

Signet-Ring Cell Carcinoma of the Urinary Bladder Mimicking Retroperitoneal Fibrosis

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ABSTRACT

We present the case of a 77-year-old white woman with a past medical history of transitional cell carcinoma of the urinary bladder that presented with symptoms of acute renal failure and duodenal obstruction and posed a diagnostic dilemma. Initially, she presented with bilateral ureteral strictures and eventually required bilateral nephrostomy tubes. Later, the patient developed intractable nausea and vomiting secondary to a duodenal stricture. The finding of a “stranding appearance” on computed tomography imaging of the retroperitoneal space raised the suspicion of retroperitoneal fibrosis. Subsequent endoscopic placement of metal stents to relieve the duodenal obstruction failed to relieve her symptoms. The patient’s poor general condition precluded an exploratory laparotomy. The patient expired shortly thereafter and an autopsy was performed. The autopsy results revealed full wall thickness signet-ring cell carcinoma of the urinary bladder with extensive metastasis to the retroperitoneum.

INTRODUCTION

Primary signet-ring cell carcinoma (PSRCC) is a rare neoplasm of the urinary bladder. Approximately 70 cases have been reported since Saphir reported the first 2 cases in 1955.^{1,2} We report the case of a woman presenting with acute renal failure (ARF) and severe nausea and vomiting who was initially suspected to have retroperitoneal fibrosis (RF), but on autopsy was found to have PRSCC of the urinary bladder that had advanced

into the retroperitoneum resulting in bilateral ureteral obstruction as well as duodenal obstruction.

CASE REPORT

A 77-year-old white woman with a past medical history significant for high-grade superficial transitional cell carcinoma (TCC) of the bladder presented at another hospital for congestive heart failure and ARF. A non-contrast abdominal computed tomography (CT) scan at that time revealed bilateral hydronephrosis with no evidence of metastatic disease in the retroperitoneum to explain her ureteral obstruction. Subsequently, a urologist was consulted and then performed a cystoscopy and placed bilateral ureteral stents. The cystoscopy was reported as normal, and urine cytology from the bladder, as well as both ureters, was negative for TCC. Initially the patient’s serum creatinine level was 6.0 mg/dl but it fell to 1.3 mg/dl 48 hours after placement of ureteral stents. A day later, the patient developed nausea and vomiting, and the serum creatinine level once again began to rise. At this point, bilateral nephrostomy tubes were placed, and the patient was transferred to our institution for further care.

On admission, the patient received supportive care including intravenous fluids, anti-emetics, and total parenteral nutrition. The patient’s laboratory studies were remarkable for a creatinine of 1.4 mg/dL, a lipase of 1445 U/L (normal 0-160), an albumin of 2.6 g/dL, and minor electrolyte abnormalities including a low bicarbonate level of 19 mmol/L. The patient had severe nausea and persistent vomiting with abdominal pain and distention but without diarrhea. The initial workup included an esophagogastroduodenoscopy (EGD) and a colonoscopy, which showed increased gastric distention and sigmoid diverticulosis. No other abnormalities were identified. A nasogastric tube was placed and the patient continued to emit a large amount of secretions.

A contrast-enhanced CT scan of the abdomen revealed abnormal tissue stranding of the retroperitoneal fat extending from the urinary bladder to the head of

