

Oncology

Renal Transplantation in the Setting of Prior Urinary Diversion: A Case of Poorly Differentiated Adenocarcinoma in an Ileal Conduit

R.S. Matulewicz^{a,*}, J.P. Fryer^b, X.J. Yang^c, R. Goyal^c, J.C. Hairston^a^a Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA^b Department of Surgery, Kovler Organ Transplantation Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA^c Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

ARTICLE INFO

Article history:

Received 8 December 2014

Received in revised form

30 December 2014

Accepted 2 January 2015

Available online 7 February 2015

Keywords:

Cystectomy

Ileal conduit

Neuroendocrine tumor

Urinary diversion

ABSTRACT

Though rare, renal transplantation into a bowel containing urinary diversion is necessary in select clinical situations. Compared to renal transplant patients with functional native bladders, patients with urinary diversion have comparable long-term graft and patient survival rates. However, compounding the increased risk of malignancy in those on chronic immunosuppression are the inherent risks of urinary diversion. We present a case report of a high grade adenocarcinoma with neuroendocrine differentiation arising in an ileal conduit and discussion on the pathophysiology, management, and screening of this highly select population.

© 2015 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Background

Renal transplantation into a bowel containing urinary diversion is necessary in select clinical situations. It is estimated that roughly 15% of patients with end-stage renal disease will have some structural abnormality of the lower urinary tract causing dysfunction, with some requiring urinary diversion.¹ Large single institution studies have shown that long-term graft and patient survival rates are comparable in renal transplant patients with urinary diversion to those with functional native bladders.² Regardless, bowel containing urinary diversions have known short and long term complications and solid organ transplants carry an increased risk of malignancy due to chronic immunosuppression. We present a case of a rare adenocarcinoma arising in a bowel containing urinary diversion draining a transplanted renal allograft.

Case report

The patient is a 47 year old male with a history of ileal conduit urinary diversion in 1978 and renal transplantation (on

azathioprine, prednisone) in 1980. His genitourinary abnormalities and end-stage renal disease were presumed to be congenital in origin secondary to posterior urethral valves, although no records were available. He first presented at our institution in June of 2009 with obstruction of the ileal conduit approximately 2.5 cm proximal to the stoma site (Fig. 1) and *Pseudomonas aeruginosa* pyelonephritis. He was treated with a percutaneous nephrostomy tube for maximal decompression and antibiotics. Subsequent dilation of the conduit stricture and placement of a single-J ureteral stent were unsuccessful secondary to early recurrence of the stricture. Definitive treatment with exploration and revision of his conduit were undertaken, which was complicated by significant and extensive scarring around the kidney and conduit. Intraoperatively a solid mass was discovered at the stricture site and was resected along with a limited lymph node dissection. The final pathologic diagnosis was high-grade adenocarcinoma with neuroendocrine features, positive margins, and all three lymph nodes negative (Fig. 2).

Follow up PET scans revealed increased uptake around the conduit area shortly after surgery. Subsequent surveillance PET scans demonstrated the development of multiple liver lesions consistent with metastasis, as well as soft tissue nodules adjacent to the prior surgical site and the abdominal wall. The patient was started on chemotherapy, but progressed on two different regimens until he entered hospice care and passed away roughly 2 years after his initial presentation at our institution.

* Corresponding author. Tel.: +1 312 695 7141.

E-mail address: Richard.Matulewicz@northwestern.edu (R.S. Matulewicz).

