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Review Article

Primary retroperitoneal mucinous cystadenocarcinoma: a case report and literature review

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Abstract: Primary retroperitoneal mucinous cystadenocarcinoma (PRMC) is extremely rare and the histogenesis of this tumor remains unclear. A 40-year-old female presented with a right retroperitoneal cystic mass (7 × 5 × 5 cm) and caused abdominal discomfort. The tumor was totally excised by the hand-assisted laparoscopic method without complications or recurrence in a follow-up period of eighteen months. Histopathologic examination after tumor excision showed a PRMC. This is the 66th case of PRMC in the world with a favorable outcome after hand-assisted laparoscopic excision. Based on 66 cases of PRMC reported in the English literature, we discussed the mural nodules, histogenesis and the appropriate treatment.

Keywords: Retroperitoneal tumor, mucinous cystadenocarcinoma, mural nodule

Introduction

Primary retroperitoneal mucinous cystadenocarcinoma (PRMC) is an extremely rare tumor. The first case was presented in 1965 [1], with only 66 cases, including our case, having been described in the English literature to date [2-8]. Six of them were male patients [6, 9-13]. Because of its rarity, the pathogenesis and biological behavior of this neoplasm is still ambiguous. It is widely accepted that total resection without rupture and careful investigation of possible origins during surgery is the best strategy. Here, we report a case of PRMC and review the literature of similar cases.

Case report

A 40-year-old woman with a complaint of abdominal discomfort was referred to our hospital in Dec 2013, with inferior abdomen pain, abdominal fullness, nausea and vomiting. The pain had been worsening over the course of several months. Family and medical history were unremarkable. Physical examination revealed a slightly tender, ill-defined mass about 7 cm in size over the right lower abdomen. The remaining systemic examination did not reveal any coexistent lesions. The laboratory tests, including the complete blood count, the chemistry profile, urinalysis, chest X-ray and electrocardiogram (ECG) were all within normal limits. The serum levels of CA125, CA72-4, CEA and CA19-9 were all within normal limits. Abdominal computed tomography (CT) scanning revealed a unilocular cystic mass with the size of 7 cm × 5 cm in the right abdominal cavity (**Figure 1**). There was no evidence of extracystic extension or distant metastasis. The preoperative diagnosis was a primary retroperitoneal mucinous tumor.

She underwent an exploratory laparotomy. A large encapsulated cystic mass about 7 cm in diameter was found in the right lower retroperitoneum. It was not connected to the bowels or other organs. The cyst was dissected off from retroperitoneal tissue without difficulty. Cyst contained approximately 300 ml of transparent mucinous fluid. No ascites were noted. Uterus and adnexa appeared normal and were medially displaced. Cytological examination for

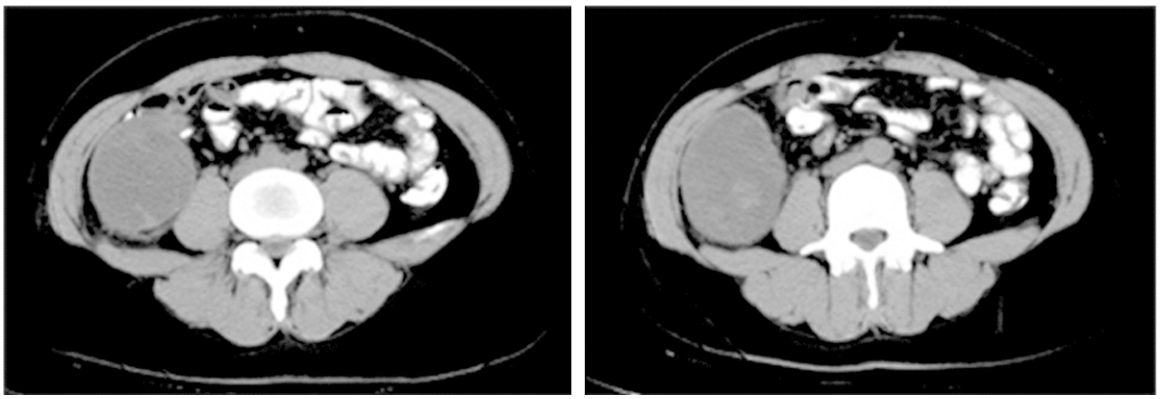

Figure 1. CT shows a retroperitoneal mass measuring approximately 7 cm × 5 cm × 5 cm in the right abdominal cavity without invasive infiltration of adjacent abdominal organs.