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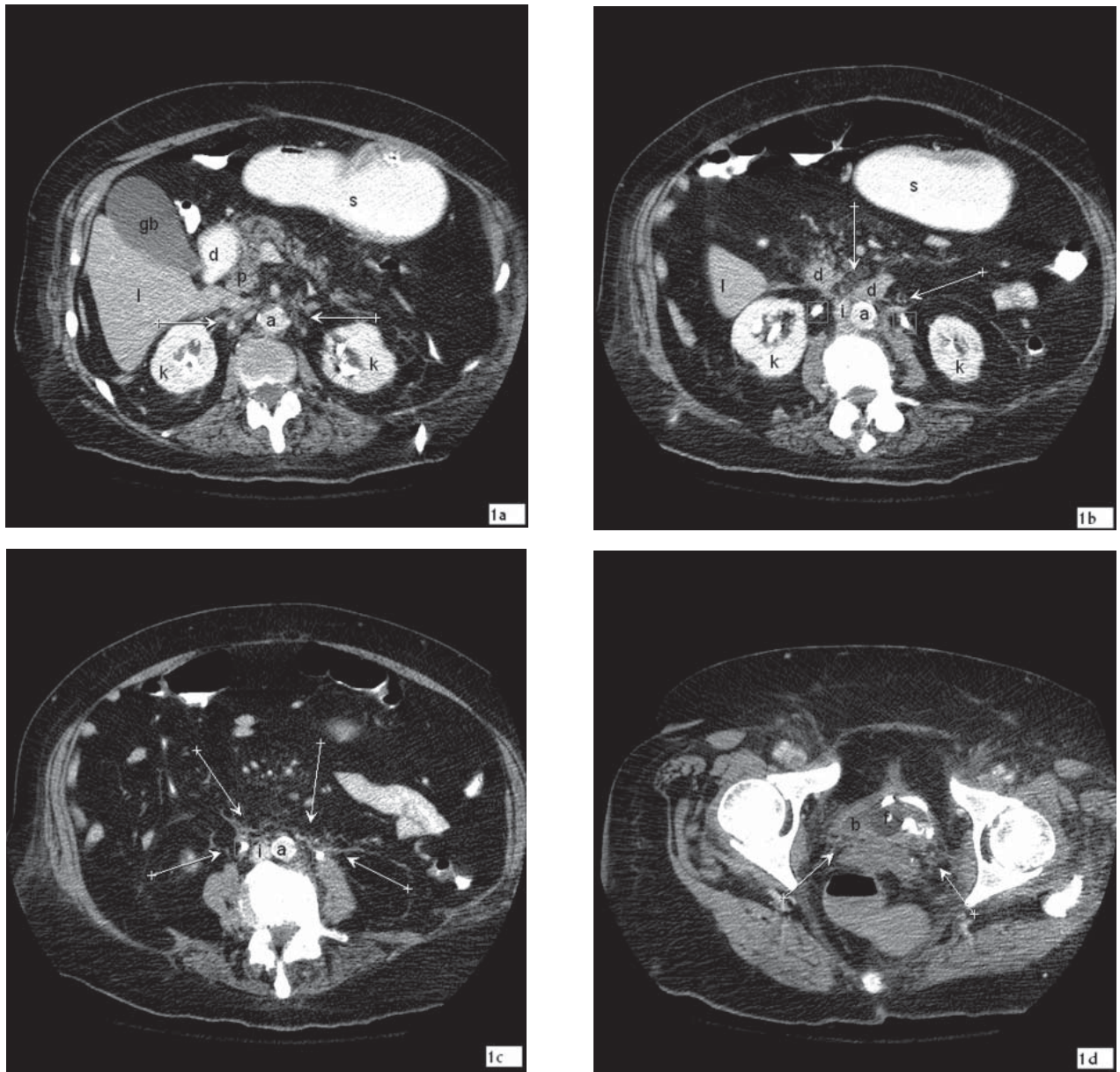


Figure 1 (a-d). Four axial CT images that show abnormal tissue (arrows) stranding the retroperitoneal fat extending from the urinary bladder to the level of the head of the pancreas. At the level of the head of the pancreas (1a), the stomach and duodenum are mildly distended. At the level of the transverse portion of the duodenum (1b), the duodenum is encased by the abnormal tissue in the retroperitoneum. Inferior to the level of the kidneys (1c), the ureters, which are of high-attenuation because of bilateral ureteral stents, are encased. At the level of the bladder (1d), strands of soft-tissue extend from the bladder into the retroperitoneal fat; high attenuation ureteral stents and a foley catheter balloon are present in the bladder. [a=aorta, b=bladder, d=duodenum, f=foley catheter balloon, gb=gallbladder, i=inferior vena cava, k=kidneys, l=liver, p=pancreas, s=stomach, the ureters are shown in boxes (1b and 1c)]