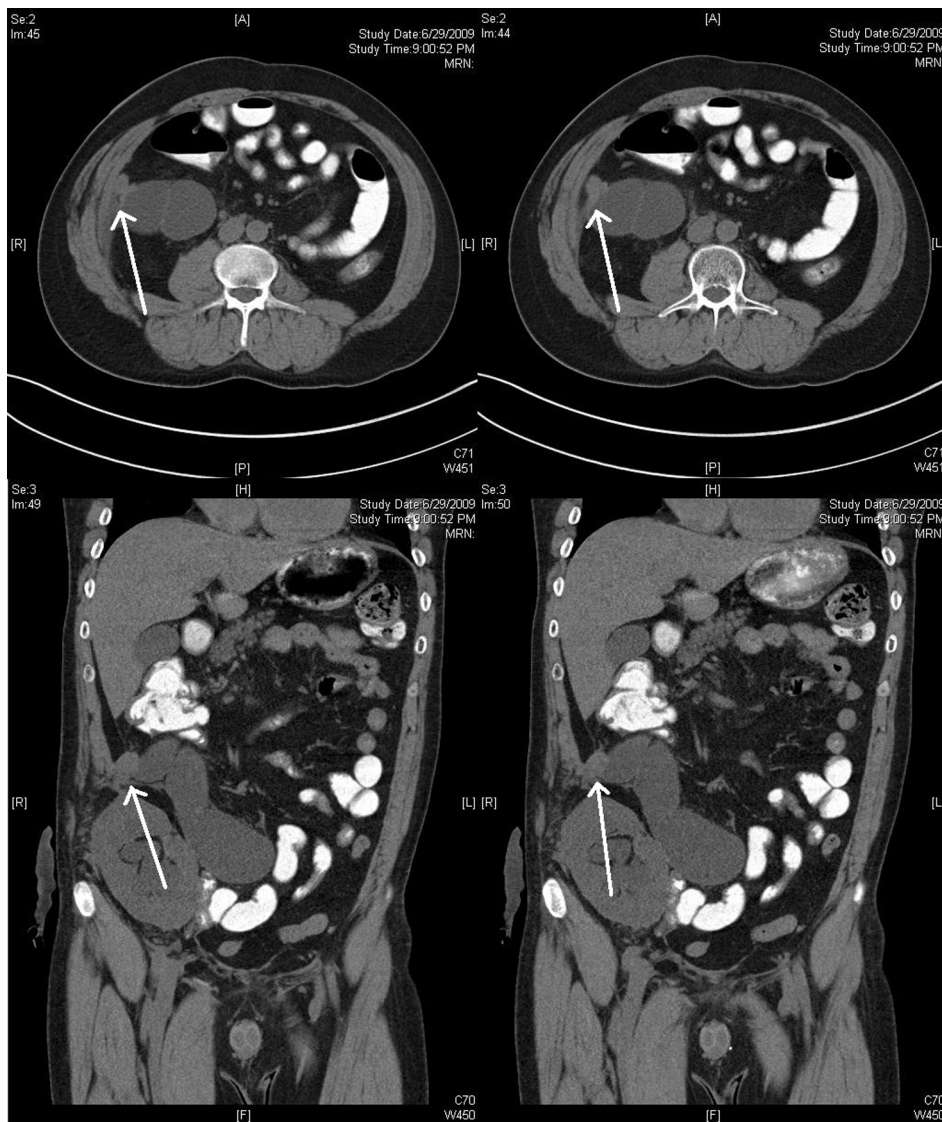


Figure 1. Representative coronal and axial images of stricture seen in ileal conduit on the patient's initial presentation. The images are notable for significant dilatation of the proximal aspect of the conduit and moderate hydronephrosis of the transplant kidney. White arrow depicts area of narrowing seen in both planes.

Discussion

Fewer than 100 cases of new primary malignancy in a urinary diversion using isolated bowel segments have been reported in the literature. In ileal conduits specifically, only twelve cases have been reported, three of which were adenocarcinomas and two were carcinoid tumors.³ Notably, none of these were in the setting of prior renal transplantation. To date, using an Ovid-Medline search, no report of a poorly differentiated neuroendocrine tumor arising in a urinary diversion has been described.

The exact mechanism of carcinogenesis in urinary diversions is unclear, but it is likely multi-factorial. Several animal studies have shown the carcinogenic effect of urine on intestinal mucosa due to the chronic stasis of urinary bacteria, especially gram-negative bacteria that are able to form N-nitrosamines.⁴ This, in addition to the known pro-inflammatory reaction formed by even sterile urine on intestinal epithelium, may explain the oncologic potential in these intestinal segments. This patient was a short-term smoker (5 pack years, quit 4 years prior to presentation) with no occupational/environmental exposures or personal risk factors known to be

associated with malignant changes to the urothelium or bowel. Importantly, he had no personal or family history of Crohn's disease, celiac disease, or familial adenomatous polyposis syndrome.

In the transplanted population however, chronic immunosuppression is a known risk factor for the development of any malignancy and the overall incidence of cancer after renal transplantation is considerably higher than the general population. The proper screening protocol for post-renal transplant patients has not yet been elucidated as limited data exists for this population. Proper screening can be inferred based on evidence based standards in both the bladder cancer population and for small bowel malignancy. Combining these principles with a high clinical suspicion for this atypical presentation will aid in earlier diagnosis. No standard screening protocols are available for primary small bowel cancers, but an early warning sign is a positive fecal occult blood test. Therefore, microhematuria in a post-transplant patient with a urinary diversion should not be ignored. In post-cystectomy patients for bladder cancer, the NCCN guidelines suggest a urine cytology test every 3 months, alongside axial imaging in the initial 2 year post-operative period with the goal of detecting upper tract

