

Oncology

Transurethral resection and surveillance of a well-differentiated neuroendocrine tumor in a ileal neobladder

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ABSTRACT

Our patient presented with a small, well-differentiated neuroendocrine tumor (NET) of the ileal neobladder 21-years after radical cystectomy for urothelial cell carcinoma. Given the rarity of NETs in urinary diversions, there are no established guidelines regarding management in this unique population. We propose that transurethral resection and close cystoscopic surveillance of the neobladder is a feasible, low morbidity approach to management of a well-differentiated, solitary ileal NET tumor.

Introduction

Small intestinal neuroendocrine tumors (NET) are neoplasms arising from intraepithelial endocrine cells with a reported prevalence of 5.25/100,000 individuals in the United States.¹ In rare cases, NETs have been reported to form in the segment of bowel used for urinary diversions. There are no established guidelines regarding management in this unique population and all prior cases have undergone extirpative therapy with either partial or complete surgical excision of the urinary diversion [Table 1]. We present a case of transurethral resection and surveillance for a patient who presented with a solitary, well-differentiated NET within his ileal neobladder.

Case presentation

A 69-year old male who had undergone radical cystectomy with ileal neobladder 21 years ago for pT2N0MxR0 urothelial carcinoma presented with new onset of nocturnal urgency. His tumor was noted to be p53 positive and he was recommended for adjuvant chemotherapy, which he declined. He was initially surveilled with cross-sectional imaging of his abdomen/pelvis and chest x-rays for two years after surgery without evidence of recurrence and was subsequently lost to follow up.

At time of presentation, his urinalysis was without hematuria and his post void residual was minimal. His renal function was normal with a glomerular filtration rate of 87 mL/min. CT urogram revealed post-cystectomy changes without evidence of recurrence or other

abnormalities. Cystoscopic evaluation of his neobladder demonstrated a small lesion of the right lateral wall and a large, capacious neobladder, likely due to chronic retention. This lesion was resected and measured 0.5 × 0.5 × 0.4 cm in size. Pathologic evaluation demonstrated amphophilic cytoplasm, bland nuclear features, stippled “salt and pepper” chromatin, + CD56, and no mitotic activity, all features consistent with a well-differentiated NET [Fig. 1]. Bladder wash cytology was unremarkable. Six weeks following his first resection, he underwent repeat biopsy of the previous resection site, which was without evidence of malignancy.

Management options were discussed with the patient, including excision of the neobladder with intraoperative examination of the small bowel and lymphadenectomy or close surveillance with cystoscopy and imaging. The patient’s nocturnal urinary symptoms resolved with more frequent emptying of his neobladder. The patient opted for observation and at 12 months from initial diagnosis, is asymptomatic and well.

Discussion

Patients with small intestinal NETs most commonly present with some combination of abdominal pain, melena, anemia, diarrhea and/or small bowel obstruction. Presentation with carcinoid syndrome is rare and only observed in 1.6% of patients with NETs. Compared to NETs of other primary sites, ileojejunal NETs are more symptomatic than NETs of other sites with higher rates of patients presenting with carcinoid syndrome and abdominal pain.² Features associated with poor prognosis

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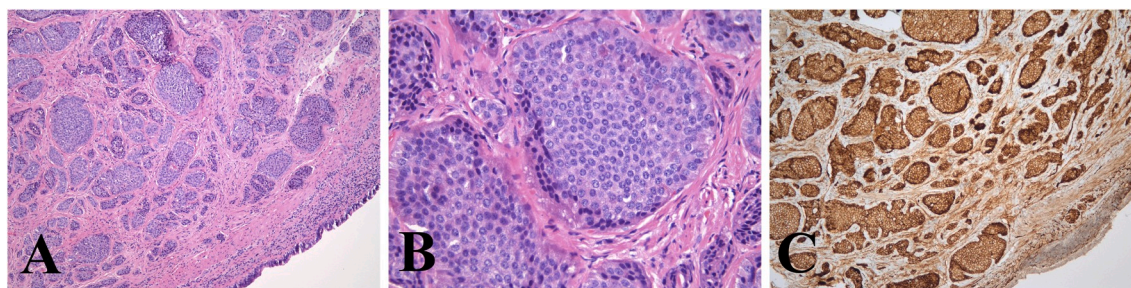
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Table 1

Case reports of NET from ileal urinary diversions.

