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Management of mucinous urachal neoplasm presenting as pseudomyxoma peritonei

Paul H Sugarbaker[1], Mohan Verghese[2], Tristan D Yan[1], and Erwin Brun[3]

[1]Washington Cancer Institute, [2]Department of Urology, and [3]Department of Pathology, Washington Hospital Center, Washington, DC, USA

ABSTRACT

Background. Mucinous neoplasms of the urachus are rare malignancies so that the physicians' index of suspicion for a timely and accurate diagnosis is low. Also, this disease may present with a wide variety of symptoms and signs.

Methods. Two patients with pseudomyxoma peritonei as the initial presentation of urachal mucinous adenocarcinoma were treated successfully. The medical literature regarding treatment options for this manifestation of the disease was searched.

Results. Two patients with large volume of pseudomyxoma peritonei originating in a mucinous urachal neoplasm were treated with cytoreductive surgery and perioperative intraperitoneal chemotherapy. Our first patient required two reoperations to palliate the accumulation of gross mucinous ascites. She died 11 years after diagnosis with progression of mucinous adenocarcinoma resulting in starvation. The second patient had ostomy closure with second look surgery at one year after definitive treatment; four small tumor nodules were seen and easily resected. The patient is currently without evidence of disease and has a normal quality of life. Seven prior manuscripts that report a single case of pseudomyxoma peritonei were reviewed to explore the full range of treatment options and survival for this rare condition.

Conclusion. Cytoreductive surgery combined with perioperative intraperitoneal chemotherapy may be a new treatment option for mucinous urachal neoplasms presenting with pseudomyxoma peritonei. Other management strategies such as systemic chemotherapy seemed to hold little promise for this group of patients.

Introduction

Several prior reports in the surgical literature have shown that pseudomyxoma peritonei can originate as a mucinous neoplasm of the urachus[1-7]. Generally, these tumors are of moderate to high malignant potential by histological examination. They progress by rupturing the urachal tumor mass into the free peritoneal cavity with the characteristic distribution pattern of mucinous carcinomatosis[8-10]. We report on two patients with urachal mucinous adenocarcinoma. In our second patient the CT showed a mass superior to the bladder and the greater omentum massively infiltrated by mucinous adenocarcinoma. Because of the prior reports on this disease, we were able to make the diagnosis of urachal pseudomyxoma preoperatively. Definitive treatment was initiated simultaneously with the histologic diagnosis through the use of cytoreductive surgery and intraperitoneal chemotherapy. This distinct clinical entity has a new treatment option that may be of benefit in selected cases.

Case reports

Patient 1

A 32 year old woman complained of infertility. With a diagnosis of uterine fibroids she was explored and a mass emanating from the superior aspect of the bladder was

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Correspondence to: Paul H Sugarbaker, MD, FACS, FRCS, Washington Cancer Institute, 106 Irving St., NW, Suite 3900, Washington, DC 20010 USA.
Tel 202-877-3908;
fax 202-877-8602;
e-mail Paul.Sugarbaker@medstar.net

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removed. One year later tumor was shown by CT layered beneath the right and left hemidiaphragms and involving the ovaries bilaterally. Tumor markers showed a carcinoembryonic antigen (CEA) of 4 ng/ml and a cancer antigen (CA) 19-9 of 182 µ/ml. A cytoreduction was performed that included a peritonectomy of the right upper quadrant, left upper quadrant and pelvis[11]. A complete omentectomy and a splenectomy were performed. A rectosigmoid colon resection with low stapled anastomosis was necessary to clear the pelvis. The cytoreduction was scored as complete. Early postoperative intraperitoneal chemotherapy with mitomycin C at 15 mg/m^2 followed by 5 days of intraperitoneal 5-fluorouracil at 600 mg/m^2 was completed. The patient recovered well and remained disease-free for 24 months. A second debulking procedure was performed and additional intraperitoneal hyperthermic cisplatin and doxorubicin chemotherapy. Again, the patient showed no evidence of disease for 3 years. At this time a third cytoreduction with hyperthermic intraperitoneal cisplatin was performed. A CT follow-up showed progression within the right pleural space and abdomen. Five years later there was no distant metastatic disease but recurrence between bowel loops was documented. The patient died 11 years after her diagnosis with progressive intraabdominal disease, intestinal obstruction, and cancer cachexia.

