a neuropsychiatry clinic for about two decades. She provided written informed consent for publication of her case report without identifying information. She had a well-documented history of bipolar disorder beginning at age 24 years. She had been successful and well-adjusted before the onset of the

disease. After an initial manic episode, she cycled into recurrent episodes of severe depression, mania and transient mixed states. Numerous medications including combinations of antidepressants (selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, monamine reuptake inhibitors), stimulants, convulsive therapy, mood stabilisers and neuroleptics were tried with, at most, partial remission. Comorbid diagnoses were mixed substance abuse, pathological gambling and obesity. The patient showed some features of borderline personality disorder and had extensive dialectical behaviour therapy. Although bipolar disorder can be comorbid with borderline personality disorder,^{3–5} her good functioning as a young adult argued against this diagnosis. She had multiple suicide attempts. She underwent many months of residential treatment under commitment to ensure safety. In 2005, she was implanted with a VNS device (Model 102, Cyberonics, Houston, Texas, USA). Because of reports that the effects of VNS may take many months with brain metabolic changes evolving even beyond 1 year,^{1–2} she was advised that major antidepressant effects from VNS might take 1 to 2 years. She would need to continue intensive psychiatric management. Her device was programmed over several months, according to manufacturer guidelines, to the final settings of 2.5 mA (milliamperes); frequency 20 Hz; pulse width 500 µs; 30 s on; 5 min off. Her depression remitted stably approximately 20 months after implantation while taking aripiprazole, topiramate, temazepam and trazodone. After 9 years of successful therapy with depression in remission and during a routine office visit, her device initially responded, but then ceased to interrogate, altogether failing communication with the programming wand. She had reported feeling stimulation 6 months earlier but had paid no attention as to whether a change in stimulation had occurred since that time. Re-implantation (Model 105 Aspire, Cyberonics, Houston, Texas, USA) occurred 6 weeks after EOBL, but stimulation (same parameters except current at 0.75 mA) was not begun until 3 months after EOBL. Two months later, she reported increased anxiety while on 0.75 mA. Thereafter, the current was increased 0.25 mA every 2–4 weeks to her previous settings while in remission. The patient reported relapsing during these weeks with Patient Health Questionnaire (PHQ-9⁶) depression score increasing to 12. A selegiline patch was followed by nardil. She remitted

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transiently 4 months later (PHQ-9=2), but affective instability required additional medication adjustments. She subsequently developed depression, mania and mixed states. She returned to a stable remission 17 months after device replacement.

DISCUSSION

VNS is used not only to treat mood disorders such as bipolar depression but also to treat refractory seizure disorders; more is known about outcomes on VNS cessation in epilepsy. There are several case reports describing outcomes of seizure patients who either (1) intentionally stop VNS or (2) have device malfunctions; or when (3) EOBL occurs. Vonck *et al*⁷ reported 14/76 of their patients treated with VNS primarily for epilepsy experienced end of effective stimulation (EOES, end of service; wand identifies near EOBL) or frank EOBL. Seven of these patients also showed loss of seizure control (N=3), decreased perception of stimulation (N=3) and recurrence of depression (N=1). Two of the three patients with loss of seizure control whose replacement was delayed by several months did not regain seizure control compared to before EOES or EOBL. Tatum *et al*⁸ reported two-thirds of epilepsy patients had similar changes in symptoms heralding estimated end of service. Waseem *et al*⁹ reported VNS device failure from broken leads most commonly increased seizure frequency. Eight of 10 seizure patients undergoing lead revisions because of device failure felt a return of their response similar to that before lead failure. Dlouhy *et al*¹⁰ described 15/16 patients undergoing lead revisions followed for 3 months who returned to the previous level of seizure control.

Less has been reported on outcomes in affective illness. To the best of our knowledge, there are two case reports of VNS device failure in treatment-resistant depression (TRD) and no previous reports of VNS failure in the treatment of bipolar disorder. Martinez and Zboyan¹¹ presented a case of a patient with TRD who showed significant improvement in depression for 3.5 years, only to later get much worse depression symptoms; the patient noted the absence of stimulation and EOBL had occurred. Restarting VNS therapy produced a fluctuating course similar to that during long-term follow-up. Conway *et al*¹² described the case of a patient with TRD treated with VNS who remitted after 1 year. After 42 months of VNS treatment, the device could not be interrogated and showed high impedance consistent with a broken lead; the battery check was normal. After 3–4 months, the patient relapsed. The lead was replaced, VNS reinitiated and the patient responded quickly with complete remission 1 month later.

The case presented teaches that stable patients in remission with VNS should be seen regularly (3–4 months) to avoid any possibility of EOBL. Newer VNS models show an icon displaying remaining battery life during interrogation. If device failure occurs, surgical replacement should proceed expeditiously. After 1–2 weeks for healing, the programming parameters should be aggressively titrated to previous levels as tolerated.

Learning points

- ▶ Vagus nerve stimulation (VNS) device failures warrant urgent replacement and expedited reprogramming as tolerated to previously successful parameters.
- ▶ Stopping VNS can result in a serious affective relapse within a couple of months.
- ▶ Re-establishing remission may prove difficult after stopping VNS, resulting in recurrence of serious affective symptoms.

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