Vagal nerve stimulator infection: a lead-salvage protocol

Clinical article

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Object. Vagal nerve stimulator (VNS) hardware infections are fraught with difficult management decisions. As with most implanted medical device–related infections, standard practice traditionally involves complete hardware removal, systemic antibiotic therapy, and subsequent reimplantation of the device. To avoid the potential morbidity of 2 repeat left carotid sheath surgical dissections, the authors have implemented a clinical protocol for managing VNS infections that involves generator removal and antibiotic therapy without lead removal.

Methods. A prospective, single-surgeon database was compared with hospital billing records to identify patients who underwent primary implantation or reimplantation of a VNS lead, generator, or both, from January 2001 to May 2010, at Oregon Health & Science University. From these records, the authors identified patients with VNS hardware infections and characterized their management, using a lead salvage protocol.

Results. In their review, the authors found a matching cohort of 206 children (age 3 months–17 years) who met the inclusion criteria. These children underwent 258 operations (including, in some children, multiple operations for generator end of life and/or lead malfunction). Six children experienced a single postimplantation infection (2.3% of the 258 operative cases), and no child experienced repeated infection. A lead-salvage protocol was used in 4 of 6 infected patients and was successful in 3 (75%), with clinical follow-up ranging from 10 months to 7.5 years. The fourth patient subsequently underwent lead removal and later reimplantation in standard fashion, with no adverse sequelae.

Conclusions. Vagal nerve stimulator lead salvage is a safe and potentially advantageous strategy in the management of VNS-related infection. Further study is necessary to validate appropriate patient selection, success rates, and risks of this approach. (DOI: 10.3171/2011.4.PEDS10556)

Key Words • vagal nerve stimulation • infection • surgical complication • treatment • functional neurosurgery

Since 1997, vagal nerve stimulation has been widely used to treat medically intractable seizures. Long-term VNS benefits may include reduction in seizure frequency, duration, and postictal period. Most clinical side effects, including localized irritation, hoarseness, torticollis, and dysesthesias, may be tolerated and often disappear or improve with time.

The infection of VNS hardware, however, requires additional surgical intervention and may result in treatment failure. As with many surgical device–related infections, standard treatment consists of complete hardware removal and systemic antibiotic therapy prior to device reimplantation. Infection is the most common serious complication following VNS implantation or revision, with an incidence of 3%–8%.

To preserve functioning VNS leads despite VNS generator pocket infection, the senior author (N.R.S.) has developed a protocol for generator removal, systemic antibiotic therapy, and generator replacements that does not require cervical lead exposure or manipulation. Implementing this protocol was successful in 3 of 4 patients in whom clinical follow-up ranged from 10 months to 7.5 years.

Methods

We undertook a retrospective review of pediatric patients in whom a single surgeon (N.R.S.) implanted VNS devices (primarily or secondarily) between January 2001 and May 2010 at a pediatric tertiary referral institution. The Oregon Health & Science University institutional review board approved the study. Following institutional review board approval, we
compared information from a prospectively collected database of all children (age < 18 years) undergoing VNS surgery with hospital billing records obtained by searching by surgeon and procedure. Generator replacements were conducted exclusively in cases of end of generator life or anticipated end of generator life, and leads were replaced for malfunction (diagnosed by the referring neurologist and confirmed using system interrogation and radiographs). A small number of cases involving an elective procedure for total device removal indicated by poor clinical response were excluded from analysis (because no hardware was left in place during these procedures). All procedures were carried out in patients for the treatment of medially refractory epilepsy, none for the treatment of depression or for other indications. Information collected included sex, age, medical history, presenting symptoms, allergies, bacterial culture results, surgical treatment, comorbidities, interval from the index surgery to presentation with infection, and antibiotic type and length and route of administration.

All surgeries, including lead salvage, were performed after induction of general anesthesia. The lead-salvage protocol consisted of the following: neck and chest VNS incisions were prepared and steriley draped in a single field. Intraoperative antibiotic therapy was delayed until after culture collection. The existing chest pocket generator incision was opened sharply and the generator pocket exposed. Culture swabs were sent for aerobic and anaerobic organisms. The generator was mobilized and then disconnected from the lead using a screwdriver (Cybernics). The generator pocket and exposed lead were then pulse irrigated (Stryker) with 1–2 L of bacitracin containing sterile saline. Bovie cautery was then used to create a small extension of the generator pocket medially, toward the sternum. The exposed lead was tucked into this area of fresh dissection, and the border between this small area and the preexisting generator pocket was closed with a single absorbable stitch, to keep the lead terminus from migrating back into the larger pocket. The lead tract was inspected at its entry into the generator pocket to ensure that no purulent material was tracking along the lead from the neck. After a small amount of additional pulse irrigation, the generator pocket was closed in layers with absorbable suture and a sterile dressing applied.

