Dysautonomia following radical cystectomy and intracorporeal orthotopic neobladder: A case report

Lan Anh S Galloway, Christopher P Dall, Lambros Stamatakis

ABSTRACT

Orthostatic hypotension and dysautonomia occur commonly after surgery, but there is little data regarding these complications in the genitourinary surgery population. This report presents the case of a 74-year-old male diagnosed with muscle-invasive bladder carcinoma who underwent radical cystectomy and creation of an intracorporeal orthotopic neobladder. Following surgery, he developed significant lightheadedness and was found to have orthostatic hypotension of unclear etiology. We postulate that this is likely multifactorial and due to a myriad of factors including postoperative weight loss, extensive lymph node dissection, presence of a hiatal hernia, and dietary contributions. This case report is the first of its kind to investigate and report on orthostatic hypotension as a postoperative complication of radical cystectomy and creation of an orthotopic ileal neobladder.

Keywords: Cystectomy, Dysautonomia, Orthostatic hypotension, Postoperative complication

INTRODUCTION

Dysautonomia and orthostatic hypotension are common postoperative complications found in up to 49% of patients undergoing a wide range of procedures, including orthopedic, bariatric, abdominal, and thoracic surgery. It can result in delayed ambulation, increased length of hospitalization, and falls [1–3]. However, there are few reported cases in the literature regarding dysautonomia following major genitourinary surgery. In this study, we present a profound case of dysautonomia and orthostatic hypotension following robotic-assisted laparoscopic radical cystectomy and creation of an intracorporeal orthotopic neobladder.

CASE REPORT

A 74-year-old male with a history of hypertension, type II diabetes mellitus, hypothyroidism, hiatal hernia, and Agent Orange exposure presented to the urology clinic with gross hematuria. The patient underwent a computerized tomography (CT) scan, which revealed asymmetric bladder wall thickening. Transurethral resection of bladder tumor (TURBT) was performed and demonstrated high grade urothelial carcinoma with invasion of the detrusor muscle (clinical stage T2). Subsequent staging revealed a lung mass and biopsy demonstrated a concurrent right lung adenocarcinoma. After multidisciplinary discussion, he underwent lobectomy with four cycles of adjuvant gemcitabine and cisplatin chemotherapy. Following this, he underwent repeat cystoscopy and bladder biopsy which demonstrated no evidence of residual carcinoma. Radical cystectomy and urinary diversion were discussed and recommended as the gold standard treatment for muscle-invasive bladder carcinoma (MIBC), but the patient opted for...
close imaging and cystoscopic surveillance in light of his age and recent treatment for lung cancer. Surveillance cystoscopy six months later revealed a new left lateral wall bladder tumor. Pathology was consistent with MIBC with micropapillary features. Restaging CT demonstrated pelvic lymphadenopathy, suggestive of possible nodal metastasis. The likelihood of nodal metastasis was discussed extensively with the patient and it was explained to him that a radical cystectomy alone would likely not be curative, but that it could be considered as part of a multimodal approach to manage his advanced bladder cancer. He met with radiation oncology and medical oncology for further management recommendations and elected to proceed with a radical cystectomy with plans to proceed with salvage immunotherapy. He was seen and evaluated preoperatively by the anesthesia team and noted to have diabetic neuropathy and hypertension but was deemed optimized for surgery.

The patient was taken to the operating room for a robotic-assisted laparoscopic radical cystoprostatectomy, extended lymph node dissection, and creation of an intracorporeal orthotopic neobladder. The neobladder was made from a section of ileum 15 cm from the ileocecal valve and consisted of approximately 30 cm of bowel. The small bowel anastomosis was performed in a side-to-side fashion using the Endo GIA stapler (Medtronic, Minneapolis, MN). The patient’s postoperative course was unremarkable, and he was discharged on postoperative day six. Surgical pathology revealed pT3aN3 urothelial carcinoma, predominantly micropapillary pattern (90%). 24/46 sampled lymph nodes were positive for carcinoma.

