Leadless intracardiac pacemaker implantation in patients with bradyarrhythmias after spinal cord injury

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Introduction

Cardiovascular instability is commonly encountered following a cervical spinal cord injury (SCI).[1] Bradycardia is almost universal, and the severity of bradycardia is greater with higher and complete spinal cord injuries.

Bradycardia may contribute to shock requiring vasopressors and may progress to asystole, necessitating cardiac resuscitation in 11%–16% of patients with complete cervical SCI.[1] The disruption of supraspinal sympathetic pathways, and the resultant parasympathetic dominance, as a consequence of a cervical SCI is the major cause of cardiovascular instability in patients with SCI. Bradycardia is noted typically 3–5 days after cervical SCI, and in most cases lasts up to 4–6 weeks, although cases describing bradycardia up to 21 months post SCI have been reported.[2]

Additionally, cardiac events are the main cause of mortality in the first year following cervical SCI.[3] Initial treatment of severe life-threatening bradycardia in SCI generally includes atropine, inotropes, and aminophylline. In refractory cases, and for those associated with life-threatening events, such as an asystole and cardiac arrest, temporary and permanent pacemakers (PPM) have been used.[3,4]

Most of the literature in patients with cervical SCI report the use of traditional PPM. To the best of our knowledge, this is the first case series describing use of leadless pacemakers in the management of these patients. The following is a case series of patients with cervical SCI resulting in hemodynamically unstable high-grade bradycardia and asystole who were managed with placement of a leadless pacemaker.

Case report
Case 1

A 20-year-old male patient with past medical history of asthma and a remote gunshot wound to the right flank presented to the emergency department (ED) after a gunshot wound to the left neck. Upon arrival, the patient had cardiac arrest, which was attributed to hemorrhagic shock secondary to active arterial bleeding at the left neck wound. Concern for airway protection necessitated intubation; and after stabilization of the patient, neurological examination was preformed and revealed a loss of rectal tone and quadriplegia.

Initial electrocardiogram demonstrated normal sinus rhythm and normal axis with nonspecific T-wave flattening in lateral leads. Computerized tomography with angiography of the cervical spine demonstrated several cervical fractures with displacement of bony fragments into the spinal canal from C3 to C4.

On hospital day 2, while on dopamine and vasopressin infusion for hypotension, the patient had persistent bradycardia with heart rate ranging from 30 to 40 beats per minute and sinus node arrest with pause of 15 seconds in duration (while he was being turned in bed). In subsequent days, bradycardia recurred repeatedly despite atropine and the patient had additional episodes of sinus node arrest with significant pauses, necessitating implantation of a PPM. The procedure was delayed until hospital day 18, as the patient continued to require aggressive respiratory and hemodynamic stabilization. In the interim, telemetry monitoring continued to demonstrate sinus bradycardia and sinus pauses. As soon as feasible, a Micra™ Transcatheter Pacing System ("Micra"; Medtronic, Minneapolis, MN) was implanted without any complication. It was set in VVI mode with a lower rate limit of 60 beats per minute and upper rate limit of 130 beats per minute. The patient had a prolonged hospital stay with concerns for respiratory failure and pneumonia but

KEY TEACHING POINTS

- Spinal cord injury (SCI) above the level of sympathetic nerve hiatus from the cervical spinal cord results in unopposed parasympathetic activity leading to dysregulation and a variety of bradyarrhythmias and asystole.

- Bradycardia is almost universal following cervical SCI, occurs 3–5 days after the injury, and lasts up to 4–6 weeks, and in some cases up to 21 months. Chronic bradycardia is often in the setting of overinflation during hypoxic episodes (pneumonia) and more likely to affect patients on chronic mechanical ventilation or tracheostomy tubes.

- Bradycardia may contribute to shock requiring vasopressors and may progress to asystole, necessitating cardiac resuscitation in 11%–16% of patients with complete cervical SCI. Bradycardia and asystole are significant contributors to morbidity, often requiring prolonged telemetry monitoring and prolonged hospital stay.