After generator removal, a course of tailored intravenous antibiotic therapy was given for 3–4 weeks via a peripherally inserted central catheter line in consultation with a pediatric infectious disease specialist. At least an additional 4 weeks were allowed to elapse after the cessation of antibiotic therapy before generator reimplantation using standard techniques was used.

**Results**

Both of the search methods that we used resulted in an identical list of 206 patients who underwent 258 procedures, including primary implantation of VNS lead and generator, or replacement of generator, lead, or both. Six procedures (6 individual patients: 2.3% of procedures and 2.9% of patients treated) were complicated by infection. All patients had postsurgical follow-up, typically at 2 weeks and 3 months after each procedure, as well as frequent follow-up with their referring pediatric neurologist.

One patient who suffered an infection after generator change for battery end of life additionally had a tracheostomy and bilateral phrenic nerve pacemakers in place. Based on written and verbal report from other physicians, we determined that this patient presented 3 weeks after surgery in another state with clinical signs of infection of the generator pocket only. Although generator removal was recommended, the physicians attempted to salvage the entire VNS using systemic antibiotic therapy only. This patient then presented to our center 11 weeks postsurgery with clinical signs of generator pocket and cervical infection. The entire VNS system was surgically explanted, and the patient was treated with systemic antibiotics. Subsequently, the entire system was successfully reimplanted (Table 1). A second patient with VNS system infection presented to our center but was treated by another surgeon with total VNS system removal.

Lead salvage was attempted in the remaining 4 cases. Three cases involved primary VNS implantation and 1 case involved generator change for end of battery life only. In each of these 4 cases, clinical evidence of infection on physical examination was limited to the generator pocket only, which is a requirement for our lead-salvage protocol. In each case the generator pocket was boggy, and gross purulence was identified within the pocket itself at surgery.

Lead salvage was successful in 3 of the 4 patients in whom it was attempted (75% success rate) (Table 1). In one patient (Case 5) lead salvage failed. In this patient, clinical signs of infection returned after generator removal, 6 weeks after the cessation of systemic antibiotic therapy. At that time, the VNS lead was surgically explanted, a further course of systemic antibiotics was administered, and a new VNS system was successfully reimplanted 8 weeks later.

The time from implantation to diagnosis of infection ranged from 1–8 weeks. Initial wound presentation generally included erythema, warmth, fluid build-up, and tenderness. Accompanying symptoms included fever in 3 patients, one of whom (Case 3) also had an elevated peripheral WBC count. Lead salvage was successful in 2 of 3 patients with these additional clinical signs, including the patient with both fever and an elevated WBC count. Both C-reactive protein and erythrocyte sedimentation rate were followed in 3 of 4 patients in whom lead salvage was attempted. Both parameters normalized before generator reimplantation in each patient, as did WBC count. No additional signs or symptoms of systemic infection were identified in any patient.

Cultures collected at surgery revealed Staphylococcus aureus in 2 patients, a combination of S. aureus and Proteus mirabilis in 1 patient, and a rare strain of Strep-tococcus viridans in 1 patient. No patient undergoing attempted lead salvage had any known local or systemic comorbidity that would have predisposed him or her to infection (such as immune suppression, diabetes, or the presence of a tracheostomy).