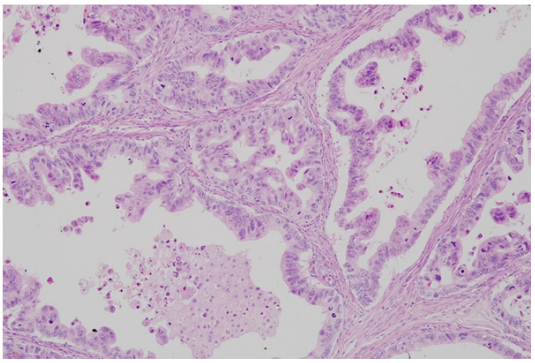

Figure 2. Pathologic diagnosis shows mucinous cystadenocarcinoma. HE × 100.

those fluids revealed no malignant cells. The cyst was lined with mucinous epithelial cells in the internal wall. There was focal involvement by adenocarcinoma in the caudal smaller cyst (**Figure 2**). The final diagnosis was a PRMC. The postoperative course was uneventful and the patient was discharged on postoperative day 7. During the eighteen month follow-up period, the patient remained completely free of symptoms and without evidence of recurrence.

Discussion

We performed a literature review of PRMC using MEDLINE and identified only 65 cases from 50 reports published since 1965 (**Table 1**). The present case is only the 66th in the literature. PRMC occurs almost exclusively in women, with the exception of 6 male cases reported in the literature. The mean age of these cases was 44.5 years (range 17-86 years), and the mean size of the cysts was 15.3 cm (rang from 3 to 28 cm). Although precise prognosis is not available, available data show a wide survival range from 2 months to 10 years. Three of the malignant patients were females with pregnancy [7, 14, 15].

Because there is no specific symptom and no available sensitive methods or reliable markers, preoperative diagnosis of PRMC is very difficult. Tumor markers, such as CA125, CEA and CA19-9, may not increase and may lack specificity. Ultrasonography, CT and magnetic resonance imaging (MRI) are often used to find and localize the tumor. However, these methods cannot easily differentiate between a benign and a malignant neoplasm [16]. Although aspiration is a good method for delineating the nature of the cyst, cytologic analysis of the aspirated fluid frequently fails to reveal the type of epithelial cells lining the cyst. Therefore, exploratory laparotomy with complete excision of the cyst is usually indicated for both the diagnosis and treatment of PRMC [17]. For this patient, abdominal discomfort and pain was first complaint. Abdominal CT examination revealed a cystic mass in right abdominal cavity. An exploratory laparotomy with complete excision was performed and adenocarcinoma cell in the caudal smaller cyst was found.

It is widely accepted that total resection is the best strategy to PRMC. Tumor excision alone is suggested by some authors, especially in patients who wish to preserve fertility [15, 18-20]. Some authors propose that treatment of PRMC, especially the malignant and mixed type, should include total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO), certainly in women who have com-