Case Report	Latency (years)	Original indication (diversion)	Presenting Symptoms	Tumor Size (mm)	Tumor Description	Tumor Site	Treatment	Reference
Klink et al. (2006)	28	Cervical adenocarcinoma (ileal conduit)	Gross Hematuria	7	Carcinoid	Midsegment ileal conduit	Excision of ileal conduit and new conduit formation	Klink J, Rutland H, Harik L, Ogan K. Primary carcinoid tumor in an ileal conduit. <i>Urology</i> . 68 (3):673e9-10, 2006.
Frese et al. (2001)	6	Urothelial Carcinoma (ileal neobladder)	Cystoscopic surveillance	8	Well Differentiated NET	Posterior neobladder	Resection and ileal conduit creation	Frese R, Doehn C, Baumgartel M, Holl-Ulrich K, Jocham D. Carcinoid tumor in an neobladder. <i>J Urol</i> . 165(5):522-3, 2001.
Kerfoot et al. (1999)	9	Adenocarcinoma of the bladder (ileal conduit)	Bilateral Flank pain, Ileal conduit stenosis	8	Carcinoid	Midsegment ileal conduit	Resection of ileal conduit stenosis with primary repair	Kerfoot BP, Steele GS, Datta MW, Richie JP. Carcinoid tumor in an ileal conduit diversion. <i>J Urol</i> . 162(5): 1685-6, 1999.
Kochevar et al. (1984)	12	Cervical adenocarcinoma causing ureteral stenosis (ileal ureter)	Pyelonephritis, Right hydronephrosis	N/A	Adenocarcinoid, goblet cell	Ureterointestinal anastomosis	Resection of stenotic ureter with ileal cuff, right ureteral reimplantation into conduit	Kochevar J. Adenocarcinoid tumor, goblet cell type, arising from a ureteroileal conduit: a case report. <i>J Urol</i> . 131(5):957-9. 1984.
Mellis et al. (2011)	3	Neurogenic bladder (ileovesicostomy)	Hematuria	8	Well Differentiated NET	Enterovesical anastomosis	Excision of proximal end and conversion to ileal conduit	Mellis AM, Parker DC, Bueth DD, Slobodov G. Primary Carcinoid Tumor of the Ileal Efferent Limb of an Ileovesicostomy: A Case Report. <i>Case Rep Urol</i> . 2011.

**Fig. 1.** Neuroendocrine Tumor of the Ileal Neobladder.

A. H&E stain (10x) – Nests of monotonous small cells beneath an intestinal-type neobladder mucosa B. H&E stain (40x) – higher magnification demonstrates amphophilic cytoplasm, bland nuclear features, stippled “salt and pepper” chromatin C. Cell stain diffusely positive for neuroendocrine marker CD 56.

include distant metastases, larger primary lesion size, high mitotic rate, tumor multiplicity, high depth of invasion, and presence of carcinoid syndrome.³ The location of the primary tumor has been shown to be a strong predictor of outcomes in patients with NET; those with primary liver NETs have the lowest overall survival rates.¹ Small bowel NETs have been traditionally divided into duodenal and ileojejunal sections for treatment and prognosis. Ileojejunal NETs are more likely to present at a more advanced stage when compared to duodenal NETs; however, the overall survival between well-differentiated duodenal and ileojejunal tumors is similar for localized, regional, and metastatic disease.^{1,2} We postulate that the difference in stage of initial presentation may be due to earlier detection with duodenal NETs. However, the malignant potential of well-differentiated duodenal and ileojejunal NETs is similar when considering overall survival.

The 2019 National Comprehensive Cancer Network (NCCN) guidelines recommend a multiphasic abdominal and pelvic CT or MRI for initial work up of NETs of the gastrointestinal tract.⁴ Further work up including endoscopic visualization with colonoscopy or EGD, biochemical evaluation, and/or somatostatin-receptor based imaging is recommended if there are clinical indications. Our patient's tri-phasic

CT urogram was unremarkable. No further work up was pursued as he did not exhibit any signs or symptoms of carcinoid syndrome, metastatic spread, or secondary tumor.

Bowel resection with regional lymphadenectomy and intraoperative examination of the entire bowel is the standard of care for locoregional NETs of the ileum. Endoscopic mucosal resection is only recommended for duodenal NETs of the gastrointestinal tract with favorable characteristics including tumors that are limited to the submucosal layer, <10mm in size, and with low mitotic rates. In contrast, endoscopic surveillance and resection of ileojejunal NETs is technically difficult compared to those of the duodenum—neither the NCCN nor the European Neuroendocrine Tumor Society (ENETS) guidelines recommend endoscopic management of ileal tumors.^{4,5} Capsule endoscopy is possible for surveillance, but does not provide full visualization of the bowel and does not allow for resection. However, in patients with ileal neobladder, both resection and surveillance of the ileum are possible through the transurethral route.

There have been five previously published case reports of NETs arising from ileal urinary diversions [Table 1]. To our knowledge, this is the first case of NET arising from an ileal neobladder managed with

transurethral resection and observation.

Conclusion

Our patient's ileal tumor demonstrated all favorable tumor characteristics: well-differentiated NET limited to the submucosa, 5 mm in size and with no mitotic activity. We confirmed complete excision with repeat resection of the biopsy site, which was without residual malignancy. Given the rarity of NETs of urinary diversions, there are no established guidelines regarding management in this unique population. We propose that in cases with favorable pathologic features and initial R0 resection, close surveillance with regular cystoscopic evaluation of the neobladder is a feasible, low morbidity approach to management of these tumors. However, we propose that cases where transurethral resection reveals NET with unfavorable pathologic features should be managed with excision of the ileal neobladder with intraoperative examination of the entire small bowel and regional lymphadenectomy.

Consent

The patient has given his consent for the publication of this case.

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Declaration of competing interest

The authors declare that they have no conflicts of interest to report.

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