Patient 2

A 47 year old man was referred to our institution after abdominal and pelvic CT suggested a diagnosis of mucinous peritoneal carcinomatosis. For 8 years the patient had intermittently experienced the urination of mucus. One year prior to diagnosis he noted increasing abdominal girth and abdominal cramping. Six months prior to diagnosis of carcinomatosis a left inguinal hernia was repaired using a laparoscopic approach and the insertion of mesh.

CT showed a cystic mass directly above the bladder and mucinous carcinomatosis with a distribution pattern characteristic of pseudomyxoma peritonei (Figures 1-3). A CT-guided biopsy of the omentum showed mildly atypical epithelial cells. A cystoscopy showed a small defect at the dome of the bladder, copious mucus in the bladder but no tumor mass was evident. A laparoscopy was performed which showed mucinous tumor located throughout the abdomen and pelvis and distributed in a characteristic fashion with large volume disease beneath the right and left hemidiaphragm, omental caking and an extensive mucoid fluid accumulation within the pelvis. Tumor marker studies showed a CA 19-9 of 594 µ/ml and CEA of 14 ng/ml.

The patient was taken to the operating room in February of 2006. At the time of surgery the primary tumor was a supravesical mass that communicated with the bladder through a patent urachus. It could be dissected

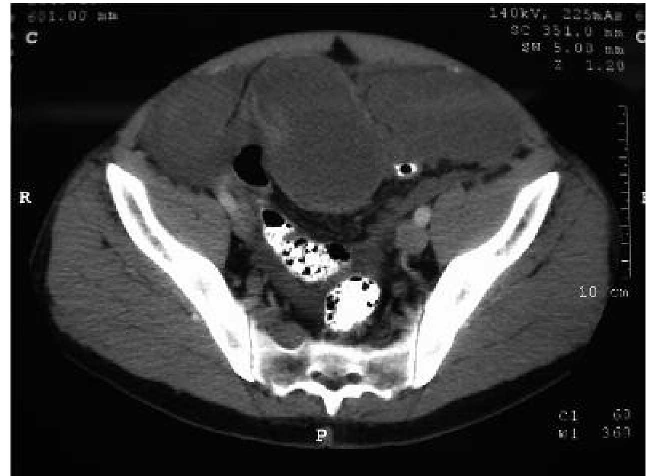

Figure 1 - CT scan through the mid-abdomen showing a cystic mass directly above the bladder.

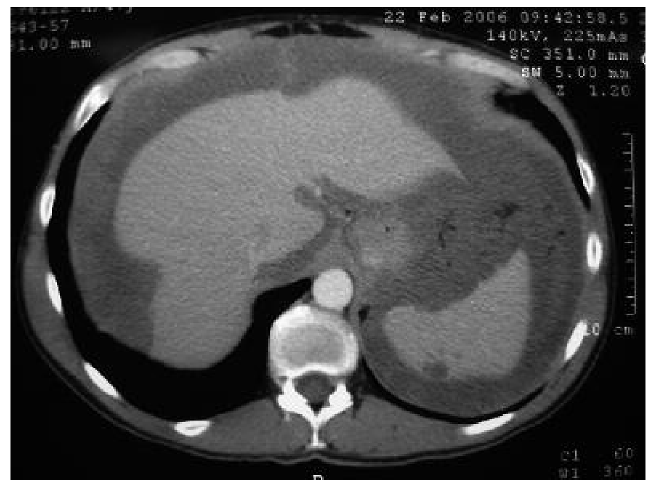

Figure 2 - CT scan through the upper abdomen showing large volume disease in the right upper quadrant, left upper quadrant, and lesser omentum.

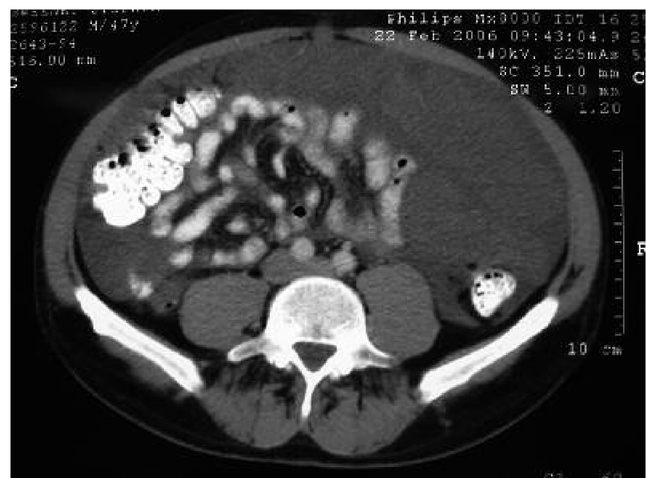

Figure 3 - CT scan through the mid-abdomen showing the "omental cake" characteristic of the pseudomyxoma peritonei. The small bowel is compartmentalized beneath the omental cake.

