Sacral Neuromodulation Unsuccessful For Pain Control After Failed Radical Cystectomy For Chronic Pelvic Pain

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Abstract
A 43-year-old female with chronic refractory interstitial cystitis (CT) and persistent pelvic pain/pressure status post-ileal conduit urinary diversion was treated successfully with sacral neuromodulation (InterStim®). Although the Food and Drug Administration (FDA) approved treatment of refractory urgency/frequency, urgency incontinence, and non-obstructive urinary retention, few patients have shown satisfactory results for the treatment of unremitting pelvic pain and pressure after cystectomy. This report of a patient with refractory urgency/frequency and pelvic pain was treated with radical cystectomy and ileal conduit urinary diversion. Her unremitting post-operative pelvic pain initially responded well to sacral neuromodulation. She underwent device removal 9 months later due to lack of efficacy.

INTRODUCTION
Refractory urinary urgency and frequency with chronic pelvic pain is a poorly understood pelvic pain syndrome with a variable presentation. It has often been referred to by some as interstitial cystitis (IC). Also, it has been under-diagnosed and confused with other gynecologic and urologic conditions. As a diagnosis of exclusion, IC may inadvertently be missed and require many years to diagnose. The relapsing nature of this chronic condition leaves most patients with few definitive treatment modalities. Patients’ pelvic pain and/or irritative urinary symptoms respond best to multimodal treatment.1,2,3,4

Patients with severely disabling symptoms, nonresponsive to more traditional treatments, require pain-management services, psychologic, and gynecologic consultations. In the past, IC patients have been subjected to neurolytic intravesical agents and/or an eventual cystectomy, with a urinary diversion to eliminate severe urinary symptoms.4,5 Unfortunately, even the most radical surgical options do not always eliminate pelvic pain.4 Likewise, sacral neuromodulation, used since 1998 as an effective treatment for refractory voiding dysfunction, has not previously been shown to have an impact on the pelvic pain.

CASE REPORT
A 43-year-old female with refractory urgency, frequency, persistent pelvic pain/pressure status, and post-cystectomy with ileal conduit urinary diversion, was first seen for treatment of her persistent chronic pelvic pain. The procedure did not include urethrectomy. Her pain was episodic, and she also complained of pelvic floor muscle spasms and irritable bowel activity with alternating constipation and diarrhea. Her surgical history was significant for lipoma removal at L5-S1, hysterectomy, and cholecystectomy. Medications included tramadol for pain control. She had no known drug allergies. Her family history was that of no abnormalities. The patient had been a 1 pack/day smoker for 20 years.

The patient's physical examination showed a cachectic female who appeared older than the stated age by approximately 15 years. Her head was normocephalic, atraumatic; neck was supple with no jugular venous distention; and the extraocular muscles were intact. Also, her heart sounds were S1 and S2 with regular rate and rhythm; respirations were clear to auscultation bilaterally; and no wheezes, rales, or rhonchi auscultated. Her abdomen was soft, nontender, and nondistended, with no suprapubic fullness. She had positive bowel sounds in all four quadrants and a healed midline scar, as well as an ileal conduit stoma in the right abdomen. The skin and lymphatic and musculoskeletal systems were within normal limits. A genitourinary examination showed an intact urethra with
anterior vaginal wall tenderness. No evidence of a pelvic floor prolapse was detected.

A computed tomography (CT) scan of her abdomen and pelvis, preformed with and without contrast, showed no evidence of abdominal or pelvic pathologic problems. Also, a colonoscopy showed no evidence of polyps or mass lesions in the colon or rectum.

The patient underwent a sacral neuromodulation trial with bilateral lead placement in the S3 foramina. She had a 75% improvement in her pelvic pain from 9 out of 10 to 2 out of 10. She also had 50% improvement in her gastrointestinal symptoms, as well as formed normal stools. Her tramadol dose of 50-mg 4 times daily was reduced to 25 mg daily. The patient underwent placement of the implantable pulse generator and initially did well for 8 months. She also had good stimulation of the impulses in the pelvis.

At her 8-month follow-up visit, she began to develop a worsening of her pelvic pain to 6 out of 10, despite excellent functioning of the InterStim® device. An examination showed no evidence of device infection. A review of the device and x-rays showed good lead placement and excellent battery function, and all circuits were functional. The patient then wanted the device removed because of lack of efficacy, despite having a 30% improvement in pain when compared to her first visit.