Table 1. PRMCs that have been reported in the literature

Patient No.	Ref	Sex	Age	Size (cm)	Treatment	Pathology	Nodules/ mass	Histology of nodules/mass	Follow up
1	Douglas et al, 1965 [1]	F	18	5	CHE	malignant			DOD
2	Tykkä and Koivuniemi et al, 1975 [29]	F	23	10	TE (spilling), left hemicolectomy	malignant			DOD 12 m
3	Roth LM et al, 1977 [18]	F	48	550 g	TE	malignant	nodules	poorly differentiated adenocarcinoma	DOD 6 m
4	Storch MP et al, 1980	F	17	17	TE, CHE	borderline			RE 21 m
5	Fujii S et al, 1986 [30]	F	69	23	TE, TAH, BSO	malignant			NED 36 m
6	Nagata et al, 1987 [31]	F	41	12	TE	borderline			LFU
7	Nelson H et al, 1988 [28]	F	35	20	TE, TAH, BSO	malignant			NED 22 m
8	Banerjee R et al, 1988 [32]	F	38	11	TE, LSO	borderline			RE 4 y
9	Banerjee R et al, 1988 [32]	F	47	13	TE, LSO	borderline			LFU
10	Chida et al, 1990 [33]	F	42	N/A	TE	malignant			LFU
11	Seki et al, 1990 [34]	F	42	11	TE	malignant			LFU
12	Park et al, 1991 [35]	F	40	25	TE, TAH, BSO	malignant			NED 3 m
13	Jorgensen LJ et al, 1991 [36]	F	38	8	TE	malignant			NED 9 m
14	Soendergaard G et al, 1991 [37]	F	37	18	TE, TAH, BSO	malignant	nodules	sarcoma-like mural nodule; anaplastic carcinoma	NED 18 m
15	Gotoh K et al, 1992 [21]	F	44	12.5	TE, CHE	malignant with sarcoma			DOD 4 m
16	Tenti P et al, 1994 [22]	F	46	20	TE, TAH, BSO, CHE	malignant			NED 33 m
17	Tenti P et al, 1994 [22]	F	45	20	TE, TAH, BSO	malignant			NED 19 m
18	Motoyama T et al, 1994 [25]	F	42	11	TE	mixed			LFU
29	Motoyama T et al, 1994 [25]	M	63	6	TE	borderline			LFU
20	Carabias E et al, 1995 [38]	F	43	15	TE, TAH, BSO	malignant			NED 2 y
21	Lee IW et al, 1996 [39]	F	55	19	TE, TAH, BSO	malignant			NED 30 m
22	Lee IW et al, 1996 [39]	F	45	17	TE, TAH, BSO	malignant			NED 15 m
23	Pearl ML et al, 1996 [40]	F	33	N/A	TE	borderline			NED 10 m
24	Dore et al, 1996 [27]	F	45	20	TE	mixed			NED 16 m
25	Papadogiannakis N et al, 1997 [41]	F	33	13	TE	borderline			NED 10 m
26	Chen et al, 1998 [19]	F	48	15	TE	borderline			NED 8 m
27	Uematsu T et al, 2000 [42]	F	86	23	TE	malignant			NED 6 y
28	Suzuki et al, 2001 [43]	F	40	15	TE, appendectomy	mixed			NED 15 m
29	Tangjitgamol et al, 2002 [44]	F	41	12	TE, TAH, BSO, CHE, appendectomy	mixed			NED 18 m
30	Kessler et al, 2002 [45]	F	38	11.5	TE	borderline			NED 60 m
31	Mikio Mikami et al, 2003 [2]	F	38	16	TE, TAH, BSO, CHE	malignant	nodules	sarcoma-like mural nodule	DOD 18 m
32	Gutsu et al, 2003 [46]	F	41	21	TE	borderline			NED 18 m
33	Song et al, 2005 [47]	F	72	12	TE	malignant			DOD 4 m
34	Matsubara et al, 2005 [16]	F	36	16	TE	borderline			NED 36 m
35	Sonntag et al, 2005 [14]	F	30	5	TE	malignant			NED 12 m
36	Thamboo et al, 2006 [9]	M	64	24	TE	mixed			NED 18 m