In Cases 1 and 3 (infected with S. aureus), a 4-week intravenous vancomycin regimen was used after the salvage procedure. In both of these patients lead salvage was
TABLE 1: Salvage therapy results in VNS patients presenting with infection*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Seizure Type</th>
<th>Initial Op</th>
<th>Initial Chest Wound Presentation</th>
<th>Associated Presenting Symptoms</th>
<th>Wks to Infection Presentation</th>
<th>Isolated Organism</th>
<th>Antibiotic &amp; Treatment Duration</th>
<th>Lead Salvage</th>
<th>FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7, M</td>
<td>Lennox-Gastaut</td>
<td>primary VNS placement</td>
<td>fluctuance &amp; warmth</td>
<td>none</td>
<td>2</td>
<td>MSSA</td>
<td>vancomycin,† 28 days</td>
<td>successful</td>
<td>7.5 yrs</td>
</tr>
<tr>
<td>2</td>
<td>11, M</td>
<td>primary generalized epilepsy</td>
<td>primary VNS placement</td>
<td>erythema, edema, tenderness</td>
<td>none</td>
<td>2</td>
<td>MSSA</td>
<td>NA</td>
<td>not attempted (primary surgeon not available)</td>
<td>NA</td>
</tr>
<tr>
<td>3</td>
<td>2.5, M</td>
<td>primary generalized epilepsy</td>
<td>primary VNS placement</td>
<td>erythema, fluctuance, tenderness</td>
<td>fever, WBC count 26.5 K/mm$^3$‡</td>
<td>1</td>
<td>MSSA</td>
<td>vancomycin, 200 mg (17.5 mg/kg) every 8 hrs, 28 days</td>
<td>successful</td>
<td>5.5 yrs</td>
</tr>
<tr>
<td>4</td>
<td>14, F</td>
<td>primary generalized epilepsy</td>
<td>end-of-life generator replacement</td>
<td>erythema, edema of both generator &amp; cervical incisions</td>
<td>none</td>
<td>3</td>
<td>MRSA</td>
<td>NA</td>
<td>not attempted (presented w/ cervical purulence)</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>2, F</td>
<td>partial epilepsy w/ secondary generalization</td>
<td>primary VNS placement</td>
<td>erythema, edema</td>
<td>fever</td>
<td>8</td>
<td>MSSA &amp; P. mirabilis</td>
<td>IV cefazolin, 200 mg (17 mg/kg) every 8 hrs, 21 days</td>
<td>failure (subsequent total removal &amp; then reimplantation)</td>
<td>NA</td>
</tr>
<tr>
<td>6</td>
<td>13, M</td>
<td>primary generalized epilepsy</td>
<td>end-of-life generator replacement</td>
<td>erythema, tenderness</td>
<td>fever</td>
<td>8</td>
<td>S. viridens</td>
<td>IV cefazolin, 1 g (20 mg/kg) every 8 hrs, 28 days</td>
<td>successful</td>
<td>10 mos</td>
</tr>
</tbody>
</table>

* FU = follow-up; MRSA = methicillin-resistant S. aureus; MSSA = methicillin-sensitive S. aureus; NA = not applicable.
† Vancomycin dose unknown.
‡ Normal range 4.8–11.8 K/mm$^3$. 

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successful. The patient in Case 5 was infected with *S. aureus* and *P. mirabilis*, and a 3-week intravenous regimen of cefazolin was used. This treatment failed, and the leads ultimately had to be removed. The patient in Case 6 was found to have *S. viridans*. He was treated with 4 weeks of intravenous cefazolin, and lead salvage was successful. A pediatric infectious disease specialist was consulted in each case to establish appropriate antibiotic selection, dose, and treatment duration.

The 10 months–7.5 years of benign clinical follow-up since VNS reimplantation in the 3 successful lead-salvage protocol cases suggest that late recurrence of infection is very unlikely to occur.

We have not performed a formal cost analysis of lead salvage compared with total VNS hardware removal. However, the following principal differential charges apply: lead salvage entails an additional 2 weeks of home intravenous antibiotic therapy (4 weeks rather than 2) prior to VNS reimplantation (an additional charge of $1659). By contrast, total VNS hardware removal entails the additional charge for a new VNS lead kit ($10,783), for approximately 1 hour of additional operating time for redo neck dissection at the time of explantation and again at the time of reimplantation of the lead ($14,800), and for a 1-day hospital stay at the time of lead reimplantation ($5975). At our institution in 2010, these principal differential costs were thus notably higher for total VNS explantation and reimplantation than for lead salvage ($1659 for lead salvage vs $31,558 for total VNS hardware removal).

The minimum duration of VNS therapy interruption is also similar when using VNS lead salvage instead of total VNS hardware removal: 8 weeks for the former and 6 weeks for the latter (due to a 2-week-shorter interval of intravenous antibiotic therapy).

### Discussion

Few studies have described the management of deep chest pocket VNS infections. Patel and Edwards suggested complete VNS hardware removal because, in their case series and their review of the literature, total hardware explanation was required to completely eliminate the infection.

