Neuroendocrine tumor causing ureteral obstruction in a patient with prior ileal conduit

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Acquired hydronephrosis following cystectomy and ileal conduit urinary diversion for bladder cancer is most commonly caused by stricture of the ureter or the ureteroenteric anastomosis. Nevertheless, malignant obstruction due to ureteral tumor recurrence must be ruled out. Neuroendocrine tumors of the ureter are extremely rare and an unlikely cause of hydronephrosis in this setting. We present the first reported case of a patient with a history of bladder cancer and an ileal conduit presenting with hydronephrosis secondary to an obstructing carcinoid tumor of the ureter.

Key Words: carcinoid tumor, neuroendocrine, ureter, ileal conduit, hydronephrosis

Introduction:

In patients with a history of bladder cancer treated with cystectomy and ileal conduit diversion, worsening unilateral hydronephrosis is typically due to upper tract stricture or disease recurrence. Ureteroenteric anastomotic strictures have been reported in up to 15% of patients and are the result of tissue ischemia at the time of surgery with resultant fibrosis.[1] Whereas benign strictures often occur in the first year after surgery, malignant strictures are more common 3 years or more after surgery. Malignant strictures have a lifetime incidence of 1%-8% following cystectomy and most commonly represent recurrent urothelial carcinoma.[2] However, cases of malignant stricture from a second primary tumor are extremely rare. The following case demonstrates an instance of ureteral obstruction due to late recurrence of metastatic carcinoid tumor, thus highlighting the need to consider alternative etiologies for ureteral stricture in patients with a history of multiple cancers.

Case report

A 62-year-old male with an ileal conduit presented to the Emergency Department with right-sided hydronephrosis and urosepsis. Five years prior, the patient underwent robotic-assisted radical cystoprostatectomy with ileal conduit diversion for T2bN0M0 urothelial carcinoma of the bladder. At the time of cystectomy, several lesions within the proximal ileum were identified and a small bowel resection was performed. Additional lesions throughout the small bowel and at the root of the mesentery were also noted but were felt to be unresectable due to the risk of short gut syndrome. Final pathology revealed well-differentiated carcinoid tumor within the small bowel as well as in a single lymph node. The patient

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was treated with octreotide injections after recovering from surgery, and a subsequent octreotide scan was ultimately negative for residual somatostatin receptor positive tumor foci.

The patient was followed routinely and did well for years until several months prior to presentation when he developed recurrent episodes of right pyelonephritis. A CT with IV contrast revealed moderate right hydroureteronephrosis without any definitive source of obstruction. Though right renal function was preserved at 44% on MAG-3 renogram with Lasix, the right hydroureteronephrosis was obstructive in nature based on a T½ greater than 20 minutes. Consequently, a right percutaneous nephrostomy tube was placed for decompression of the infected collecting system. Subsequent right antegrade ureteroscopy revealed a distal right ureteral stricture due to an irregular soft tissue mass. Biopsies of the mass and ureteral washings for cytology were negative for urothelial carcinoma. Suspicion for tumor recurrence was low based on the long postoperative interval and unremarkable work up, so the patient underwent robotic-assisted laparoscopic right distal ureterectomy with ureteral reimplantation into the ileal conduit. An appendectomy was also performed due to concern for devascularization of the appendix after ureterolysis. Final pathology of both the ureteral and appendiceal specimens revealed well-differentiated neuroendocrine carcinoma (carcinoid tumor) within the muscular propria with negative margins and no evidence of urothelial carcinoma. Overall, the patient did well postoperatively and did not undergo any genetic testing. He was last seen in clinic 6 months after surgery with no evidence of disease, no further episodes of pyelonephritis, and a MAG-3 renogram with Lasix showing no ureteral obstruction.

Discussion

Well-differentiated neuroendocrine tumors (NETs), or carcinoid tumors, represent the benign end of a spectrum of neoplasms that include moderately-differentiated (atypical carcinoids) and poorly-differentiated NETs (malignant carcinoids). Carcinoid tumors are rare NETs with an age-adjusted incidence of 4.7/100,000 nonpancreatic primaries in the United States, but the incidence is rising.[3] These tumors are found most often in the gastrointestinal tract—typically the ileum or appendix—or lungs, but may occasionally originate from or more rarely metastasize to the genitourinary tract. NETs represent only about 0.05% of genitourinary tract malignancies and usually originate within the bladder. Primary ureteral NETs are exceptionally uncommon with fewer than 40 cases described in the literature.[4] To our knowledge, our patient represents only the second case of metachronous carcinoid tumor metastasizing to the ureter reported in the literature. It is unique not only because of the patient's late relapse, but also because it represents the first description of ureteral carcinoid tumor in a patient with an ileal conduit.