37	Fan et al, 2006 [48]	F	68	17	TE, TAH, BSO	malignant	nodules	osteoid-forming sarcoma-like mural nodule	LFU
38	Law et al, 2006 [26]	F	35	11	TE	mixed			NED 60 m
39	Green et al, 2007 [10]	M	83	26	TE	malignant			NED 6 m
40	Lee et al, 2007 [49]	F	32	10	TE, CHE	malignant	nodules	sarcoma-like mural nodule	NED 42 m
41	de León et al, 2007 [50]	F	36	19	TE, CHE	mixed			RE 8 m
42	de León et al, 2007 [50]	F	21	26	TE	mixed			NED 6 m
43	Kashima et al, 2008 [15]	F	28	17	TE	malignant			NED 13 m
44	Bakker et al, 2007 [51]	F	45	20	TE	borderline			NED 12 m
45	Cottrill and Roberts et al, 2007 [51]	F	22	20	TE	borderline			LFU
46	Bifulco et al, 2008 [52]	F	35	28	TE, appendectomy, partial omentectomy	borderline			NED 24 m
47	Moral Gonzales et al, 2008 [53]	F	47	24	TE	malignant			NED 8 m
48	Tjalma et al, 2008 [20]	F	74	3	TE, CHE	malignant			RE 8 m, DOD 31 m
49	Roma and Malpica et al, 2009 [3]	F	35	N/A	TE	malignant	nodules		NED 91 m
50	Roma and Malpica et al, 2009 [3]	F	20	N/A	TE	malignant	mass	anaplastic carcinoma	LFU
51	Roma and Malpica et al, 2009 [3]	F	40	15	TE	malignant	nodules		NED 58 m
52	Roma and Malpica et al, 2009 [3]	F	31	18	TE, CHE	malignant	mass	sarcomatoid carcinoma	RE 26 m
53	Roma and Malpica et al, 2009 [3]	F	43	10	TE	malignant	nodules	anaplastic carcinoma	DOD 6 m
54	Roma and Malpica et al, 2009 [3]	F	49	11	TE	malignant	nodules		NED 131 m
55	Roma and Malpica et al, 2009 [3]	F	63	7.5	TE	malignant	mass		NED 14 m
56	Roma and Malpica et al, 2009 [3]	F	48	26	TE	malignant	nodules		RE 59 m
57	Roma and Malpica et al, 2009 [3]	F	47	21	TE	malignant	nodules		NED 2 m
58	Hrora et al, 2009 [12]	M	42	multiple masses	TE	malignant			NED 6 m
59	Dierickx et al, 2010 [4]	F	50	13	TE, TAH, BSO, omentectomy, appendectomy + lymphadenectomy after 6 weeks, chemotherapy	malignant			NED 58 m
60	Haiping Jiang et al, 2011 [54]	F	21	14.6	TE, CHE	malignant			NED 4 m
61	Tomoko Kanayama et al, 2012 [5]	F	40	25	TE, PLN, PAN	malignant	nodules	sarcoma	NED 6 m
62	Shiau J.P. et al, 2013 [6]	M	59	7.5	TE	mixed			NED 79 m
63	Feng Jf et al, 2013 [13]	M	63	4	TE	malignant			NED 13 m
64	Hanhan HM et al, 2014 [7]	F	37	22	TE	malignant			NED 24 m
65	H-K et al, 2015 [8]	F	62	4 cysts 10, 9.5, 6.5, 3	TE	malignant			DOD 15 m
66	This case	F	40	7	TE	malignant			NED 18 m

TE = tumor excision; CHE = chemotherapy; TAH = total abdominal hysterectomy; BSO = bilateral salpingo-oophorectomy; LSO = left salpingectomy and ovariectomy; PAN = paraaortic lymphadnectomy; PLN = pelvic lymphadenectomy; NED = no evidence of disease; DOD = died of disease; RE = recurrent; LFU = lost to follow-up; mixed = borderline + malignant.

Table 2. Treatment of borderline PRMCs and their prognosis (n = 14)

Borderline	NED	DOD	RE	LFU	Total
TE without CHE	8	0	1	4	13
TE with CHE	0	0	1	0	1
Total	8	0	2	4	14

TE = Tumor excision; CHE = chemotherapy; NED = no evidence of disease; DOD = died of disease; RE = recurrent; LFU = lost to follow-up; mixed = borderline + malignant.