the pancreas (Figure 1a-1d). An upper GI series revealed partial obstruction of the second and third segments of the duodenum. A diagnosis of RF was suspected. A few days later, a repeat EGD was performed, which revealed a tight stricture in the second segment of the duodenum. Enlarged folds of the duodenum suggested extrinsic compression. Multiple biopsies were obtained, all of which were negative for malignancy.

The patient's atenolol was discontinued due to a rare association of β -blockers with RF, and steroids were started per the rheumatology consultant's recommendations. A laboratory workup for a connective tissue disease had no positive findings. The patient's hospital course was further complicated with a diagnosis of bilateral deep venous thrombosis, a urinary tract infection, which grew *Candida*, and a gram-negative rod identified as *Morganella morganii*.

An EGD was repeated and a self-expanding metal enteral stent was placed (Wallstent 22mm wide and 90mm long) across the duodenal narrowing. However, the stent did not expand completely, secondary to a tight narrowing of the small bowel. Hence, the success of the gastric outlet obstruction relief was only partial. The stent closed completely in 48 hours and was removed. At this time, a second stent was placed endoscopically. It also failed to remain patent and closed within 24 hours. The patient refused to undergo a biopsy of the retroperitoneum for further workup of suspected RF. The urology consultant recommended surgery to intraperitonealize the ureters and construction of an ileal conduit for urinary diversion. However, the patient did not consent to any further surgical procedures and the goals of care were changed to palliation. The patient expired shortly after discharge from the hospital.

An autopsy was performed, revealing signet-ring cell carcinoma involving the full thickness of the urinary bladder, right ovary, bilateral fallopian tubes, omentum and peri-adnexal, peri-adrenal, and peri-pancreatic soft tissue. Immunohistochemistry (IHC) studies show that the tumor cells are positive for cytokeratin (CK7), and CK20, but negative for CK903, ER, PR, Breast (GCDFFP-15) and S-100. (CK7 and CK20 staining patterns are used to differentiate tumor types. CK903 is a high molecular weight cytokeratin. Estrogen and progesterone receptor stains are seen in cells that express those hormone receptors, including breast tissue. S-100 staining generally stains nerves and nerve tissue.) Further IHC studies with villin (a stain that highlights the cellular membrane and cytoplasm of neoplastic signet-ring cells) was performed on various sections of the tumor and found to be positive.³ No masses were present in the urinary bladder, but the signet-ring cell tumor was seen to extend through the full-thickness of the bladder wall including the urothelial lining. The tumor was also present, encasing the pancreas with extension into the pancreatic parenchyma.

DISCUSSION

In this case, bilateral ureteral obstruction, gastric outlet obstruction, and the abnormal appearance of the retroperitoneum on CT imaging led to the suspicion of RF. As described by Ormond, the classic presentation of RF is a middle-aged woman with back pain, anuria, weight loss, and malaise.⁴ To some degree, all patients have compression of the retroperitoneal structures from an inflammatory mass. Approximately 70% of cases of RF are idiopathic,⁵ but most remaining cases have been associated with drugs or medications (Table 1).

