

# Pseudomyxoma Peritonei: A Case Report of an Incidental Finding at Cesarean Section

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## Abstract

Pseudomyxoma peritonei (PMP) is a rare neoplasia, the approach to which was largely palliative until recently. A 27-year-old nulliparous patient with a presumed dermoid cyst and pelvic pain related to pregnancy was incidentally found to have disseminated PMP during cesarean section at term for a breech presentation. The patient underwent surgical cytoreduction, operative heated intraperitoneal chemotherapy and early postoperative intraperitoneal chemotherapy, a novel approach known as “the Sugarbaker technique”. A literature review of this rare clinical scenario and a discussion of diagnosis and management are presented.

**Keywords:** Pseudomyxoma peritonei; Cytoreductive surgery; Cesarean section

## Introduction

Cancer during pregnancy is rare, occurring in approximately 1 in 1,000 women. The cancers most likely occurring during pregnancy are those of the breast, uterine cervix, ovary, lymphomas and the colorectum, in declining order [1]. Of the colorectal neoplasms, approximately 1% are appendiceal in origin [2]. Some of these tumors arise from mucin-2 expressing goblet cells and in some cases, the appendix may perforate and goblet cells proliferate throughout the abdominal cavity. Large volumes of mucinous material can rapidly amass within the peritoneum. This is a condition known as pseudomyxoma peritonei (PMP).

The case reported below is a rare presentation of an incidental finding of PMP at cesarean section. As Donegan (1983) [1] attests to, and this case illustrates, symptoms of cancer are

too often mistakenly attributed to the changes of pregnancy.

A review of the literature in light of the case presentation is discussed. Suggestions are made regarding diagnosis and management of this extremely rare disease.

## Case Report

A 27-year-old nulliparous patient was found to have a right-sided 7.6 cm heterogenous adnexal mass on routine antenatal ultrasound (morphology scan) at 20 weeks gestation. She was given the tentative diagnosis of an ovarian dermoid cyst and a follow-up ultrasound was arranged at 28 weeks gestation. The follow-up ultrasound was subsequently abandoned given that the working diagnosis was a dermoid cyst, the patient was asymptomatic and the fetus was growing normally.

Aside from a reassuring review for decreased fetal movements at 31 weeks, her pregnancy continued uneventfully. At 36 weeks gestation, the fetus was found to be breech on a routine antenatal visit. This was confirmed sonographically and, at the same time, it was observed that the “dermoid cyst” had grown to 18 cm and was occupying the pouch of Douglas.

Following an unsuccessful external cephalic version, she was consented for an elective cesarean section and right ovarian dermoid cystectomy at 38 weeks. On the day prior to surgery, she attended hospital for an anesthetic assessment. She reported ongoing pelvic pain, exacerbated with movement, which was attributed to her dermoid cyst.

The following day, she underwent an elective cesarean section. Under spinal anesthetic, the abdomen was entered through a Pfannensteil incision and routine entry, and was found to be grossly abnormal. Both ovaries were enlarged, multicystic and mucinous. A right salpingo-oophorectomy and left ovarian cystectomy were performed. The appendix similarly demonstrated enlarged mucinous cysts. Cystic deposits were evident throughout the omentum and palpable over the right side of the liver and the right diaphragm. The findings were consistent with PMP.

Intraoperative pathology samples confirmed low grade mucinous adenocarcinoma likely of appendiceal origin. Following delivery of a healthy male infant, she made an uneventful postoperative recovery.

The subsequent staging CT abdomen showed a ruptured mucinous tumor of the appendix with no appreciable metastasis.

Manuscript accepted for publication August 18, 2015

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doi: <http://dx.doi.org/10.14740/jcgo332w>

ses within the liver, surrounding bone or beyond the peritoneal cavity. Low density material was associated with the left ovary and pouch of Douglas but it was unclear whether this was free fluid or tumor deposits.

The patient was referred to St George's Hospital in Sydney for further assessment and management.

A plan was made for cytoreductive surgery. This was initially delayed for social reasons but at 6 months following her cesarean section, the patient underwent extensive cytoreductive surgery. She had extensive "jelly-like" disease intra-abdominally; the appendix was the obvious site of primary disease. Bilateral diaphragms, the liver surface, her pericardium and her pelvis were stripped of deposits. Due to the extent of disease, a splenectomy, cholecystectomy, right hemicolectomy, terminal ileectomy and greater and lesser omentectomy were performed. She then received 90 min of intraoperative intraperitoneal heated chemotherapy (mitomycin C at 41.5 °C). The peritoneal cancer index (PCI) score was 24. Early postoperative intraperitoneal chemotherapy (EPIC) was performed the following day.

