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Microbial colonization of sacral nerve stimulators pseudo-capsule: A single institution experience

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Purpose: To evaluate the incidence and type of microbial colonization of the pseudo-capsule (PC) that forms around sacral nerve stimulators (SNS) and consequently the significance of surgical excision of this PC at time of SNS revision or removal.

Materials and Methods: A cohort of 31 patients who underwent SNS revision or removal from January 2018 to June 2021 were retrospectively reviewed. The baseline demographics, rate and type of PC microbial colonization and development of SNS insertion site infection were reported.

Results: A cohort of 31 patients who underwent "InterStim device (Medtronic)" revision or removal were included. The majority were females (93.5%). The most common indication for SNS insertion was refractory overactive bladder (67.7%). Nine patients (29.0%) underwent SNS revision due to malfunctional device, and 9 patients had SNS removal for the need of MRI procedures. Four patients (12.9%) had positive tissue culture growing Coryneform bacillus (50.0%), Cutibacterium acnes (25.0%) and Pseudomonas aeruginosa (25.0%).

Conclusions: PC colonization was uncommon at the time of SNS explant. However, more research is needed to better understand the role of PC-positive culture in increasing the risk of SNS device infections if strict adherence to sterile techniques is adopted.

Keywords: Capsules; Electric stimulation; Host microbial interactions; Implantable neurostimulators; Sacrum

INTRODUCTION

The application of neurostimulation has evolved over the past decades as a third line of management for refractory lower urinary tract dysfunction not responding to behavioral and pharmacological options [1]. Neurostimulation techniques for abnormal bladder function have evolved from the simple application of anogenital electrodes and transcutaneous electrical nerve stimulation to the more advanced implantable neurostimulation devices [2]. Sacral nerve stimulator (SNS) can treat fecal incontinence, detrusor overactivity, underactive bladder, and bladder pain with a proven efficacy in controlling the bothersome lower urinary tract symptoms [3-5]. The rechargeable and recharge-free "InterStim™ II device (Medtronic)" as well as the rechargeable "Axonics r-SNM System™ (Irvine)" are the currently available implantable pulse generators (IPGs) applied for SNS.

Despite the great benefits of SNS, the procedure is not without adverse effects including local site pain, leg pain, lead migration, and local site or device infection which, although rare with a very low risk of sepsis, mostly prompts device removal [3,6,7]. The mechanism of SNS device infec-

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tion can be understood based on the data available on similar implantable medical devices like cardiac pacemakers, prosthesis, and indwelling vascular catheters in which the lack of self-cleansing capacity leads to biofilm formation that forms the basis for microbial colonization in these devices [8,9]. Beside the general measures applied to minimize infections in prosthesis and indwelling medical devices [10,11], there is increased tendency among urologists to prophylactically resect the pseudo-capsule (PC) that forms around SNS during SNS explant [10]. The hypothesis is that this PC can be a rich environment for microbial colonization, which can theoretically increase the risk of implantation site infection during SNS revision. This PC is common with implantable medical devices due to inflammatory and fibrotic reactions to implanted foreign materials [12]. Neuro-prosthetics including SNS are more vulnerable to these fibrotic reactions. While this fibrotic capsule can impede electrical impulse propagation and induce damage to nearby structures which can eventually lead to neuro-prosthetics failure [13,14], its role in increasing infection rate in SNS is still unclear. We sought to evaluate the incidence and type of microbial colonization in PC among patients who underwent SNS explant at our institution.

Objective

The primary aim of this study is to evaluate the incidence of microbial colonization of the PC that forms around SNS and consequently the significance of surgical excision of this PC at time of SNS revision or removal. The Secondary aim is to correlate between PC colonization and re-implantation infection or post-removal surgical wound infection rates.

MATERIALS AND METHODS

Approval was obtained from the University of Cincinnati Institutional Review Board (approval number: 2018-3363). The authors also certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. Exemption from patient consent form was obtained from the University of Cincinnati Institutional Review Board since the study is just a retrospective review of medical records without any potential harm to the patients or sharing of any patient's personal information.

After approval by the Institutional Review Board at the University of Cincinnati, we started reviewing the charts of all patients who underwent SNS revision or removal at University of Cincinnati Hospitals in the period between January 2018 to June 2021. Prior to SNS revision, all patients received antibiotic prophylaxis in the form of cefazolin with dose adjusted to patient body weight and had the surgical site isolated with Ioban™ (3M) which is designed with continuous broad-spectrum antimicrobial activity in the drape adhesive where it can't be washed away. Also, all patients underwent subcutaneous pocket irrigation with a mixture of sterile water and Neomycin sulphate antibiotic prior to SNS insertion. The device PC was excised and tested. All tissue specimens were tested for gram stain and tissue culture, including aerobic, anaerobic, and fungal cultures. Patients with active acute infection were excluded from our study. Demographic information and baseline characteristics including age, sex, body mass index (BMI), smoking status, diabetes mellitus, and immunosuppressive therapy, rate of PC microbial colonization, and development of SNS insertion site infection were reported.