The CT appearance of RF is variable; it can present as

a bulky retroperitoneal mass, as a fibrous sheet, or with no visible abnormality.⁶ The retroperitoneal soft-tissue stranding in our case was relatively mild. Visualization of RF as minimal soft-tissue stranding has been considered rare but may become significantly easier with current technology thin-section CT imaging.⁷ Because the morphology and contrast-enhancement characteristics can be identical, differentiation between benign fibrosis and retroperitoneal malignancy may not be possible on CT examinations.⁸ Magnetic resonance imaging was not performed in this case but may be useful in differentiating benign fibrosis from retroperitoneal malignancy. Benign RF, at least in the absence of acute inflammation, has homogeneously low signal intensity on both T1- and T2-weighted images. Malignant RF has higher signal intensity on T2-weighted images.⁹

Adenocarcinoma of the bladder is rare, comprising 0.5%-2.0% of all primary bladder cancers.¹⁰ PSRCC of the urinary bladder is a rare histologic variant of adenocarcinoma. Like other bladder cancers, PSRCC normally arises in the sixth decade of life and is most common in men.¹¹ Common presenting symptoms for PSRCC include hematuria and dysuria, neither of which was seen in the present case. As in our case, PSRCC presenting as ARF has been previously described.¹² One possible cause for the lack of urinary symptoms in this patient is the histologic subtype of the disease. PSRCC may manifest as classic mucosal tumors that give rise to common symptoms such as hematuria or irritation. However, some cases manifest as rapidly growing tumors that infiltrate the submucosa without projecting into the lumen of the bladder.¹² These patients, as in our case, tend to have normal cystoscopic examinations.¹¹ In the linitus plastica-like variants, patients tend to present with symptoms of advanced disease.¹³

Surgical treatment options for PSRCC of the bladder include transurethral resection or partial cystectomy for small tumors and radical cystectomy with urinary diversion for diffuse tumors. Radiotherapy and chemotherapy have also been used; however, they have had limited success and are mostly used as adjuvant therapy to surgery.¹³ However, case reports have been published that describe the use of arterial infusion of carboplatin to treat PSRCC of the bladder.^{14,15} One report showed a complete remission lasting 44 months.¹⁵ Because PSRCC is an aggressive tumor, most patients (up to 65%) tend to present with locally advanced disease.¹¹ In these patients, surgery is not a cure, but should be considered for palliation along with urinary diversion.

Based on the aforementioned IHC studies and on the lack of involvement on autopsy of other organ systems

Table 1. Causes of Retroperitoneal Fibrosis¹⁶

Drugs	Periarthritis
Methysergide	Aortic aneurysm
Hydralazine	Collagen vascular disease
Reserpine	
Haloperidol	Inflammatory Processes
LSD	Ascending lymphangitis
Methyldopa	Chronic IBD
β Blockers	
Ergotamine alkaloids	Radiation Injury
Phenacetin	
Amphetamines	Chemicals
	Avitene
Retroperitoneal Tumors	Methyl methacrylate
Sarcoma	Talcum powder
Lymphoma	
Metastatic carcinoma	Hemorrhage
	Abdominal surgery
	Ruptured viscera
Infection	
Gonorrhea	Other
Tuberculosis	Sarcoidosis
Chronic UTI	Endometriosis
	Biliary tract disease

LSD=lysergic acid diethylamide; UTI=urinary tract infection; IBD=inflammatory bowel disease. Reprinted with permission.

(such as gastrointestinal, gynecological, and pulmonary) as a primary site for this high-grade tumor, we believe that this is a primary signet-ring cell carcinoma of the urinary bladder. An interesting finding in this case is the prior history of high grade superficial TCC of the bladder. The simultaneous presence of high-grade TCC of the bladder accompanied by signet-ring cell carcinoma in a cystectomy specimen has been previously reported, raising the possibility of differentiation of adenomatous metaplasia of bladder TCC into signet-ring cell carcinoma.¹⁷

CONCLUSION

RF is a clinical syndrome characterized by obstructive symptoms of retroperitoneal organs mainly consisting of the urologic and gastrointestinal systems. The appearance of RF on diagnostic imaging studies is variable, and definitive diagnosis is made by biopsy of the retroperitoneum. In this case, RF was caused by the metastatic infiltration of a PSRCC of the urinary bladder into the retroperitoneum, despite a normal-appearing cystoscopic examination. PSRCC of the urinary bladder is a rare histologic variant of adenocarcinoma.

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