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Peritonectomy in the Management of *Pseudomyxoma peritonei* Arising from Ovarian Mucinous Tumors - A Case Series

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Background: Pseudomyxoma peritonei (PMP) is a rare condition that is more commonly seen in females and is characterized by the development of massive amounts of mucinous ascites. It is believed to originate mostly from mucocoeles of the appendix. However, other mucin-producing tumors in other organs such as the ovary have been implicated in its etiology. Due to the rarity of this condition, there have been no formal trials to provide guidelines for optimum treatment.
Objectives: To determine the efficacy and safety of peritonectomy procedures in the treatment of patients with pseudomyxoma peritonei.
Methods: A retrospective review of patients diagnosed with pseudomyxoma peritonei was done. Demographic data and clinical outcomes of patients who underwent peritonectomy procedures were compared to those who did not undergo peritonectomy. Descriptive analysis of the data collected using frequency and percentages was used.
Results: There were a total of 14 patients with pseudomyxoma peritonei from 2006-2009. Of the 11 patients with disseminated peritoneal adenomucinosis (DPAM), 4 patients (43%) underwent peritonectomy while the remaining 7 (67%) did not undergo the said procedure. All 4 patients with DPAM and the patient with benign ovarian mucinous tumor with PMP not otherwise specified as to whether DPAM or peritoneal mucinous carcinomatosis (PMCA) who underwent peritonectomy are currently alive with no evidence of disease. Survival in this group of patients ranged from 18-48 months, with a median survival of 29 months. There were no recurrences noted in this group of patients. Seven patients with DPAM did not undergo peritonectomy: 2 developed recurrent disease, 4 became lost to follow-up, while 1 continue to have no evidence of disease. Recurrences were noted between 13-29 months from the time of diagnosis of PMP. There were 2 cases of PMCA, both arising from malignant ovarian neoplasms. One died 5 months after surgery (without peritonectomy) while the other one who was treated with peritonectomy was lost to follow-up.
Conclusion: Peritonectomy is a safe treatment modality for pseudomyxoma peritonei arising from mucinous ovarian new growths which may have a potential benefit in terms of disease-free interval.

Key words: pseudomyxoma peritonei, peritonectomy

Pseudomyxoma peritonei (PMP) is an intriguing but often confusing disease, partly because of its rarity.[1] PMP is a rare disease with an estimated incidence of 1-2 per million per year.[2] It occurs in approximately 2 out of every 10,000 laparotomies, and is more common in women.[3] It is a progressive disease of the peritoneum characterized by the production of copious amounts of mucinous fluid that gradually fills the peritoneal cavity, resulting in the characteristic "jelly belly"[4]. Over time, accumulation of mucin in the peritoneal cavity results in massive symptomatic distention and associated mechanical and functional gastrointestinal obstruction.[5] The pathogenesis of this rare disease has generally been attributed to rupture, leakage, or metastasis of an intraperitoneal mucinous neoplasm.[4] The precise origin of the tumor has been debated throughout the years, with both appendiceal and ovarian origins being considered. Interestingly, simultaneous occurrence in both the appendix and ovaries has been noted in the vast majority of women with this condition.[6]

The evolution of treatment strategies of PMP still remains debated though the current mainstay of the treatment remains surgical extirpation of the lesion.[7] Observation alone will eventually result in bowel obstruction and consequent death of the patient by cachexia or complications related to obstruction.[1] Traditional treatment of PMP consists of serial cytoreductive surgery with removal of all mucinous ascites with or without additional modalities. In the second half of the previous century the Memorial Sloan-Kettering Cancer Center (n=17) and the Mayo Clinics (n=56) reported on serial celiotomy and cytoreductive surgery. These studies suggest that survival could be achieved by surgery alone,

even though gross disease was present at the end of most procedures. Aggressive surgical debulking as the sole treatment modality was further explored by the Memorial Sloan-Kettering Cancer Center. An analysis of surgical therapy in 97 patients, aiming at symptom management rather than cure, demonstrated a mean of 2.2 debulking operations to reach a complete cytoreduction in 55% of patients. The median overall survival was 9.8 years. Survival was independently associated with low-grade pathologic subtype and the ability to achieve complete cytoreduction.[1]