- Initial treatment of bradycardia generally includes atropine, inotropes, and aminophylline; and in intractable cases or if with asystole/cardiac arrest, pacemakers are used. Because of the mortality benefit in patients receiving pacemakers, several researchers recommend aggressive pacemaker implantation over medical therapy.

- Leadless pacemakers (LPMs) eliminate lead- and pocket-related complications such as pneumothorax/pocket infection seen with traditional pacemakers. Additionally, the femoral approach for LPM insertion might be uniquely beneficial when compared to the jugular approach for traditional pacemakers, in patients with cervical SCI.

Figure 1 Portable chest radiography demonstrates partially visualized cervical fixation hardware with C-collar in place and a leadless pacemaker implanted in the right ventricle.

tection. Initial imaging demonstrated a nondisplaced fracture of the left lamina of C5, anterior superior angle of T3 vertebral body, cervical epidural hematoma at the foramen magnum, and left neural foraminal stenosis with cord compression at C6–C7 level. The patient underwent posterior cervical decompression and a C3–C7 laminectomy, hardware placement, and posterior spinal fusion was performed. On hospital day 4 the patient had an episode of sustained atrial fibrillation with rapid ventricular response at a heart rate in the 130s, followed by sinus bradycardia with heart rate in the 30s and 40s (beats per minute), with long conversion pauses. Owing to concern for sick sinus syndrome, the patient was determined to be a candidate for pacemaker and a leadless pacemaker was inserted (Figure 1). The mode was set to VVI, with a lower rate limit of 60 beats per minute. The patient had a prolonged hospital stay with ventilator dependence, respiratory failure, and acute respiratory distress syndrome. The patient was finally transferred to a long-term acute care facility for rehabilitation without further incidence of bradycardia.

Case 3

This case involved a 70-year-old man with a past medical history of hypertension and arthritis who was taken to an outside facility after he was found unconscious on the sidewalk. Initial work-up there revealed a blood alcohol level of 291, hypothermia, bradycardia, and severe cord compression at C3–C4 level and cord contusion at C2–C5 level. He was intubated at that facility for airway protection and later extubated successfully. After extubation, he was unable to move his extremities and was transferred to our hospital for further management of quadriplegia and cord decompression. On hospital day 2, cardiology service was consulted for telemetry monitoring, which revealed sinus bradycardia with intermittent atrial tachycardia and heart rate ranging between 30 and 128 beats per minute. The heart rate was

was finally transferred home under the care of his family and visiting nurse services. There were no further instances of sinus bradycardia or sinus pauses.

Case 2

A 71-year-old male patient with past medical history of coronary artery disease with regional wall motion abnormality, atrial fibrillation, and hypertension was brought into the ED after his family found him lying on the floor at home after a presumed fall. The patient was unable to recall events and, upon arrival, was unable to move his extremities and had no sensation below the axilla. Pooled blood was found in his airway and he was intubated in the ED for airway pro-
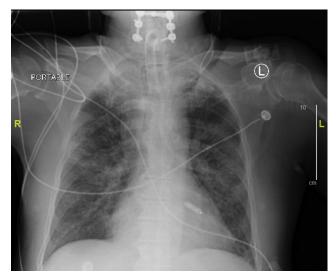
unrelated to the patient's being turned in bed and fluctuated spontaneously. Later that day, the patient had an episode of syncope lasting about 90 seconds while his heart rate was in low 30s. Presence of tachycardia-bradycardia syndrome was thought to be the cause of syncope and a Micra pacemaker was placed without complication. The mode was set to VVI with a lower rate limit of 60 beats per minute. His hospital course was prolonged and complicated by chronic respiratory failure with ventilatory support required. He was eventually stabilized and transferred to a nursing home facility without further incidence of sinus bradycardia.

