Case of Delayed Ileal Conduit Necrosis Related to Infiltrative Diffuse Large B-cell Lymphoma

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The ileal conduit (IC) is the most common form of urinary diversion, accounting for 33%-84% of all diversions performed in the United States.[1,2] IC is an excellent reconstructive option for patients who require cystectomy for bladder cancer, other pelvic malignancies or benign conditions such as neurogenic bladder/spina bifida, refractory radiation cystitis, and bladder fistulae. While IC is the simplest form of urinary diversion to construct and manage long-term, early and late complications are not uncommon.[3] In one series of 1057 patients who underwent IC following radical cystectomy, 61% experienced complications, most commonly related to bowel (20%), renal (20%), infectious (17%), stomal (15%), urolithiasis (15%), metabolic (13%), or other nonstomal structural issues (12%).[4] Stomal complications typically include stenosis, prolapse, skin breakdown, and parastomal hernia. Stoma and conduit necrosis is very rare and requires urgent surgical management. Herein, we present an unusual case of late stomal necrosis in an IC.

CASE

The patient is a 46-year-old female with a history of sacral spina bifida and up shunted hydrocephalus who underwent cystectomy and IC at the age of 2. She is otherwise healthy, although is an active smoker, and her conduit had been functioning well for many years. She presented to the urology clinic with new onset protrusion around her IC stoma and intermittent lower back pain. A computed tomography (CT) scan was obtained, which revealed bilateral nonobstructing kidney stones, a long tortuous conduit and a thick-walled edematous stoma above the fascia (Fig. 1). She subsequently underwent treatment for her 8 mm left renal stone with Electrohydraulic Shockwave Lithtripsy (ESWL) and returned to the urology clinic to re-evaluate the bulge around her stoma. At that time the stoma was healthy, with a surrounding nontender bulge. While it was not a true parastomal hernia, there appeared to be redundant bowel between the fascia and skin. She was counseled that she would likely require revision, but chose to delay surgery.

One month later, she returned with increasing pain, induration, purple discoloration, and ulceration of the stoma. Endoscopy of the conduit was performed which revealed distal ischemic changes (gray-white mucosa), stenosis at the level of the fascia, and proximal healthy pink conduit mucosa. She was scheduled for elective repair, but returned to clinic several days later with an obvious necrotic stoma and severe abdominal pain. On examination at that time, the entire stoma was necrotic with sloughing tissue and a urinary-cutaneous fistula where the conduit was separating from the skin. She was admitted to the hospital for pain control and a bowel prep before taking her to operating room the following day.

She underwent exploratory laparotomy and take down of her old IC stoma (Fig. 2A) via a midline incision. We found a necrotic, friable stoma, and ischemic bowel wall above the fascia with surrounding purulent drainage. A 22 French Robnel catheter could not be passed proximally into the conduit due to a tight stricture. Once fully delineated, the conduit was spatulated along the antimesenteric border proximally, and 2 tight mid-conduit strictured areas were identified. Thus, the decision was made to resect the old IC and create a new one. Of note, during this dissection, several enlarged lymph nodes were identified in the small bowel mesentery and were assumed to be reactive. The new IC was fashioned from 20 cm of ileum in standard Bricker fashion and the stoma was placed on the left side, away from the previous infected stoma site on the right (Fig. 2B). The old stoma site fascia was closed primarily and the skin packed open.

Postoperatively course was uneventful until the fourth postoperative day. She developed significant tachycardia, tachypnea, and green-tinged drainage from her Jackson-Pratt drain but no peritoneal signs. CT scan at that time was inconclusive, and she was then transferred to the ICU for resuscitation. She then underwent celiotomy for presumed bowel leak. Two

Financial disclosures: None.