Statistical analysis

All statistical analyses were conducted using the SPSS software (ver. 26; IBM Corp.). Quantitative variables are presented as means±standard deviation, and qualitative variables are expressed as frequencies with percentages. Results were compared between the two groups using Student's t-test for quantitative variables and Fisher's exact test for qualitative variables. A p-value of <0.05 was considered significant.

RESULTS

Between January 2018 and June 2021, 31 consecutive patients underwent SNS explant with PC excision. Most of the study population were females (93.5%, n=29), the mean age was 51.6±13.8 years with a mean BMI of 31.5±8.1 kg/m^2. Eight patients (25.8%) were active smokers, five patients (16.1%) had diabetes, and five patients were under immunosuppressive therapy (Table 1). Indications for SNS insertion were refractory overactive bladder (n=21, 67.7%), bladder pain syndrome (n=5, 16.1%), neurogenic bladder (n=4, 12.9%), and refractory urinary retention (n=1, 3.2%) (Table 2). Indications for SNS explant were device malfunction (n=9, 29.0%), need of a magnetic resonance imaging (MRI) (n=9, 29.0%), leg or insertion site pain (n=6, 19.3%), failure to control symptoms (n=6, 19.3%), and patient desire (n=1, 3.2%) (Table 3). All excised PC were sent for gram stain and tissue culture, including aerobic, anaerobic, and fungal cultures.

Overall, four (12.9%) out of the 31 patients had positive tissue cultures in the excised PC. Two microbial cultures grew Coryneform bacillus, one grew Cutibacterium acnes,

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Table 1. Patient demographics

Variable	Total (n=31)	NPCC (n=27)	PPCC (n=4)	p-value
Age (y)	51.6±13.8	50.6±13.6	58.5±15.2	0.294
BMI (kg/m^2)	31.5±8.1	32.5±8.1	24.3±4.0	0.056
Sex				
Male	2 (6.5)	1 (3.7)	1 (25.0)	0.245
Female	29 (93.5)	26 (96.3)	3 (75.0)	
Diabetes mellitus	5 (16.1)	4 (14.8)	1 (25.0)	0.525
Smoker	8 (25.8)	8 (29.6)	0 (0.0)	0.550
Immunosuppressive therapy	5 (16.1)	4 (14.8)	1 (25.0)	0.525

Values are presented as mean±standard deviation or number (%).
NPCC, negative pseudo-capsule culture; PPCC, positive pseudo-capsule culture; BMI, body mass index.

Table 2. Indications for SNS insertion

Indication	Value
Refractory overactive bladder	21 (67.7)
Bladder pain syndrome	5 (16.1)
Neurogenic bladder	4 (12.9)
Refractory urinary retention	1 (3.2)

Values are presented as number (%).
SNS, sacral nerve stimulator.

Table 3. Indications for SNS removal

Indication	Value
Revision of malfunctional device	9 (29.0)
Need for MRI	9 (29.0)
Insertion site or leg pain	6 (19.3)
Failure to achieve symptom control	6 (19.3)
Patient request	1 (3.2)

Values are presented as number (%).
SNS, sacral nerve stimulator; MRI, magnetic resonance imaging.

Table 4. Pseudo-capsule positive cultures

Pseudo-capsule positive cultures	Value
Total	4 (100.0)
Coryneform bacillus	2 (50.0)
Cutibacterium acnes	1 (25.0)
Pseudomonas aeruginosa	1 (25.0)

Values are presented as number (%).

and one grew Pseudomonas aeruginosa (Table 4). Two of the four patients with positive tissue cultures required removal for revision of a malfunctional device and two for the need of an MRI. All four patients underwent delayed SNS re-implantation using the same subcutaneous pocket. The reasons for the delayed reimplantation were the need to undergo MRI without the device in two of the patients. Both of whom refused to try the MRI-compatible device as they felt comfortable with their devices. The other two patients needed a device-free interval to decide if they would need re-implantation. At a follow-up of 16.3±8.3 months, none of these patients developed surgical site/device infection.

Among the 27 patients with negative tissue cultures, 19 patients underwent SNS re-implantation and none of them developed surgical site/device infection at a follow-up of 14.8±5.7 months.

Patients with positive culture were older than patients with negative culture (58.5±15.2 y vs. 50.6±13.6 y, p=0.294) and had a lower BMI (24.3±4.0 kg/m^2 vs. 32.5±8.1 kg/m^2, p=0.056). Rate of immunosuppression therapy was higher among positive culture group (25.0% vs. 14.8%) but not statistically significant (p=0.525). Eight patients (29.6%) of negative culture group were smokers and 14.8% (n=4) of them were diabetic (Table 1).

DISCUSSION

SNS revision or removal due to complications or device malfunction is not uncommon. End of battery life, lead migration, insertion site discomfort and decreased response are the most common indications for revision while persistent insertion site or leg pain, MRI, failure to maintain function and infection are the most encountered complications mandating device removal [3,15].