**DISCUSSION**

Sacral neuromodulation was a significant breakthrough in management of refractory urgency/frequency, urgency incontinence, and non-obstructive urinary retention. Initially, it was approved by the Food and Drug Administration (FDA) in 1997, based in part on published research regarding the value of sacral neuromodulation in management of the neurogenic bladder.\[7\] Likewise, Hassouna and colleagues noted its preliminary efficacy in urinary urgency, urgency-frequency, and retention.\[8\] Thereafter, sacral neuromodulation was adapted to treat the variable urinary symptoms attributed to refractory urgency/frequency (IC). Many IC suffers experience debilitating relapses, with limited responses to commonly used traditional pharmacologic therapies.

Typical patients with IC are seen by health professionals in their 20's to 50's (mean: 40 years old) with symptoms that include—but not limited to—bladder, pelvic or perineal pain and discomfort, dyspareunia, nocturia, urinary frequency, and/or urgency.\[9\] Chronic, non-remitting pelvic pain (with or without urinary, symptoms) that last more than 9 months without a neurologic or malignant component are commonly considered to be a component of IC.

Most treatments determined to be of value in management of IC are typically temporarily efficacious for the majority of patients. Mast cells in the tissues of some patients suggest an allergic or autoimmune reaction, at times responsive to antihistamines such as hydroxyzine hydrochloride.\[10\] Theories that implicate inflammation secondary to bacterial or viral causes suggest antibiotics or anti-inflammatory medications are valuable.

Functional abnormalities that include bladder wall defects and pelvic floor dysfunction also are being considered.\[11\] Hydrodistention can provide short-term symptomatic relief, whereas nonsteroidal anti-inflammatory drugs (NSAIDs), muscle relaxants, and anti-depressants (such as amitryptiline) also can have mediating effects. Neurogenic pain appears to be a common finding in many of the most severe cases. Tricyclic antidepressants, anti-epileptics, or opioids may alleviate some patients’ neurogenic pain.

Intravesical treatments with heparin, dimethyl sulfate (DMSO), or bacillus Calmette Guerin (BCG) also may provide short-term solutions for symptomatic pain relief, likely through neural modulation. They can be caustic, may cause tissue damage, and the pain may return or symptoms worsen.

Unfortunately, as many as 50% of IC patients’ status post cystectomy continue to have pelvic pain, presumably secondary to the centralization of pain.\[12\] If sacral neuromodulation could prove to consistently control pelvic pain in IC patients with or without pelvic organs, it would be a huge success. The mechanism for this approach to pain control may result in pain relief by bypassing the spinal cord and peripheral nerves.

To date, results as in this case have been minimally successful. Zabahi and coworkers described short-term results with bilateral sacral neuromodulation for IC, painful bladder syndrome, and chronic pelvic pain. Whereas, in 23/30 patients who received an implantable generator, only a 40% improvement in pain symptoms was noted at a mean follow-up time of 15 months.\[12\]

Peters and Konstadt showed a reduction in morphine dose
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 equivalents by 36% in patients with refractory IC and chronic pelvic pain at a mean follow up of 15 months.\(^{13}\) Approximately 20% of patients were actually able to stop their narcotic medications.

Unfortunately, these results, as well as this patient, suggest the difficulties encountered in treating patients with refractory IC and chronic pain. Positive initial results can be short lived. The authors believe that patient expectations for success with this procedure must be carefully explained at the outset.

Nevertheless, the challenges of refractory IC with chronic pain need further investigation. Sacral neuromodulation may continue to be a viable option for those with unremitting pain. Perhaps bilateral sacral neuromodulation, pudendal nerve stimulation, dorsal genital nerve stimulation, and posterior tibial nerve stimulation may prove successful either as a single or part of a multimodal treatment for this challenging condition.

CONCLUSION

The challenges of treating patients with IC and chronic pelvic pain represent a significant challenge for the practicing physician. Sacral neuromodulation is a promising modality that has shown some success in limited studies by improving chronic pain in the short term. Whereas initially successful in this patient, her desire for more significant improvement lead to explantation of the InterStim® device.

Nevertheless, this modality remains worthy of consideration in this challenging patient population.

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