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Submitted: September 10, 2018, accepted (with revisions): September 18, 2018

https://doi.org/10.1016/j.urology.2018.09.015
0090-4295

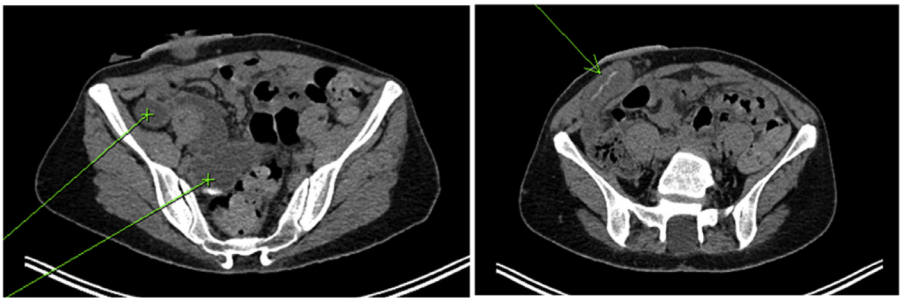

Figure 1. Preoperative CT scan (Left: arrows show redundant and elongated ileal conduit. Right: arrow shows edematous and thick-walled suprafascial conduit). (Color version available online.)

perforated areas of small bowel were found: one 10 cm proximal to the ileal-ileal stapled functional end-end anastomosis, and the other just distal to the ligament of Treitz in the proximal jejunum. The prior ileal-ileal anastomosis was resected along with the perforation and a new end-end stapled anastomosis created. Similarly, the jejunal perforation was resected and a stapled anastomosis was performed. The abdomen was washed out and was left open with a temporary abdominal closure Vacuum Assisted Closure (VAC) system in place (AB-Thera, KCI, San Antonio, TX) as part of a planned damage-control management. She was then resuscitated in the ICU and remained on vasopressors and broad-spectrum antibiotics. She was taken back to the operating room twice more; once for a washout and a second time for abdominal closure with a biologic collagen matrix. The wound and previous stoma site were left open and a wound VAC was placed. She improved clinically thereafter, was transferred to the floor and slowly advanced in diet. She was severely deconditioned from prolonged ICU stay and required extensive physical and occupational therapy.

Pathology from the initial operation and the second bowel resection returned transmural diffuse large B-cell lymphoma (DLBCL) in the IC specimen as well as the 2 perforated bowel segments. Histologic sections contained multifocal, diffuse proliferation of lymphoid cells with transmural intestinal involvement associated with mucosal ulceration and serosal changes. Immunohistochemistry was positive for proto-oncogene (MYC) (30% subset weak), CD20, BCL2 (small subset weak), BCL6, MUM1, and Ki67 (proliferative index 80%) and was negative for CD3, CD10, CD21, and CD163 (Fig. 3).

Restaging CT scan at 2 weeks postoperative noted enlarging retroperitoneal adenopathy and several subcentimeter pulmonary nodules. Seventeen days after her last surgery, she was started fractionated RCE (cyclophosphamide, etoposide, and rituximab). She tolerated her first cycle of chemotherapy well, and 3 months later was able to receive a second cycle of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone. Unfortunately, her course over the next months was complicated by multiple issues including neutropenic sepsis, enterocutaneous fistula requiring

Figure 2. Left: Preoperative appearance of necrotic stoma. Right: Immediate postoperative appearance of new left-sided ileal conduit stoma. (Color version available online.)

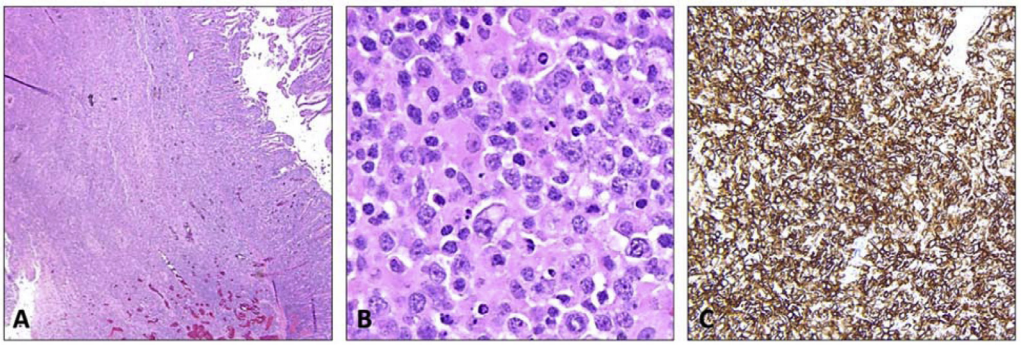

Figure 3. Histology of small bowel and lymph node specimens. (**A**) Hemotoxylin and eosin (H&E) stained section of small bowel (mucosa upper right) showing lymphoma infiltrating and disrupting the submucosa. (**B**) High power view of H&E-stained lymph node showing large, highly atypical lymphocytes, diffuse apoptotic debris, and mitotic figures, indicating rapid proliferation. (**C**) CD20 IHC stain confirming neoplastic cells are of B-cell origin [T-cell markers were negative]. (Color version available online.)

prolonged Non Per Os (NPO) status and total parenteral nutrition, persistent abdominal abscesses requiring drain placement, and intravenous antibiotics, and poor wound healing requiring skin grafting. To date, the patient is alive, receiving palliative care with no further plans for additional chemotherapy.