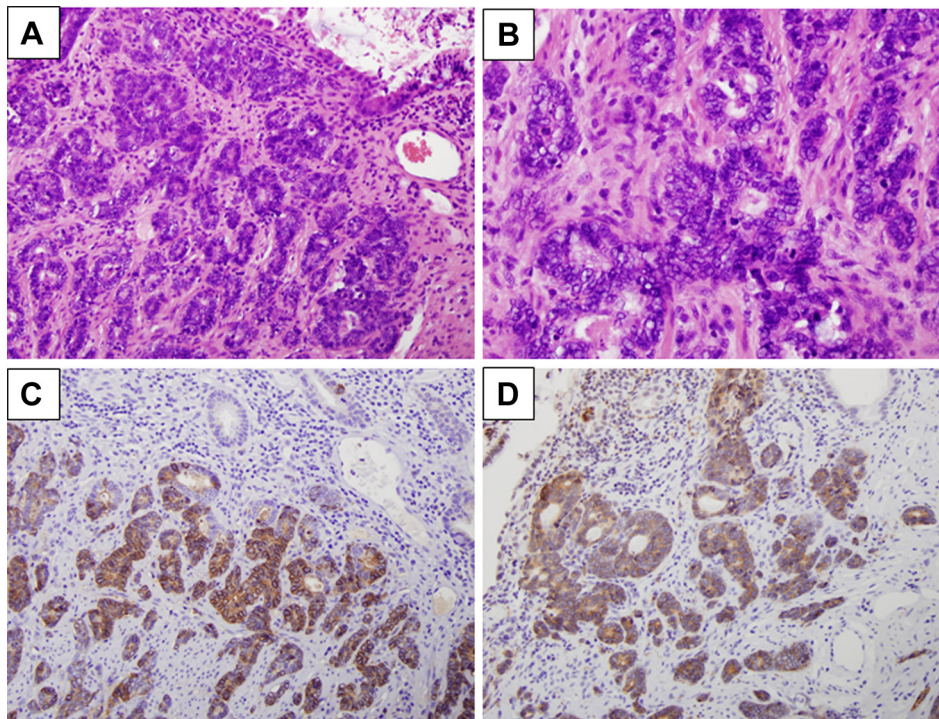


Figure 2. Adenocarcinoma with neuroendocrine differentiation (grade 3) of the ileal conduit infiltrating the lamina propria (A) and muscularis propria. The tumor shows glandular differentiation and high mitotic activity (B). The tumor cells are positive for chromogranin (C) and synaptophysin (D).

recurrences (typical prevalence between 1% and 6%). This surveillance protocol would be minimally invasive, but repeated contrast administration could potentially threaten the transplant allograft. It should be noted that it would be less necessary to screen for upper tract urothelial carcinoma in patients without a history of bladder cancer, as in this population.

There are differences in the timing of surgical complications seen with anastomotic strictures versus conduit strictures. This timing difference could help differentiate whether there is a technical issue (early stricture at anastomosis) or something more concerning like a cancer recurrence (in conduit). In a large series with long-term follow up a rate of anastomotic stricture was seen roughly 10% of the time at a median of 1.1 years. Conduit stricture was much less common, occurring 2.4% of the time at a median of 9.4 years.⁵

Clinical suspicion must be high in patients presenting with worsening hydronephrosis, hematuria, or recurrent UTIs. Although no evidence based screening regimen is available, the authors suggest a combination of urinalysis to check for microhematuria, urine cytology, axial imaging, and direct visual surveillance with looposcopy or loopogram to follow these patients.

Disclosures

The authors of this manuscript have no conflicts of interest to disclose.

Acknowledgment

None.

References

1. Cerilli J, Anderson GW, Evans WE, Smith JP. Renal transplantation in patients with urinary tract abnormalities. *Surgery*. 1976;79:248.
2. Surange RS, Johnson RW, Tavakoli A, et al. Kidney transplantation into an ileal conduit: A single center experience of 59 cases. *J Urol*. 2003;170:1727.
3. Austen M, Kalble T. Secondary malignancies in different forms of urinary diversion using isolated gut. *J Urol*. 2004;172:831.
4. Malone MJ, Izes JK, Hurley LJ. Carcinogenesis. The fate of intestinal segments used in urinary reconstruction. *Urol Clin North Am*. 1997;24:723.
5. Shimko MS, Tollefson MK, Umbreit EC, Farmer SA, Blute ML, Frank I. Long-term complications of conduit urinary diversion. *J Urol*. 2011;185:562.