Cytoreductive surgery involves peritonectomy procedures. Peritonectomy is a surgical technique that allows resection of all parietal peritoneum involved by peritoneal seeding. The visceral peritoneum invaded by tumor may require organ resection. Likewise, these intend to reduce peritoneal surface dissemination to a microscopic level. In brief, peritonectomy procedures are performed on the basis of disease extension by the following steps: 1) greater omentectomy and right parietal peritonectomy with or without right colon resection, 2) pelvic peritonectomy with or without sigmoid colon resection as well as hysterectomy and bilateral salpingo-oophorectomy, 3) lesser omentectomy and dissection of the duodenal-hepatic ligament with or without antrectomy and cholecystectomy, 4) right upper quadrant peritonectomy and glissonian capsule resection, 5) left upper quadrant peritonectomy and left parietal peritonectomy with or without splenectomy, and 6) other intestinal resection and/or abdominal mass resection.[8]

The natural history of this disease has been drastically modified since the introduction of a new surgical approach, proposed by Sugarbaker who defines it as a peritonectomy procedure consisting of the complete removal of the tumor. Surgery is followed by local drug administration aimed at eliminating microscopic and/or minimal residual disease left in the abdominal cavity following surgical manipulations. The additional effects of hyperthermia, through the use of a special pump, increase local tissue drug concentration and consequently antiblastic drug activity. This technique has been defined as hyperthermic intraperitoneal chemotherapy (HIPEC).[9]

The negative side of combined modality treatment is the relatively high morbidity and mortality rate in comparison with less aggressive treatment. Although most complications are related to surgery, intraperitoneal chemotherapy is not performed without any side effects. In particular, the lowest point of the white blood cell count, usually around the 10th day, as a result of bone marrow toxicity, endangers any surgical complication.[10]

Surgical expertise and postoperative management entail the experience of the entire medical team with all aspects of demanding surgery. Increasing experience with the surgical procedure, postoperative care, and handling complications has been shown to decrease operation duration, blood loss with need for transfusion, treatment-related morbidity and mortality and consequent intensive care unit stay and total in-hospital stay.[19]

This study was conducted to determine the efficacy and safety of peritonectomy procedures in the treatment of patients with PMP.

Methods

Clinical records and follow-up data of patients diagnosed with pseudomyxoma peritonei which originated primarily from the ovary were reviewed. All patients were treated surgically in a single institution and patients were grouped into those who underwent peritonectomy procedures and those who did not undergo peritonectomy procedures. For this study's purpose, peritonectomy is defined as stripping and removal of the anterolateral abdominal peritoneum, paracolic gutter peritoneum and pelvic peritoneum. Diaphragmatic peritoneum excision and resection of the gastric, intestinal, liver, gallbladder and/or spleen were not included in this study's peritonectomy procedures. Information on patient demographic characteristics, histologic subtypes of pseudomyxoma peritonei, nature of the mucinous ovarian tumors, dates of surgery and current status of the patient were collected and entered into a case registry form.

Due to the rarity of the condition, a case series study design was employed. Descriptive analysis of the data collected using frequency and percentages was employed for this study.

Results and Discussion

There were a total of 551 cases of mucinous tumors of the ovary seen at the tertiary government hospital

from 2006 to 2009. Majority of these were mucinous cystadenomas (64%). Its malignant counterpart, the mucinous cystadenocarcinoma, comprised 22% while the remaining 13% were mucinous tumors of low malignant potential. (Table 1)

Table 1. Mucinous tumors of the ovary seen in UP-PGH from 2006-2009.

Histology of Ovarian New Growth	Year 2006	2007	2008	2009	Total
Mucinous tumor of LMP	8	19	20	25	72
Mucinous cystadenoma	86	99	94	75	354
Mucinous cystadenocarcinoma	18	36	33	38	125
TOTAL	112	154	147	138	551

Majority of the patients diagnosed with PMP were between the ages of 31-40 years old (36%) and had a mean parity of 1-3 (43%). Majority had no co-morbidities (57%). At the time of diagnosis of PMP, 50% of the patients were already postmenopausal while the other half was still menstruating regularly. The most common complaint on admission was abdominal distention or enlargement, occurring in 57 percent of the cases. (Table 2)

Half of the cases with PMP had tumors of low malignant potential while 4 had benign ovarian new growths. The remaining 3 had frankly malignant mucinous tumors of the ovary. (Table 3)