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Of the typical delayed complications related to IC construction, stomal necrosis, and lymphoma are exceedingly rare. In the literature, there have only been 2 reported cases of DLBCL presenting in an ileal urinary diversion—1 patient was a 76-year-old man with a 12-year-old IC and the other patient was a 78-year-old man with a 15-year-old ileal neobladder.[5,6] This is the youngest patient, first woman, and first life-long urinary diversion to develop lymphoma of the conduit.

Primary gastrointestinal non-Hodgkin's lymphoma (PGI NHL) is the most common extranodal lymphoma (30%-45%), and DLBCL is the most common type of PGI NHL (59%-71%).[7,8] The incidence in the United States is approximately 7 cases per 1,00,000 people per year. In fact, DLBCL is a heterogenous group of tumors that consists of morphologically and genetically unique lymphomas which are defined by large, transformed B cells with diffuse growth patterns and high proliferation rates. These cases typically present with abdominal pain, B-symptoms (weight loss, fever, and night sweats), GI bleeding, obstruction and/or bowel perforation.

There are several known predisposing conditions to PGI NHL including *Helicobacter pylori* infection, autoimmune disease, immunosuppression, Celiac disease, and inflammatory bowel disease.[9] Ultimately, the cause of intestinal lymphoma in most patients is unknown. Interestingly, in a Middle Eastern series of adults with primary small intestinal lymphoma, lower socioeconomic status, poor sanitation, endemic parasite infection, and infantile infectious enteritis were identified as risk factors.[10] Perhaps by similar mechanisms, chronic inflammation and recurrent infections within an IC could contribute to lymphoma risk.

Overall prognosis of patients with DLBCL is variable. The disease is curable in about half of patients using the rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone chemotherapy regimen. Rituximab has revolutionized the treatment of DLBCL. The drug is a monoclonal antibody that targets CD20 on the cell surface of B-cell lymphomas. In multiple clinical trials, the drug confers a 10%-15% increased overall survival advantage with minimal additional toxicity as compared to standard chemotherapy.[11] Unresponsive or relapsed cases of DLBCL are treated with high-dose chemotherapy and autologous hematopoietic cell transplantation. The International Prognostic Index score is widely used to determine risk.[12] The International Prognostic Index is a 5-point scale that includes the following factors: age (above or below 60), lactate dehydrogenase (elevated or normal), performance status Eastern Cooperative Oncology Group (ECOG) above or below 2), Ann Arbor stage (I/II or III/IV), and the number of extranodal involvements (0-1 or >1). Given our patient's poor performance status, high grade tumor and multiple extranodal sites, her score of 3 predicts a 5-year overall survival of only 43%.

While bowel perforation is rare, occurring in 9%-25% of PGI NHL, it is a devastating complication with about half of patients dying from sepsis.[13,14] In our patient, resection of her necrotic IC was unfortunately followed by multisite bowel perforation related to DLBCL. There is a lack of evidence as to the optimal timing of surgery and subsequent chemotherapy for patients with perforated PGI NHL, but in a sick patient with a bowel perforation, source control must be attempted. The largest reported series of bowel lymphoma perforations is 92 patients from the Mayo Clinic.[15] In these patients, half of perforations occurred as the initial presentation of intestinal

lymphoma and the other half occurred during treatment with chemotherapy. Ultimately, 60% of patients with perforation died, with half of those related to the perforation or subsequent complications, and the other half related to disease progression or relapse.

CONCLUSION

Awareness of PGI NHL and DLBCL is important for urologists who care for patients with ICs. Stomal complications and bowel perforation related to these conditions can result in significant morbidity and mortality.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.urology.2018.09.015.

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