Six weeks after surgery, the patient presented to the emergency department with fever, nausea, and vomiting. He complained of dizziness and lightheadedness exacerbated by movement and sitting up. Admission vitals were notable for a fever to 38.5°C, a heart rate of 97 beats per minute (bpm), and a blood pressure of 169/76. Labs were significant for a leukocytosis to 24 $\times$ 10^3 cells/µL and a lactatemia of 3.7 mmol/L. He was admitted for evaluation of possible sepsis and continued following his hospitalization.

Despite improvement in his fevers, leukocytosis, and clinical appearance, the patient continued to complain of lightheadedness and dizziness. Upon further questioning, he reported these symptoms had started soon after surgery and had not improved. He complained of worsening symptoms with distension of his neobladder prior to catheterization and relief with catheter placement. He reported difficulty ambulating secondary to the dizziness and several episodes of pre-syncope.

Orthostatic vitals were notable for a sitting blood pressure of 128/73 and heart rate of 70 bpm and a standing blood pressure of 88/52 and heart rate of 85 bpm. This did not resolve after fluid resuscitation and resolution of his sepsis and continued following his hospitalization.

Therefore, he was started on fludrocortisone and noted significant improvement in his symptoms, described by the patient as a “miraculous” resolution. Endocrinology was consulted and believed his orthostasis may have been due to adrenal insufficiency. However, his work-up was negative and no clear cause was identified. He did note a weight loss of 8 kilograms since his cystectomy. Nutrition was consulted and recommended nutritional supplements and a high-protein diet. Following his hospitalization, salvage pembrolizumab was initiated.

He continued to follow with the urology clinic and reported slow improvement in his dizziness and lightheadedness on ambulation. However, 11 months after surgery, he developed a small bowel obstruction and upon surgical exploration he was found to have metastatic bladder cancer implants on his small bowel. He aspirated on extubation and was admitted to the Surgical Intensive Care Unit (SICU). His family ultimately decided to withdraw care and the patient expired shortly thereafter.

**DISCUSSION**

Orthostatic hypotension is defined as a decrease in systolic blood pressure by 20 mmHg or decrease in diastolic blood pressure by 10 mmHg within 3 minutes of standing [4]. Normally, standing activates a physiologic response in carotid baroreceptors, which increases sympathetic tone and decreases parasympathetic tone via the vagus nerve [5]. Maintenance of blood pressure is dysfunctional in those with orthostatic hypotension and blood pressure does not increase upon standing, impairing cerebral perfusion. This can lead to lightheadedness and dizziness, and loss of consciousness if cerebral hypoperfusion is severe [5]. Orthostatic hypotension is often mediated via cardiac, neurologic, or drug-related pathways. Diagnostic work-up includes autonomic testing, investigations into patient drug regimens, and the head-up tilt test if the patient demonstrates symptoms but no difference in blood pressure upon standing [5]. The incidence of orthostatic hypotension has been found to be as high as 40% following any surgery and roughly 33% of abdominal surgeries [1]. Although there has been extensive research in other fields examining orthostatic hypotension, there is little data reported on the condition in the genitourinary surgical population.

Orthostatic hypotension has been well documented in the bariatric surgery population [6, 7]. In one retrospective chart review of 741 patients undergoing bariatric surgery, researchers found postoperative orthostatic intolerance to be a chronic and persistent issue in up to 4.2% of these patients [8]. Researchers hypothesized that decreased sympathetic nervous system (SNS) activity occurred following weight loss, manifesting as orthostatic intolerance or hypotension. In the same study of bariatric patients, 21 of the 31 patients experiencing orthostatic intolerance underwent specialized autonomic testing that demonstrated impaired SNS activation with a Valsalva...
The authors suggested that these patients may have had a pre-existing autonomic neuropathy unmasked by significant weight loss and given our patient's significant weight loss, this may have been a significant contributor to his symptoms. Urinary diversion with ileum is associated with many metabolic complications including a hyperchloremic, hypokalemic, metabolic acidosis [9]. Our patient was acidic with a pH of 7.29 during his postoperative admission. Nearly nine months later, he continued to have a metabolic acidosis with a pH of 7.30. Additionally, the ileum is responsible for absorption of water, bile salts, and B12. Although there is little literature on the relationship of these metabolic sequelae, they may be associated with postoperative orthostatic hypotension.