An important prognostic factor in PMP is its histology. The classification described by Ronnet, et al. categorized PMP into 2 groups with different prognosis: DPAM, PMCA, and an intermediate/hybrid group. PMCA seems to behave like peritoneal carcinomatosis and has a very poor prognosis. In their analysis, the authors found that the histologic classification of PMP was found to have prognostic significance with five year age-adjusted survival rates of 84% for DPAM, 37.6% for tumors with intermediate or discordant features and 6.7% for classical PMC[14] In this study, there were 2 cases of PMCA, both arising from malignant ovarian neoplasms. One died 5 months after surgery (without peritonectomy) while the other one who was treated with peritonectomy was lost to follow-up thus her current status is unknown. (Table 3)

Furthermore, Ronnet, et al. found that DPAM was more common, accounting for 59.7% of cases compared to PMCA which accounted for only 25.7%. The rest were of the intermediate type.[14] In this study, majority (78%) of the patients with PMP had DPAM as the histologic classification on final biopsy result. There were only 2

Table 2. Socio-demographic characteristics of patients with PMP.

Patients with PMP (N=14)			
Variable		Number	%
Age	20-30	0	0
	31-40	5	36
	41-50	2	14
	51-60	1	7
	61-70	1	7
	>70	5	36
Parity	0	3	21
	1-3	6	43
	4-6	1	7
	7-9	3	21
	≥10	1	7
Civil Status	Single	4	29
	Married	7	50
	Widowed	3	21
Co-morbidities	Hypertension	1	7
	Diabetes mellitus	2	14
	Bronchial asthma	1	7
	Bronchial asthma and hypertension	1	7
	PTB	1	7
	None	8	57
Menstrual Status at Time of Diagnosis	Premenopausal	7	50
	Postmenopausal	7	50
Chief Complaint	Vaginal bleeding	1	7
	Hypogastric pain	1	7
	Abdominal pain	3	21
	Abdominal enlargement/ distention	8	57
	Abdominal enlargement and abdominal pain	1	7

Table 3. Patients with PMP diagnosis by selected characteristics.

Patient Code	Date diagnosed with PMP	Nature of mucinous ovarian new growth	Histo-logy of PMP	Perito-nectomy done	Follow-up course	Additional treatment	Present status	Date present status noted	Time period from diagnosis to present status (Months)
B	7/5/2006	Malignant	PMCA	No	Lost to follow-up	None	Dead	12/1/06	5
C	1/12/2008	Benign	DPAM	No	Recurrent disease	Herbal/ Alternative meds	Alive with disease	6/17/10	29
D	12/21/2008	Malignant	DPAM	No	Lost to follow-up	None	Alive with NED	7/27/10	20
H	12/9/2008	Benign	DPAM	No	Recurrent disease	None	Dead	1/1/10	13
I	7/10/2009	Benign	DPAM	No	Lost to follow-up	None	Unknown	-	-
L	8/11/2009	LMP	DPAM	No	Lost to follow-up	None	Unknown	-	-
M	5/15/2009	LMP	DPAM	No	NED	None	Alive with no disease	1/22/10	8
N	9/24/2009	LMP	DPAM	No	Lost to follow-up	None	Unknown	-	-
A	2/4/2006	Benign	NOS	Yes	Lost follow-up	None	Alive with NED	5/12/10	48
E	7/9/2008	LMP	DPAM	Yes	NED	None	Alive with NED	7/26/10	36
F	8/14/2008	LMP	DPAM	Yes	NED	None	Alive with NED	4/17/10	20
G	8/6/2009	LMP	DPAM	Yes	NED	None	Alive with NED	7/27/10	23
J	1/30/2009	LMP	DPAM	Yes	NED	None	Alive with NED	6/16/10	18
K	12/2/09	Malignant	PMCA	Yes	Lost to follow-up	None	Unknown	-	-

cases of PMCA (14%) and one case wherein the histologic classification of DPAM was not specified. (Figure 1)

Of the 11 patients with DPAM, 4 patients (43%) underwent peritonectomy while the remaining 7 (67%) did not undergo the said procedure. (Figure 2)

All 4 patients with DPAM and the patient with benign ovarian mucinous tumor with PMP not otherwise specified as to whether DPAM or PMCA who underwent peritonectomy are currently alive with no evidence of disease. Survival in this group of patients ranged from 18-48 months, with a median survival of 29 months. (Table 3)

Of the remaining 7 patients with DPAM who did not undergo peritonectomy, 2 developed recurrent disease, 4 were lost to follow-up, while 1 continued to have no evidence of disease. (Figure 4) Recurrences were noted between 13-29 months from the time of diagnosis of PMP. The sole patient who continued to have no evidence of disease had been disease-free for 8 months. (Table 3) The current status of the 4 patients who were lost to follow-up is unknown.