Case 4

A 30-year-old patient with no known past medical history presented to the trauma bay in hemorrhagic shock after sustaining gunshot wounds to the neck and left abdomen. He was intubated for airway protection and a massive transfusion protocol was initiated. He was emergently taken to the operating room for exploratory laparotomy. He underwent several sequential operations including an ileocolic anastomosis, right hemicolectomy, gastric repair, and gastrostomy. Computerized tomography of the cervical spine demonstrated a posteriorly displaced fracture of the C6 inferior endplate with displacement into the spinal canal and severe spinal stenosis secondary to the fracture fragments with a bullet lodged at the C5–C6 level. On day 3 of admission, the patient was found to be quadriplegic. He had a prolonged hospital course complicated by uremia, septic bacteremia, fascial necrosis, compartment syndrome, and pneumothorax requiring several corrective procedures. On day 23 of hospitalization, the patient was noted to have several episodes of bradycardia with a heart rate in the 30s–40s. On telemetry review, he was sinus bradycardic and also found to have a 4-second pause. Bradycardia recurred despite transient improvement with atropine administration. In light of his sustained injuries with increased risk for asystole and bradycardic events, the patient underwent implantation of a leadless pacemaker. The mode was set to VDI with a lower rate limit of 60 beats per minute and upper rate of 130. The patient was managed in the hospital for another 12 days for multidrug-resistant *Acinetobacter* pneumonia. The patient acutely desaturated and became hypotensive despite adequately paced pulse response. Aggressive resuscitation efforts and vasopressor support were unsuccessful and the patient died.

Discussion

Annually, between 250,000 and 500,000 people suffer SCI globally.[4] Although the 85% mortality rate for acute SCI reported during the First World War has substantially decreased in the current era, SCI still remains a devastating condition.[5] The incidence, prevalence, and cause vary between developed and developing countries, with the highest prevalence being that of the United States at 906 per million

population.[5] Traffic accidents are typically the most common cause of SCI, followed by falls in the elderly population. Subsequently, males younger than 30 years of age were the most affected demographic, followed by elderly men.

Cardiovascular effects of SCI

Cardiovascular effects of SCI are well described. The autonomic nervous system regulates many functions, including control of cardiovascular functions such as coronary blood flow, cardiac contractility, heart rate, and peripheral vasomotor responses. Heart rate at rest is controlled almost exclusively by the parasympathetic nervous system. For the autonomic innervation of the heart, the preganglionic sympathetic fibers exit the spinal cord at the first through fourth thoracic level, while parasympathetic control is exerted through the vagus nerve originating at the level of the medulla oblongata.[6] Hence, high SCI in the cervical region may completely disrupt cardiac sympathetic influences from higher centers while parasympathetic control remains intact.[1]

Following SCI, there is an initial transient pressor response. This is followed by spinal shock syndrome, which is the period after injury characterized by a marked reduction or abolition of sensory, motor, or reflex function of the spinal cord below the level of injury. Additionally, deficits in the autonomic nervous system include an extended period of neurogenic shock characterized by hypotension, bradycardia, and hypothermia.[6] Neurogenic shock is primarily caused by a disrupted sympathetic flow to the heart and the vessels, while the parasympathetic influence is preserved. This imbalance is exaggerated transiently by activities that increase the vagal tone, such as tracheal suctioning, belching, defecation, or passive movement. Without the usual sympathetic counteraction, these activities often lead to severe bradycardias and cardiac arrest in these patients.[1] In about 48%–90% of these patients, after resolution of the neurogenic shock, abnormal recovery of the sympathetic nervous system below the level of injury may lead to bouts of apparent sympathetic hyperactivity associated with bradyarrhythmias and tachyarrhythmias, referred to as autonomic dysreflexia.[7]

Management of SCI-induced bradycardia

In the acute phase of SCI, the management of bradycardia has mostly been pursued from a medical/neuropharmacologic approach rather than an electrophysiologic approach. As uninhibited vagal activity is the cause of bradycardia, atropine is well established as the first-line agent in these patients. The proportion of patients with SCI who experience bradycardia that can be successfully managed with atropine alone is unknown.[8]