With the increasing application of implantable medical devices like cardiac pacemakers, prosthesis and indwelling vascular catheters, the risk of the associated infections that can be life-threatening in certain circumstances became very concerning. Zheng et al. [8] and VanEpps and Younger [9] attributed the highly prevalent microbial colonization of these implantable medical devices to the lack of self-cleansing capacity with subsequent microbial adherence and formation of microbial biofilms that form the basis of infection in these devices. In specific, several factors have been shown to be implicated in increasing the risk of infection in SNS and have been identified in literature as the risk factors of

infection in SNS. These include length of stage 1 testing, longer operative time for stage 2, and non-obstructive urinary retention. SNS is frequently performed via a two-staging testing procedure to examine the efficacy of the device in treating the individual patient's symptoms. During the initial testing phase (stage 1), the device leads are exposed from the patient's skin. Several studies reported an increased risk of infection with prolonged testing [16,17] while other studies denied the association between prolonged device testing (>14 d) and increased risk of infection [18,19]. Additionally, Guralnick et al. [20] reported longer mean operative time for stage 2 procedure (IPGs placement) in patients with infection compared to those without (68.8 minutes versus 52.4 minutes), thereby identifying it as the sole risk factor for subsequent infection. Also, Clifton et al. [21] identified the preoperative diagnosis of non-obstructive urinary retention, in which patients often require self-catheterization for bladder management, as the only significant preoperative predictor of infection.

Additionally, the implant site or device infection associated with SNS were looked at in many studies. Noblett et al. [22] found that out of 340 subjects, only 13 patients developed implant site infection, eight of them required surgical intervention while the remaining responded well to antibiotics. Similarly, van Kerrebroeck et al. [23] reported 7.9% rate of infection at the implant site in 152 patients who underwent sacral neuromodulation for refractory voiding dysfunction and Hijaz et al. [3] reported 5% infection rate in 214 patients who underwent sacral neuromodulation therapy.

Proper handling of the device and decontamination of skin and surfaces before insertion are the cornerstone for infection prevention in implantable medical devices [24]. Amongst prosthetic surgeons, there is a tendency to prophylactically resect the PC that forms around SNS. This tendency came mostly from the rationale that this PC can be a rich environment for microbial colonization.

PC is common with implantable medical devices. The fibrotic reactions that lead to formation of this PC in neural tissues were investigated by Carnicer-Lombarte et al. [12] and Salatino et al. [13] who reported a higher tendency of glial tissues for PC formation. Additionally, Polikov et al. [14] highlighted the role of this PC as a main reason for failure of implanted neural electrode. However, the colonization rate of the PC and its relation to infection after SNS insertion were not adequately reported and to our knowledge, this is the first study to investigate the rate of microbial colonization of the PC and the feasibility of its resection in the absence of associated clinical infection.

Our results revealed a low rate of PC colonization (12.4%) as positive culture results were reported in only 4 cases. The rate of colonization was found to be higher in older patients and patients on immunosuppressive therapy. Interestingly, none of these patients developed infection at the implant site during the follow-up duration.

Since the virulence of microorganisms can play a role in the severity of subsequent clinical infection, the positive culture samples in our study revealed that Coryneform bacillus represented most isolated microorganisms followed by Cutibacterium acnes and Pseudomonas aeruginosa.

Generally, Coryneform bacillus and Cutibacterium acnes are low-virulence organisms that are unlikely to cause life-threatening infections; however, some fatal infections were reported [25-27]. Conversely, pseudomonas aeruginosa is not uncommon cause of serious infections [28].

We reported a low rate of PC colonization at the time of SNS revision (12.9%). In addition, this colonization was not associated with implant site infection, diabetes, or smoking status. It was rather correlated with patient's age and use of immunosuppressive therapy. None of our patients with positive PC culture developed surgical site infection following device revision despite using the same pocket. Accordingly, we hereby question the relevance of the ongoing trend to excise the PC during SNS explant. More research is needed to better understand the role of PC-positive culture in increasing the risk of SNS device infections if strict adherence to sterile techniques is adopted.

Study limitations

In addition to the relatively small sample size, the lack of a comparative group of infection rate in patients who did not undergo PC removal can affect the generalizability of our study results.

CONCLUSIONS

PC colonization was uncommon at the time of SNS explant. However, more research is needed to better understand the role of PC-positive culture in increasing the risk of SNS device infections if strict adherence to sterile techniques is adopted.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose except mentioned below:

Ayman Mahdy:

-Axonics: principal investigator

-Medpace: consultant

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-FirstThought: consultant

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AUTHORS' CONTRIBUTIONS

Research conception and design: Mostafa M. Mostafa, Mohamed Kamel, and Ayman Mahdy. Data acquisition: Mostafa M. Mostafa. Statistical analysis: Mostafa M. Mostafa and Mohamed Kamel. Data analysis and interpretation: Mostafa M. Mostafa, Mohamed Kamel, and Ayman Mahdy. Drafting of the manuscript: Mostafa M. Mostafa and Mohamed Kamel. Critical revision of the manuscript: Mohamed Kamel and Ayman Mahdy. Obtaining funding: Ayman Mahdy. Administrative, technical, or material support: Mostafa M. Mostafa, Mohamed Kamel, and Ayman Mahdy. Supervision: Mohamed Kamel and Ayman Mahdy. Approval of the final manuscript: all authors.

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