Pseudomyxoma Peritonei Associated With Primary Mucinous Borderline Tumor of the Renal Pelvicalyceal System

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● Primary mucinous cystic neoplasms are extraordinarily rare tumors of the kidney. Herein, we present a case of a 52-year-old man who presented with painless hematuria and mucusuria. The nephrectomy showed a markedly enlarged kidney replaced by a large cystic mass filled with mucin and with almost complete destruction of the renal parenchyma. Histologically, the mass was lined primarily by simple mucinous epithelium and showed foci of adenomatous (borderline) change with focal areas exhibiting intraepithelial carcinoma. No invasion was documented after extensive sampling of the tumor. A pathologic diagnosis of intraepithelial carcinoma arising in a mucinous neoplasm of borderline malignancy was rendered. One year later, the patient presented with pseudomyxoma peritonei. This case illustrates that, in a patient with pseudomyxoma peritonei, the absence of an appendiceal, gastrointestinal, or ovarian primary tumor raises the possibility of a primary neoplasm at an unusual site such as the kidney.

(Arch Pathol Lab Med. 2009;133:1472–1476)

The most common neoplasms in the renal pelvis are urothelial in origin, although less commonly, squamous and glandular lesions may arise within the renal pelvicalyceal system through metaplastic change of the urothelium. From this metaplasia, glandular lesions such as mucinous cystadenoma, adenocarcinoma, and villous adenoma are thought to arise.

Invasive mucinous adenocarcinoma with enteric features has been well documented in the literature since 1946. In contrast, mucinous cystic neoplasms are exceedingly rare primary neoplasms involving the kidney, with only 5 benign, 3 borderline, and 3 malignant cases reported in the literature. Because these have been published as isolated case reports, experience and knowledge with renal mucinous cystic neoplasms is extremely limited and they have not been recognized formally in the World Health Organization classification of tumors of the pelvicalyceal system. The consensus, in few reported cases, is that these tumors most likely represent neoplasms arising from the pelvicalyceal mucosa as a result of mucinous metaplasia. The spectrum of mucinous cystic neoplasms involving the pelvicalyceal system is similar to the more common ovarian mucinous neoplasms and includes benign mucinous cystadenoma, mucinous borderline tumor with or without intraepithelial carcinoma, and mucinous cystadenocarcinoma. We present the case of a 52-year-old man whose condition had an aggressive clinical course that resulted in the development of pseudomyxoma peritonei after he presented at nephrectomy with borderline mucinous neoplasm arising in a background of extensive mucinous metaplasia of the pelvicalyceal urothelium secondary to chronic nephrolithiasis. We describe the clinical, radiologic, and histologic findings of this unique case and review the differential diagnosis and distinguishing features of this entity.

REPORT OF A CASE

A 52-year-old man presented with long-term hematuria, mucusuria, abdominal flank pain, and occasional bouts of nausea and vomiting. The patient had no significant past medical history. The physical examination was remarkable for left-flank tenderness. A computed tomography scan was performed and showed a cystic renal mass involving the left kidney (Figure 1). A thorough clinical and radiologic workup did not reveal any other mass lesions in the abdomen. A nephrectomy was subsequently performed. No adjuvant therapy was given to the patient after surgery. One year after nephrectomy, the patient had widespread pseudomyxoma peritonei and died as a result of complications related to sepsis a few months later. No other primary tumor was identified. No postmortem examination was performed.

PATHOLOGY

On gross examination, the resected left kidney weighed 2750 g and measured 35 × 28 × 20 cm. Except for a very thin rim of recognizable renal parenchyma, the cut surface showed a complete cystically dilated, multiloculated, mucin-filled mass that measured 24 × 22 × 19 cm. The tumor was completely excised (confirmed by the presence of microscopically uninvolved renal parenchyma at the periph-
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were lined by simple mucinous epithelium, which showed basally located nuclei, devoid of nuclear atypia or mitosis (Figure 3, B). Other areas were lined by mucinous epithelium, which showed presence of goblet cells (Figure 3, C). Scattered among the smooth walled areas were more architecturally complex foci—designated as borderline, with finger-like projections of tumor cells into the luminal aspect—which comprised approximately 10% of the overall tumor (Figure 3, D). Less than 5% of the tumor showed greater nuclear stratification with loss of polarity as well as moderate to severe cytologic atypia in the form of nuclear hyperchromasia, prominent nucleoli, and increased mitotic activity. By applying the criteria used to classify ovarian mucinous cystic neoplasms, these areas were designated as foci of intraepithelial carcinoma, on the basis of the presence of severe cytologic atypia. Copious mucin was present within the cysts as well as in patches extravasated within the wall of the tumor as acellular pools of mucin within a fibrotic stroma (Figure 3, A). Extensive sampling did not reveal any evidence of invasive carcinoma. Ovarian-type stroma was not identified in the multiple sections examined. There was no residual urothelium identified in any of the histologic sections sampled from the pelvicalyceal system. Immunohistochemical stains showed that the tumor cells coexpressed cytokeratin (CK) 7 and CK20 and were negative for CDX2.