Historically, pacemakers have been used in patients refractory to medical therapy or in cases with asystole and cardiac arrest, although there are no clear guidelines for their use. Published case series indicate pacemaker implantation

rates ranging from 2% to 16%, across a wide spectrum of ASIA functional classification and anatomic level of injury.[4] PPM placement has been reported as early as 2 weeks after injury and up to 21 months post SCI.[2,9] Chronic bradycardia is often in the setting of overinflation during hypoxic episodes (pneumonia) and more likely to affect patients on chronic mechanical ventilation or tracheostomy tubes.[2] Several researchers recommend aggressive pacemaker implantation in patients with severe/persistent bradycardia, suggesting intervention even earlier than 2 weeks post SCI.[4] This approach has shown promising results, and Moerman and colleagues[4] described reduction in cardiac events from 35 to zero and the use of atropine from 9 to zero, among the 6 patients who received PPM. Additionally, limited data suggest the safety of pacemakers in patients with spinal cord injury on functional electrical stimulation programs for assistance in muscle activation and recovery.[10]

The case for leadless pacemakers

Permanent pacing has been a longstanding effective therapy for symptomatic bradycardia, with up to 350,000 procedures performed each year in the United States alone. Conventional traditional pacemakers (T-PPM) consist of a pacemaker device and battery typically implanted in a subcutaneous pocket in the chest. One or more leads threaded from the device pocket through veins into the heart conduct the pacing to the desired cardiac site. Despite a reduction in complications over the years, serious adverse events are still encountered. Complications are reported in about 20% of patients at 5 years, with highest complications related to the pacing lead (11%) and pocket (8%).[11,12] These include pocket hematoma, erosion or infection, pneumothorax/hemothorax after subclavian vein puncture, vein stenosis or occlusion, endocarditis, tricuspid valve trauma, lead connection troubles, and lead fractures.[13]

In an effort to address the demerits of T-PPM, leadless pacemakers (L-PPM) were introduced in 2012. Since then L-PPM therapy has been well adopted and their use has consistently increased because of elimination of lead- and pocket-related complications.[14] L-PPM are miniaturized single-chamber PPM that are implanted directly in the right ventricle, usually via femoral access. The Micra Transcatheter Pacing System (Medtronic) currently is the only FDA-approved and available L-PPM device. The Micra L-PPM is associated with a 51% lower risk of complications in the first 6 months after implant compared with T-PPM, including a lower risk of infection.[14]

There are several unique qualities of survivors of SCI that make them ideal candidates for an L-PPM as compared to T-PPM. These patients have an increased propensity for infections because of high *Staphylococcus aureus* colonization rates, immunosuppression secondary to autonomic dysreflexia, and increased oral flora in the neck region from secretion leak at tracheostomy sites.[15] L-PPM implantation

via the femoral route does provide for a safer approach in these patients compared to T-PPM, which often require a jugular approach for the procedure. Additionally, after cervical SCI a cervical collar is in place for 6 weeks or more to offer stability, as even slight movements in the neck may further compromise an already injured spinal cord and vertebral column. The collar itself may be a barrier to early placement of a T-PPM and neck immobility may also preclude the turning of the patient's head to access the left subclavian vein. In our experience reported in this study, we were successfully able to implant the Micra L-PPM device in the 4 patients early after their SCI, which then resolved their respective arrhythmias.

Summary/Conclusion

The authors acknowledge the need for published consensus treatment recommendations for bradyarrhythmia management in patients with SCI. We agree with the initial use of medical therapies in the management of these patients. With this study we add to the growing literature demonstrating the success of early PPM implantation in patients with severe and recurrent bradyarrhythmias. This is especially relevant because of the well-documented failure of medical therapy in bradycardia management. Ours is the first report to show successful use of L-PPM in the management of patients with bradycardia in the setting of cervical SCI. L-PPM may offer advantages over T-PPM in these patients by providing easier procedural access as well as potentially decreasing the infectious complications post procedure. We encourage more reports and studies to validate our experience here.

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