At present, there is no international consensus regarding the most beneficial treatment strategy for PMP. Due to the rarity of this condition, there have been no formal trials to provide guidelines for optimum treatment. However, proponents of surgical extirpation point out that there are certain features of PMP that makes it amenable to curative surgery. These include early peritoneal dissemination and accumulation in anatomically resectable sites by peritonectomy.[15]

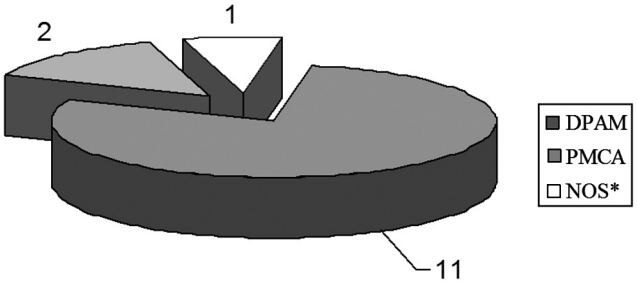

Figure 1. Distribution of patients based on histological classification of PMP (N = 14).

* NOS - not otherwise specified

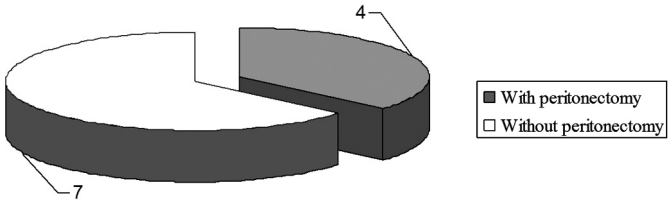

Figure 2. Distribution of patients with DPAM based on the inclusion of peritonectomy in the surgical procedure performed (N = 11).

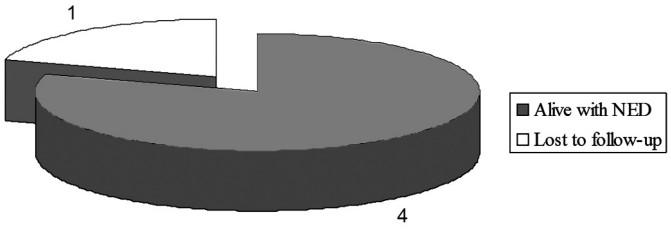

Figure 3. Current status of patients with DPAM and benign mucinous ovarian new growth, NOS treated with peritonectomy (N = 5).

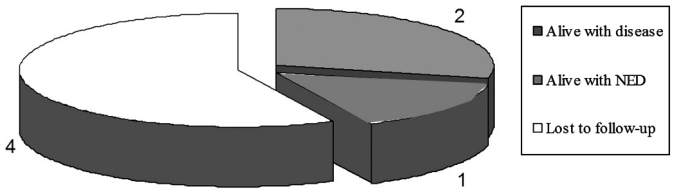

Figure 4. Current status of patients with DPAM who did not undergo peritonectomy.

Taking into account the considerable morbidity, if not mortality, which combined modalities may entail coupled with the prohibitive cost of chemotherapy, peritonectomy as part of a maximal cytoreductive effort may be a feasible option for this group of patients. This study has shown that the patients with PMP on whom peritonectomy was done as part of the surgical management are currently alive and with no clinical evidence of disease.

Although the cases of PMP treated with peritonectomy at the UP- PGH from 2006 and 2009 have been limited, it can be seen from the results of this study that there may be a therapeutic benefit in doing peritonectomy in this group of patients.

Conclusion

Peritonectomy as a treatment modality for pseudomyxoma peritonei arising from mucinous ovarian new growths may have a potential benefit in terms of disease-free interval. In this study, median disease-free interval was 29 months from the time of diagnosis. Furthermore, no recurrences were noted in this group of patients. However, further follow-up is on-going for 5-year survival analysis.

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