Table 3. Treatment of malignant and mixed PRMCs and their prognosis (n = 52)

Malignant and mixed	NED	DOD	RE	LFU	Total
TE without CHE	22	5	1	4	32
TE with CHE	2	1	3[a]	0	6
TE + TAH + BSO without CHE	8	0	0	1	9
TE + TAH + BSO with CHE	3	1	0	0	4
CHE	0	1	0	0	1
Total	35	8	4	5	52

TE = tumor excision; CHE = chemotherapy; NED = no evidence of disease; DOD = died of disease; RE = recurrent; LFU = lost to follow-up; mixed = borderline + malignant. [a]one patient developed recurrence of disease at postoperative 8 month, and died at postoperative 31 month.

Table 4. Difference of prognosis in maligant and mixed patients with and without nodules

	NED	DOD	RE	LFU	Total
Malignant and mixed with nodules	7	3	1	1	12
Malignant and mixed without nodules	28	5	3	4	40
Total	35	8	4	5	52

NED = no evidence of disease; DOD = died of disease; RE = recurrent; LFU = lost to follow-up; mixed = borderline + malignant.

pleted their child bearing or are postmenopausal [4]. The review showed 14/66 patients (21%) with a borderline tumor, and none of them was treated with TAH and BSO. Malignant and mixed patients were present in 52/66 patients (79%), and thirteen of these patients were treated with TAH and BSO (**Table 3**). Of these thirteen patients treated with TE + TAH + BSO, 1 died, 1 lost follow up, and 11 were no evidence of disease during follow up (**Table 3**). Removal of the uterus and adnexa makes young women infertile. The mean follow-up of patients treated with TE + TAH + BSO is only 24.5 months (range 3-58 months). So the prophylactic effect of TAH and BSO is not yet validated by long-term results. TAH and BSO were not performed in this patient, because the patient was in reproductive age and her uterus and adnexa appeared normal. A role for adjuvant chemotherapy is controversial [21, 22]. Chemotherapy can be reserved for those cases that there was spilling of cystic fluid during the operation [22] or in the presence of metastases or local recurrence. In the literature review, one borderline patient performed chemotherapy after tumor excision (TE + CHE), and developed recurrence of disease (**Table 2**). In the malignant and mixed group (**Table 3**), 11 patients performed TE + CHE, 3 developed recurrence, and 3 died (including 1 recurrence). One malignant patient performed CHE only, and died. Benefits of adjuvant chemotherapy have yet to be established.

In the literature review, 12 malignant patients had mural nodules, which were considered to be signs of malignancy [5]. Mural nodule was not found in this case. Histologically, mural nodules are classified as reactive lesions (sarcoma-like nodule) and tumors (carcinoma, sarcoma and mixed carcinoma/sarcoma). Of these 12 patients with nodules, histology of four was tumor (carcinoma or sarcoma). Prognosis of patients with mural nodules was that 3 died of disease, 1 developed recurrence (**Table 4**). The rate of die and recurrence in malignant patients with nodules was 33.3% (4/12), and 20% (8/40) in malignant patients without nodules. Compared with malignant without nodules, the rate of die and recurrence in malignant with nodules raised. This is in concordance with previous studies that the presence of mural nodules in a PRMC may indicate a worse prognosis [5].

Due to its rarity, the histogenesis of PRMC remains to be undetermined and five main hypotheses have been proposed to explain the histogenic origin of the tumor. (1) heterotopic ovarian tissue [7, 14, 15], (2) monodermal variant of teratomas [23], (3) embryonal urogenital remnants [8], (4) intestinal duplication [24], (5) coelomic metaplasia [9, 18, 20, 25, 26]. The hypothesis of coelomic metaplasia is the most

appropriate etiology. During embryogenesis, the coelomic epithelial cells from the urogenital ridge are deposited along the retroperitoneal area during embryonic descent [27]. The peritoneal epithelium may act as epithelial ovarian tissue and conduct the process of mullerian differentiation. Then, these epithelial cells cluster and form the inclusion cyst [10]. Subsequently, the coelomic epitheliums of these cysts undergo metaplasia and develop a spectrum of histological cells in different stages [28].

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Disclosure of conflict of interest

None.

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