Radiologic studies confirmed that there was no detectable primary tumor in the appendix or the gastrointestinal tract. One year later, the patient had widespread pseudomyxoma peritonei (Figure 4). Sections from the omentum showed widespread deposition of mucin with presence of isolated tumor cells, small nests, and well-formed glandular structures embedded within the pools of mucin. The epithelial cells showed minimal to mild nuclear pleomorphism, similar to the nuclear features of the cells in the benign areas of the tumor in the kidney (Figure 5). Immunohistochemical stains were not performed on the omental specimen.

**COMMENT**

It is well recognized that the urothelium can undergo squamous and glandular metaplasia. Metaplasia of the urothelium typically occurs in reaction to chronic irritation from infection, hydronephrosis, or nephrolithiasis. From this metaplasia, dysplasia and carcinoma are postulated to develop; this is the likely carcinogenic sequence in the development of neoplastic mucinous lesions of the renal pelvis. Several cases of borderline and malignant mucinous tumors of the renal pelvis, previously reported in the literature, have had a history of long-standing renal calculi, as was also seen in our case (Table). It is plausible that in all these cases, chronic irritation and subsequent glandular metaplasia was a precursor to the development of the tumor. On the basis of this collective experience, we believe that mucinous neoplasms involving the kidney arise from glandular metaplasia of the pelvicalyceal mucosa. Other proposed theories for mucinous neoplasm involving the kidney include a possible teratomatous origin or coelomic epithelial origin because of a striking resemblance to ovarian mucinous neoplasms. Alternatively, the propensity of this lesion to arise in anomalous kidneys has also led authors to postulate that these tumors may arise from sequestered renal pelvic epithelium within the parenchyma, as a consequence of maldevelopment.
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Figure 3.  A, Low-power view of the smooth areas of the cyst wall. The lining epithelium is mucinous in nature with a single to a few layers of epithelial cells with basally polarized nuclei. Note the pools of mucin present within the cyst wall (arrows). B, Higher-power view of the cyst wall lined by simple mucinous epithelium, showing lack of nuclear atypia. C, Areas lined by intestinal-type mucinous epithelium. D, Areas designated as “borderline,” showing nuclear stratification and nuclear atypia (hematoxylin-eosin, original magnifications ×10 [A] and ×20 [B, C, and D]).

Figure 4.  Image showing gross appearance of the omentum with involvement by pseudomyxoma peritonei.

The cystic nature of the current pelvicalyceal neoplasm distinguishes this tumor from the more recognized adenocarcinomas of the urothelial tract, which are overtly invasive with widespread involvement of the renal parenchyma in a destructive manner. Further, the tumor in our case lacked well-defined papillary architecture—as noted with villous adenoma of the renal pelvis—which is histologically similar to its intestinal counterpart. No ovarian-type stroma was identified in the wall of the tumor in the multiple sections examined; this feature, along with the absence of solid areas, excluded a diagnosis of mixed epithelial-stromal tumor.

Mucinous adenocarcinoma of the renal pelvis was first described in 1946 by Ackerman.6 The author described an invasive adenocarcinoma arising in the renal pelvis of a hydronephrotic kidney. The tumor demonstrated extensive mucinous metaplasia of the epithelium of the renal pelvis and was interspersed by papillary epithelial projections described by Dr Ackerman as “not unlike the papillary projections of a rectal polyp.” Since, there have been several reports of “papillary mucinous adenocarcinomas” of the renal pelvis.20 In a detailed literature review of 32 cases of glandular neoplasms of the renal pelvis, Auferheide and Streitz comment that these tumors tend not to form discrete mass lesions on gross examination.7 Many of these tumors appear to be overtly invasive mucinous adenocarcinomas with enteric morphology. They contrast...
Figure 5. A, Low-power view of the omentum shows well-differentiated glands lacking cytologic atypia and floating in large pools of mucin. B, Higher-power image highlighting the bland nuclear features of the epithelial cells (hematoxylin-eosin, original magnifications ×4 [A] and ×10 [B]).