To our knowledge, only 2 individual case reports and 1 other case series have described techniques to preserve VNS hardware despite the presence of purulent infection. Ortler et al. described a single case in which they undertook debridement of an infected generator pocket, leaving the entire VNS system in place. In their case, the wound was then packed with 3% iodoform gauze and laved daily with 1.5% hydrogen peroxide for an extended period. Systemic antibiotics were also given during this lengthy hospitalization and VNS salvage was successful. Liechty and colleagues described a single case of generator pocket infection in which they used a surgically implanted sump antibiotic (vancomycin) irrigation system for 7 days. During this period, systemic vancomycin was also administered, and this was followed by a subsequent 7 days of outpatient oral antibiotics. In this single case, VNS salvage was also successful.

Air et al. reported a series of 10 patients with VNS infections, representing an infection rate of 5.2% in their series, with all infections initially clinically apparent at the generator site only. Using generator pocket needle aspiration and systemic antibiotics only, they attempted to salvage both the VNS lead and generator despite the presence of purulent infection in 7 cases. In 5 of these 7 patients in whom hardware salvage was attempted (71%), it failed, and the patients underwent hardware removal, sometimes after repeated intermittent courses of antibiotic therapy for as long as 16.5 months. In the 2 patients in whom hardware was not ultimately removed, the duration of postantibiotic therapy and clinical follow-up was not stated. Of note, in 1 case of ultimate hardware removal, the authors were not able to remove the lead tip coils due to extensive scar formation around the vagus nerve.

In contrast, the present study demonstrated successful lead salvage in 3 of 4 patients with purulent generator pocket infections. Although patients treated with our protocol do require surgical intervention for generator removal and subsequent replacement, they avoid the potential morbidity and scar formation associated with multiple carotid sheath dissections required for lead removal and replacement.

Of note in our series, 5 of 6 patients with VNS system infections presented with clinical signs of generator pocket infection only, consistent with the observations of Air et al. One of these patients (Case 4), however, was treated at another institution with systemic antibiotics, but that therapy failed, and the patient presented much later to our clinic with both chest and cervical incision purulence. Our observations suggest that the generator pocket is particularly at risk for perioperative infection and that early, aggressive, and combined surgical/medical management may obviate the need for lead removal in many cases.

Combined, the present series and that of Air et al. report an overall population of 15 patients, all of whom presented with clinical signs of infection in the generator pocket only. The reason for this predilection is not known but may involve the large size of the surgical pocket and/or the implanted hardware itself. Although the proximal end of the VNS lead is present in the generator pocket and is therefore contaminated, we have successfully cleared this contamination in 3 of 4 cases.

The principal rationale for lead salvage is to avoid 2 repeated dissections within the carotid sheath, which may promote the formation of additional scar tissue around the vagus nerve and result in the potential for neurovascular injury. Although it is relatively straightforward to dissect the involved segment of vagus nerve free by following existing VNS leads, exposure of a new segment of vagus nerve is often required at the time of lead reimplantation because hardware is not then in place to serve as a roadmap through dense scar tissue. Exposure of this additional segment may limit future options for replacement of a malfunctioning lead.

There are a number of possible explanations for the failure of our lead-salvage protocol in Case 5. First, it was the youngest patient in the series. Second, infection in this case was caused by the only gram-negative bacteria in our series, although it was sensitive to the antibi-
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Afonso used. Perhaps most important, this child received the shortest course of antibiotics of the 4 undergoing attempted lead salvage (3 weeks rather than 4 weeks) and at a lower dose than in the patient in Case 6 who also received cefazolin instead of vancomycin. Further study is clearly needed to elucidate factors critical to patient selection and optimal medical management for this lead-salvage protocol, in addition to more definitely establishing risks, overall success rates, and cost effectiveness.

Conclusions

In a small series, 75% of the patients with pediatric epilepsy successfully underwent therapy that involved a lead-salvage protocol to treat purulent VNS generator pocket infection. This approach appears to be safe and to offer potentially higher success rates than local or systemic antibiotic therapy alone, with potentially reduced cost. This protocol has the advantage of obviating the need for 2 carotid sheath dissections. However, further study is needed to validate this protocol and more carefully define appropriate treatment criteria and parameters of the associated systemic antibiotic therapy.

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Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: all authors. Critically revising the article: all authors. Statistical analysis: Wozniak. Study supervision: Selden.

References


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