Ureteral carcinoid tumors tend to present in the sixth or seventh decade of life without a clear gender predilection. Much like upper tract urothelial carcinoma, initial presentation frequently includes unilateral flank pain and hematuria, but symptom severity is highly variable. Interestingly, the classic triad of flushing, diarrhea, and wheezing described in other non-midgut carcinoid tumors is generally not associated with genitourinary carcinoids. In fact, upper tract NETs may be asymptomatic and are most often detected on computed tomography or magnetic resonance imaging. Incidentally, these imaging modalities are also helpful for staging, as up to 45% of patients may have locally advanced disease and/or lymph node metastasis at the time of diagnosis.[5]

Urine cytology may reveal malignant neuroendocrine cells in cases of malignant carcinoids, but cytology is typically negative in well-differentiated carcinoids, as in this case. Similarly, tumor markers are of little utility.

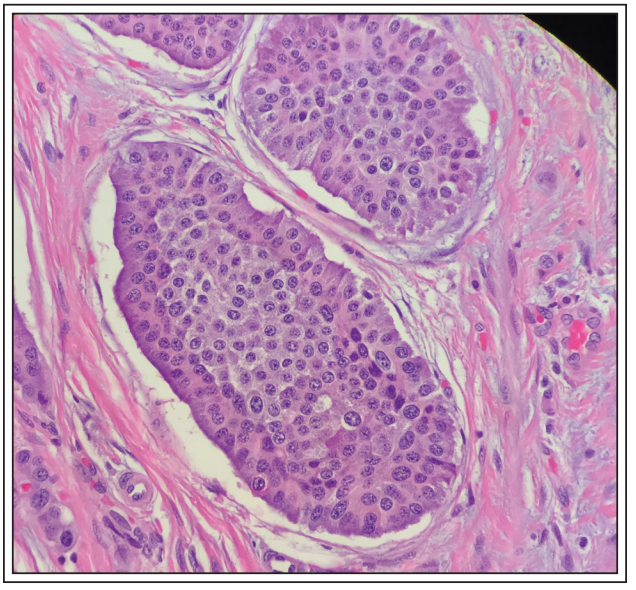

Figure 1. Microscopic examination of right ureter at 400X magnification using H&E stain demonstrating the characteristic features of carcinoid tumor with nests composed of small cells with uniform, round nuclei and "salt and pepper" chromatin in the submucosa and muscular propria.

Instead, definitive diagnosis requires tumor resection and histopathologic examination. Well-differentiated carcinoids differ from malignant carcinoids by having fewer mitoses, a lower Ki-67 index, and low-grade nuclear atypia with "salt-and-pepper" chromatin, Figure 1. Cell patterns include rosettes, nests, and trabeculae and an accompanying desmoplastic reaction is frequently seen.[6] As with other NETs, immunohistochemical staining is classically positive for synaptophysin, chromogranin A, CD-56, and neuron-specific enolase. Uroplakin III positivity, often seen in urothelial carcinoma, may rule out the presence of NETs, which are negative for uroplakin III.[7]

Regarding treatment, traditional therapeutic regimens for primary ureteral NETs tend to incorporate either neoadjuvant or adjuvant cisplatin-based chemotherapy along with nephroureterectomy. Alternate regimens have included neoadjuvant irinotecan or alternating ifosfamide/doxorubicin and etoposide/cisplatin. In general, chemotherapy combined with surgery has yielded favorable survival relative to surgery alone. In the case of known metastatic disease, however, chemotherapy alone may be preferred.

Previous studies suggest a poor prognosis for ureteral NETs with frequent relapses and overall survival typically less than 24 months. Stage at diagnosis remains the biggest predictor of long term survival. During our literature review, however, we identified five cases of carcinoid tumor in the setting of prior intestinal urinary diversion (three in an ileal conduit, one in an ileal neobladder,[8] and one in an ileovesicostomy[9]), and in most cases outcomes were excellent, requiring no further treatment beyond tumor resection. Similarly, our patient has fared well thus far with no evidence of recurrence since surgery. This suggests that solitary carcinoid lesions of the urinary tract, whether representing a new primary malignancy or an isolated recurrence, may be effectively treated with surgery alone. □

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