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Abbreviations: NED, no evidence of disease; DOD, died of disease.

with the largely intracystic growth seen in our case whose spectrum, for the same lesion, ranged from cystadenoma to a borderline lesion to intraepithelial carcinoma, much like ovarian mucinous tumors.4,6,20 Unlike mucinous cystic neoplasms of the pancreas, which show a strong female preponderance, mucinous cystic neoplasms of the kidney occur in patients of both sexes. Also, the ovarian stroma that typifies mucinous cystic neoplasms of the gastrointestinal tract is absent in cases that have been reported in the kidney, thus suggesting that these neoplasms are distinctly different.

On the basis of our experience in this case, and from what we can learn from descriptions and illustrations of prior published cases, tumors similar to the one seen in our case have a distinctive morphology and are best classified by applying the nomenclature used for ovarian neoplasms: cystadenoma, borderline mucinous tumor with or without intraepithelial carcinoma, and cystadenocarcinoma.19 Therefore, very thorough sampling of the cyst wall in borderline tumors is necessary to identify potential areas of stromal invasion. Because of the rarity of primary mucinous cystic neoplasms involving the kidney, secondary involvement from the more common sites, such as ovary and gastrointestinal tract, should be thoroughly excluded. Since mucinous neoplasms involving the kidney arise from the pelvicalyceal system, meticulous gross examination and adequate sampling are crucial in the diagnosis. Interestingly, the immunohistochemical profile of the current tumor is similar to the immunohistochemical profile of ovarian mucinous neoplasms, which is CK 7/CK 20 positive and CDX2 negative.21

Pseudomyxoma peritonei is a clinical phenomenon characterized by the accumulation of mucin within the abdomen and/or pelvis and is a well-documented occurrence associated most frequently with appendiceal mucinous neoplasms as well as with gastrointestinal malignancies, and rarely with borderline and malignant mucinous ovarian tumors.22 Ronnett et al attempted to propose a pathologic definition for tumors clinically characterized by pseudomyxoma peritonei. They proposed 2 diagnostic categories for pseudomyxoma peritonei: disseminated peritoneal adenomucinosis (DPAM) and peritoneal mucinous carcinomatosis (PMCA). Cases that were classified as DPAM were characterized by scant, simple mucinous epithelium demonstrating minimal cytologic atypia and mitotic activity, whereas those classified as PMCA showed mucinous epithelium with architectural and cytologic features of carcinoma, embedded within a mucinous background. It is critical to distinguish between these 2 entities, as the 5-year survival for patients with DPAM is significantly better, at 74% compared to 14%, for patients with PMCA.23

A limiting factor of our study is the fact that the appendix was not examined histologically. Appendiceal mucinous neoplasms may occasionally present as occult neoplasms, which may be difficult to identify grossly, and
often, histologic evaluation of the entire appendix is necessary to exclude a mucinous adenoma or a microscopic focus of rupture.22 In our case, it would be unlikely that this rare event could provide an explanation for the development of pseudomyxoma peritonei because a large mucinous cystic neoplasm involving the kidney was present, with abundant extravasation in the renal parenchyma. Further, the absence of a clinical and radiologically detectable primary lesion in the appendix, during the year after the nephrectomy, points to the kidney as a likely source for pseudomyxoma peritonei. To our knowledge, no association between the phenomenon of pseudomyxoma peritonei and mucinous tumors involving the kidney has been reported in the literature. In our case, the pathologic features of the omentum befitted a diagnosis of DPAM. On the basis of our unique case report, the pathologist should be aware of the kidney as a possible source of neoplasm in patients with pseudomyxoma peritonei for which no appendiceal, gastrointestinal, or ovarian neoplasm is found.

Because of the rarity of mucinous cystic neoplasms, the latter have not been formally recognized, thus far, in the World Health Organization classification of tumors of the pelvicalyceal system.17 Our case, and the few similar cases reported in the literature, suggest that these tumors represent a unique clinicopathologic entity that merit inclusion in future classification systems of tumors of the renal pelvis.

References