clear of the bladder. Large volumes of intravesical mucus were suctioned through the opening of the dome of the bladder. No other bladder abnormalities were identified. The appendix, dissected free of the surrounding tissue, was determined to be normal. The findings at surgery showed massive tumor in omentum, beneath hemidiaphragms, and in the pelvis. The small bowel was free of disease (Figure 4).

Cytoreductive surgery required total anterior parietal peritonectomy, right upper quadrant peritonectomy, left upper quadrant peritonectomy, greater and lesser omentectomy, right colectomy and pelvic peritonectomy including a rectosigmoid colectomy[9]. Segmental cystectomy and closure of the bladder was performed. The tumor was reduced to no visible evidence of disease. A diverting ileostomy was performed to protect a low colorectal anastomosis. In the operating room the patient received hyperthermic intraperitoneal mitomycin C (15 mg/m^2) and doxorubicin (15 mg/m^2). Simultaneous intravenous 5-fluorouracil at 600 mg/m^2 and leucovorin at 20 mg/m^2 was utilized. Tubes and drains were positioned so that patient could receive early postoperative intraperitoneal 5-fluorouracil using 600 mg/m^2 x 4 days.

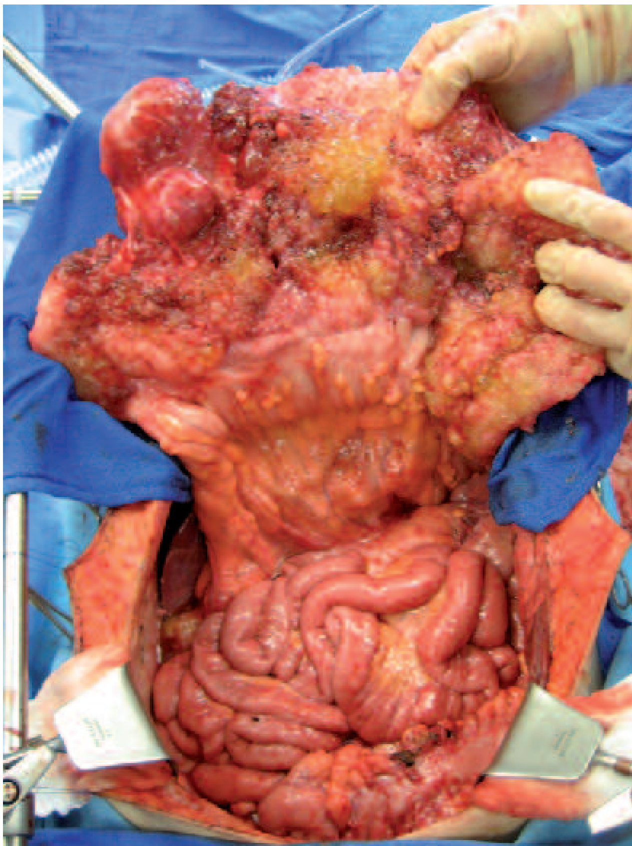

Figure 4 - Intraoperative photograph of the omental cake and the normal appearing small bowel beneath.

Histopathologic examination showed a mucinous adenocarcinoma that was well-differentiated (Figure 5).

The patient's postoperative course was uneventful. The ileostomy was closed one year later. Four small tumor nodules were visualized and removed without difficulty. The patient is currently disease-free at 18 months from the initial cytoreduction.

Literature review of urachal adenocarcinoma presenting with pseudomyxoma peritonei

The medical literature was searched using PubMed for publications that reported a urachal adenocarcinoma concomitant with peritoneal carcinomatosis. The results of this survey are presented in Table 1[1-7]. Mendeloff and McSwain[1] recognized the direct relationship of mucinous carcinomatosis and the urachal primary cancer. Loggie *et al.*[3] was the first to report a definitive treatment plan for the local-regional component of this disease. In his patient metastases became evident at 20 months from diagnosis; the large volume intraperitoneal component of the disease never recurred despite systemic progression of disease. Also, in the report by de Bree[4] and in our two patients, perioperative intraperitoneal chemotherapy was used. Our 32 year old female patient died of disease at 11 years. The patient reported by De-Bree *et al.* is alive and well at nine years after treatment.