Pathology results concluded low grade appendiceal mucinous neoplasm with perforation. The intraoperative peritoneal deposits confirmed low grade PMP equivalent to disseminated peritoneal adenomucinosis (DPAM).

At 5 weeks postoperatively, she developed a transient small bowel obstruction that was conservatively managed. By 3 months postoperatively, she had returned to her activities of daily living at home, was eating well, exercising and had returned to paid work.

At 5 months postoperatively, repeat CT demonstrated no residual or recurrent disease.

## Discussion

PMP is a rare condition with approximately 500 cases discussed in the medical literature [3]. To our knowledge, there are only four cases of this entity occurring in pregnancy, only one of which was discovered at cesarean section [4].

## Etiology

The notable Bohemian physician and pathologist, Carl von Rokitansky, first described PMP in 1842 [5]. The understanding of PMP pathogenesis has evolved considerably since then. As in our patient, the vast majority of cases are primary appendiceal mucinous neoplasms [6-8], but there are cases that have been related to an ovarian primary [9]. The pathologic process begins with neoplastic transformation of the appendiceal goblet cells that, upon appendiceal perforation, continue to proliferate into the peritoneal cavity. Through maintenance of mucin expression, intraperitoneal mucin amasses resulting in voluminous PMP [10].

## Clinical presentation

The clinical presentation of PMP is highly variable and non-

**Table 1.** Frequency of Symptoms and Signs of Pseudomyxoma Peritonei [13]

	Men (n = 105)	Women (n = 112)
Appendicitis	36 (34%)	22 (20%)
Increased abdominal girth	28 (27%)	21 (19%)
Ovarian mass	N/A	44 (39%)
Hernia	26 (25%)	4 (4%)
Ascites	5 (5%)	4 (4%)
Abdominal pain	5 (5%)	3 (3%)
Other	5 (5%)	14 (13%)

specific with up to 20% of cases diagnosed incidentally at laparoscopy or laparotomy [11, 12]. The most common symptom in both men and women is gradually increasing abdominal girth (Table 1) [13]. Twenty to thirty percent of patients will present with non-specific symptoms such as lower abdominal pain, pelvic pressure and nausea [14, 15]. Women often develop an ovarian mass, usually on the right side, which is commonly diagnosed at a routine gynecological examination, and men can have new-onset hernia as the primary complaint [13]. Pregnancy can mask and misconstrue the interpretation of all these symptoms and signs.

## Diagnosis

In diagnosing PMP, CT appears to be the most useful diagnostic tool. Diffuse loculations with mucin deposits exhibiting densities higher than non-mucinous or typical ascites are suggestive of PMP. The mucin deposits are loosely adherent to underlying surfaces; therefore, there is characteristic sparing of motile viscera such as the small bowel, and accumulation over non-motile organs, such as the liver and spleen [13, 16, 17]. Visceral "scalloping" arising from mucinous compression and fibrosis of organs [18] is pathognomonic of PMP.

Though CT may be of most diagnostic utility, its use in pregnancy is heavily guarded. To complicate diagnosis further, imaging by ultrasound can be misleading because the mucinous ascites can be mistaken for free intraperitoneal fluid [12]. However, there are sonographic features that can assist the clinician in distinguishing PMP (Table 2). When surrounded by benign ascites, the bowel floats freely and demonstrates positional shifting. Conversely, in PMP the gelatinous mucin tends to fix the bowel in position [19]. Koyama et al suggested that the finding of ascitic septations should alert the experienced clinician to the possibility of PMP [20]. Certainly, ascites, if present, is typically complex with multiple foci of echogenicity reflecting the mucinous composition [21]. Thus, in contrast to benign ascites, PMP varies in its gravity dependence due to its organ adherence. Lastly, the scalloping of hepatic margins evident on CT can typically be seen sonographically as well [19].

The role of tumor markers remains unclear but, as with most cancers of gastrointestinal origin, carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) are fre-

**Table 2.** Sonographic Features of Pseudomyxoma Peritonei

Classically unilateral
Cysts are typically
Large (up to 50 cm)
Filled with mucin (echogenic in appearance)
Distinct fluid-fluid level occasionally present (demarcation between free fluid and mucinous aggregate)
Bowel fixing (typically in the presence of ascites)
Complex ascites (often with septations) with variable gravity dependence
Organ margin scalloping (especially hepatic margins)

quently elevated in appendiceal neoplasms [13].

Therefore, a step up approach to investigation of lesions identified during pregnancy appears to be the safest and most sensible. Sonography is effective in routine screening and follow-up. CT is crucial in surgical evaluation. The risk of teratogenesis after 15 weeks gestation is extremely low [22]. The risk of carcinogenesis is less clear but certainly a single abdominal CT scan falls well below the carcinogenic dose estimated for a fetus [22]. In retrospect, this should have been the follow-up our patient received of the “dermoid cyst” uncovered at routine antenatal scan at 20 weeks gestation. If surgery is warranted, this is often safest in the second trimester, when the risk of spontaneous abortion or preterm labor is least [23].