Another study of bariatric surgery patients demonstrated that high protein diets can result in decreased norepinephrine levels, which can decrease venous return to the heart and affect cardiac output. This decrease in norepinephrine can lead to orthostatic hypotension [10]. Patients undergoing radical cystectomy and ileal neobladder creation, including our patient, are often instructed to eat a protein-rich diet following surgery to help combat the catabolism seen after this complex surgery. It is possible that a high-protein diet and the resulting changes in autonomic signaling may have contributed to our patient's symptoms.

Lymph node dissection may be associated with postoperative dysautonomia. One recent case series described two cases of patients with testicular and renal masses that underwent retroperitoneal lymph node dissection and subsequently developed orthostatic hypotension [11]. These cases were thought to be due to the extent of sympathetic denervation that occurred with significant dissection of the superior mesenteric ganglia and fibers near the spinal muscular atrophy (SMA). Authors theorized that the sympathetic denervation of the SMA ganglia led to an inability of the bowel to vasoconstrict, thus impairing venous return when a patient stands or sits up. Our patient did not have a significant superior mesenteric ganglion dissection but did have an extended pelvic and iliac lymphadenectomy (up to the inferior mesenteric artery) which may have affected his autonomic function in a similar way.

Comorbid conditions may have also predisposed our patient to postoperative orthostatic hypotension. Deglutition syncope, or swallow syncope, occurs when there is increased intrathoracic pressure causing vgal nerve stimulation and syncope [12]. This phenomenon is well documented in cardiac literature and hiatal hernia has been known to contribute to increased vagal nerve activity. Our patient's hiatal hernia may be contributing to his orthostatic hypotension by increasing vagal tone.

Sepsis and infection are also known causes of orthostatic hypotension. Our patient's orthostatic hypotension was diagnosed during his admission for sepsis; however, he reported his symptoms started prior to that admission. Additionally, his symptoms persisted after his infection improved, making this infection an unlikely cause of his orthostatic hypotension.

In autonomic dysreflexia, patients with spinal cord injuries experience hypertension with urinary retention and bladder irritation due to increased sympathetic nervous system stimulation. While the clinical scenarios are very different, the triggering of autonomic dysreflexia with bladder overdistention could provide a corollary to explain our patient's symptoms. In our case, the patient insisted that his hypotensive symptoms worsened with neobladder distention and improved with catheterization. While speculative, perhaps some of his symptoms are related to similar neural pathways with parasympathetic nerve involvement. Further investigation with formal urodynamic testing and concomitant blood pressure monitoring could have helped further define this proposed etiology of his symptoms.

**CONCLUSION**

Literature searches have not identified other instances of similar cases or an obvious explanation for our patient's symptoms following radical cystectomy and intracorporeal neobladder creation. In summary, the etiology of this patient's dysautonomia is likely multifactorial and could be related to postoperative weight loss with decreased SNS response, surgical disruption of important autonomic neural pathways during the lymphadenectomy, and unusual autonomic dysregulation related to distention of the ileal neobladder. Awareness of this case could help future clinicians who encounter similar scenarios and perhaps lead to further investigation of this unusual phenomenon related to orthotopic continent urinary diversions.

**REFERENCES**

6. Rubinshtein R, Clubotaru M, Elad H, Bitterman H. Severe orthostatic hypotension following

Author Contributions
Lan Anh S Galloway – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved
Christopher P Dall – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved
Lambros Stamatakis – Conception of the work, Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved
Guarantor of Submission
The corresponding author is the guarantor of submission.

Source of Support
None.

Consent Statement
Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

Copyright
© 2021 Lan Anh S Galloway et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.
Submit your manuscripts at
www.edoriumjournals.com