Discussion

In the 7 patients reported in the medical literature and our own 2 patients the urachal mucinous neoplasm oc-

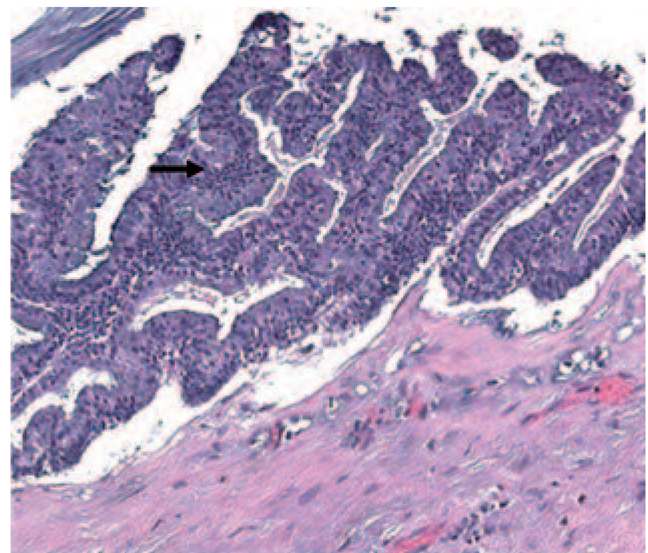

Figure 5 - Photomicrograph of the wall of the primary tumor mass showed a well-differentiated mucinous malignancy of the primary tumor.

Table 1 - Literature review of urachal adenocarcinoma presenting with pseudomyxoma peritonei

Author	Year	No. patients	Age/Sex	Pathology	Cytoreduction	Cystectomy	HIPEC	Survival (months)	CEA/CA 19-9 preoperative	Current status
Mendeloff and McSwain[1]	1971	1	49/M	Mucinous adenocarcinoma	Debulking	No	No	28	NA/NA	DOD
Sasano *et al.*[2]	1997	1	45/M	Cystadenoma	None	No	No	NA	5.7/135	NA
Loggie *et al.*[3]	1997	1	35/M	Signet ring	Extensive	Yes	Mitomycin C 40 mg	31	NA/NA	DOD
De Bree *et al.*[4]	2000	1	34/M	Low grade mucinous	Extensive	No	Mitomycin C	108	NA/NA	NED
Yanagisawa *et al.*[5]	2003	1	50/F	Mucinous cystadenocarcinoma	Oophorectomy	No	No	NA	NA/NA	NED
Stenhouse *et al.*[6]	2003	1	55/M	Low grade mucinous	NA	No	No	NA	28/NA	NA
Takeuchi *et al.*[7]	2004	1	82/M	Mucinous adenocarcinoma	Minimal	No	No	NA	7.9/38	NA
Sugarbaker *et al.**	2007	2	32/F	Mucinous adenocarcinoma	Extensive	No	EPIC	132	4/182	DOD
			47/M	Mucinous adenocarcinoma	Extensive	No	Mitomycin C	20	14/594	NED

HIPEC, hyperthermic intraperitoneal chemotherapy; EPIC, early postoperative intraperitoneal chemotherapy using mitomycin C and 5-fluorouracil, units for CEA = ng/ml, units for CA 19-9 = μ/ml; NA, not available; DOD, died of disease; NED, no evidence of disease.
*Present study.

curred along with the pseudomyxoma peritonei. In the patient reported by de Bree and colleagues the pseudomyxoma peritonei was found at laparotomy two years after the prior excision of a mucinous urachal primary tumor[4]. Ohira and colleagues have collected literature reports on 3 women who had adenocarcinoma of the urachus with ovarian tumor masses[12]. In a majority of these reports the ovarian tumor mass was several times larger than the primary urachal mass. Usually, ovarian involvement was bilateral. Also, many patients had synchronous or metachronous metastatic disease. Nevertheless, it is likely that these "ovarian adenocarcinomas" were not the result of metastatic disease through lymphatic channels or blood-borne metastasis. Rather they are caused by ovarian implantation into a corpus hemorrhagicum or urachal mucinous adenocarcinoma cells[13]. Growth stimulation at this metabolically hyperactive site in the ovary causes the ovarian masses to progress more rapidly than in the primary tumor mass. Even though obvious rupture of the primary tumor into the peritoneal cavity is not detected, mucinous cells can dissect through tissues under pressure for release into the peritoneal cavity. This local extension may explain the pseudomyxoma peritonei described by Stenhouse *et al.* that was associated with a urachal cystadenoma that did not obviously communicate with the peritoneal cavity[6].

The diagnosis of urachal mucinous adenocarcinoma is rarely made prior to exploratory surgery so that the necessary plans to definitively treat the disease do not occur. In our second patient prior experience with this disease led to a diagnosis preoperatively and definitive treatment occurred as a single event. The symptom of mucus noted upon urination should be recognized as an unusual complaint distinctively associated with this rare disease. Also, CT showing a cystic mass anatomically related to the position of the urachus can confirm the diagnosis. In some patients this primary tumor mass should be noted prior to the development and progression of the extensive mucinous ascites described as pseudomyxoma peritonei. In our patient an elevated CA 19-9 tumor marker was helpful in making a diagnosis of mucinous carcinomatosis and has been utilized in follow-up.

Urachal remnants are usually lined by transitional-type epithelium but focal glandular metaplasia may give rise to mucinous adenocarcinoma similar to that seen with colon cancer. In patients with a radiologic and histologic diagnosis of pseudomyxoma peritonei, the clinical suspicion usually points to a primary appendiceal or colonic mucinous neoplasm. However, in patients who present with mucosuria and a cystic lower midline abdominal mass on CT or MRI, a primary urachal adenocarcinoma should be suspected. During the prolonged course of this disease prior to diagnosis the urachal mucinous neoplastic cells gain access to the peritoneal cavity. In this environment they continue to disseminate as neoplastic cells in mucinous ascites moving with peritoneal fluid throughout the peritoneal cavity. This characteristic pattern of tumor dissemination associated with pseudomyxoma peritonei is known as "redistribution phenomenon"[8, 9]. In some patients the mucus from

the primary tumor mass is also forced down a patent urachus into the bladder causing mucosuria. A definitive treatment approach to this disease using cytoreductive surgery and perioperative intraperitoneal chemotherapy similar to that used for patients with pseudomyxoma peritonei of appendiceal mucinous neoplasms may be of greatest benefit to these patients.

There seems to be no doubt that complete excision of a urachal adenocarcinoma with clear margins is the treatment of choice if primary cancer resection alone can achieve negative margins. The mucinous nature of this neoplasm and the possibility for stray cancer cells developing at a later time as pseudomyxoma peritonei must be considered. An *en bloc* resection is the preferred surgical strategy. The decision to proceed with a cystectomy *versus* simple resection of the superior aspect of the bladder with negative margins will depend on the anatomic extent of the disease and its biological aggressiveness. In the proper clinical setting cystectomy is not mandatory[14]. In patients with pseudomyxoma peritonei arising in a primary urachal adenocarcinoma, the disease is associated with a cystic primary cancer that produces copious mucus. In this type of primary cancer deep invasion into the bladder is less likely to occur. In our two patients and in the other six reported in the literature, cystectomy was not required. Although the primary urachal cancer is usually manageable by surgical resection, the peritoneal spread presents a special problem in management.

A large proportion of these patients have an elevated carcinoembryonic antigen and cancer antigen CA 19-9 at the time of diagnosis of the pseudomyxoma peritonei. In our first patient the tumor markers increased with disease recurrence and declined to normal with complete cytoreduction. These tumor markers should be used in a serial manner in follow-up. Also, these mucinous tumors are well imaged by CT, especially if the bowel is filled by oral contrast. We recommend for follow-up tumor markers CEA and CA 19-9 every 3 months and chest, abdominal, and pelvic CT every 6 months for 5 years post-cytoreduction.

These tumors are similar to appendiceal neoplasms in that there is a great histological variation between patients. In some patients the epithelial cells are described as bland, well-differentiated, non-invasive, and thought to be of borderline malignancy[6]. In other reports, an aggressive signet ring histomorphology is reported[3]. In order to include this broad range of histologic types, both benign-appearing and invasive-appearing, we have suggested that the term "mucinous urachal neoplasms" be used to describe this clinical entity.

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