### Classification

Classification of the PMP entity has been shrouded with controversy and lacks standardization.

In 1997, Ronnett and colleagues [7], based on the findings from 109 cases, devised a classification system for PMP based on malignant potential and histopathology results. Under this system, PMP is sub-classified into three groups, with cases in each group exhibiting homogenous histology. DPAM exhibits histologically benign peritoneal lesions that follow an indolent course progressing over several years. In contrast, peritoneal mucinous carcinomatoses (PMCA), usually with signet ring morphology, exhibit poor cellular differentiation and a rapid aggressive clinical course. A refinement of Ronnett et al’s original classification introduced the third sub-classification of PMCA-I (intermediate) describing lesions that would behave like PMCA but with a less aggressive course and therefore better survival outcomes.

Bradley et al [24] in a case series of 101 patients with PMP found no difference in survival outcomes at 1, 3 and 5 years between patients classified as DPAM or PMCA-I (but found PMCA patients had significantly worse clinical courses). Based on these findings and some confusion over terminology, they suggested classifying PMP as either low or high grade mucinous adenocarcinoma based on the grade of epithelium within the peritoneal mucin. In 2010, the American Joint Committee on Cancer (AJCC) and the World Health Organization (WHO) adopted Bradley’s classification system. However, it has not been widely adopted by the medical community and Ronnett’s revised classification remains commonly reported

by pathology services.

### Treatment

The importance of accurate classification and terminology has implications for the management of this disease.

Traditionally, appendiceal neoplasms with associated PMP carried a median survival of 3 years [13]. Serial surgical debulking was the mainstay of management and was repeated until no further benefits for the patient were achieved. The treatment was largely considered to be a palliative one.

Over the last three decades, a new standard of care has emerged. The “Sugarbaker technique” involves extensive abdominal surgery comprised of peritonectomy, heated intraoperative peritoneal chemotherapy (HIPEC) and EPIC. Systemic chemotherapy is rarely indicated because lymphatic and hematogenous metastasis is rare in appendiceal neoplasms [12, 25]. It may be of use in patients with recurrent or progressive disease [26].

No double blinded trials have been undertaken to compare the traditional approach versus the Sugarbaker technique. However, with serial surgical debulking alone, only 3-4% of patients will be disease-free at 10 years [27]. In a case series of 60 patients managed according to the Sugarbaker technique, 70% of patients remained disease-free 10 years postoperatively [28]. Understandably, the treatment itself is risky. Butterworth and colleagues reported a morbidity and mortality rate of 56% and 11%, respectively associated with intraperitoneal chemotherapy [29]. Complications included prolonged ileus, enteric fistulae, pancreatitis, pulmonary embolism, chronic abdominal pain and intra-abdominal abscesses. Given the considerable risks involved with this procedure, it is imperative to assess suitability to this management.

Research is increasingly turning to the crucial role of mucin in the pathogenesis of this disease. Amini and co-workers explored several novel approaches to mucin production including glucocorticoids and COX inhibition amongst others [10]. This may present an adjunct area of treatment in the future.

### Prognosis

Prognosis is dependent on the histologic grade of disease and whether operative cytoreduction is complete or not. In a case

report of 385 patients, partial cytoreduction did not confer any survival benefit over grossly inadequate cytoreduction [13]. A review of 274 cases of PMP classified according to the AJCC/WHO criteria revealed a 5-year survival of 63% for low grade mucinous adenocarcinoma and 23% for high grade mucinous adenocarcinoma [30].

In our patient, a delay in definitive treatment undoubtedly allowed an increase in tumor volume to occur. Initial exploration of the abdomen at cesarean section gave a PCI of 6. Six months later, at the time of peritonectomy, the PCI was 24. However, since the disease was low grade and surgical cytoreduction was complete, minimal compromise in the prognosis was expected. Early identification of the histological grade of the disease and subsequent completeness of cytoreduction are imperative in prognostication of PMP.

If a pregnant patient, in their second trimester or beyond, is diagnosed with low grade disease, definitive treatment can be deferred until 34 - 35 weeks when the infant can be delivered safely. If a cesarean is obstetrically warranted at this time, a vertical incision carries a lower risk of mucin deposits seeding into the abdominal wall [23]. Haase and colleagues reported a case of a patient diagnosed with PMP at 17 weeks gestation. Pregnancy was preserved till 35 weeks gestation and she underwent cytoreductive surgery at 2.5 weeks post-delivery. At 5-year follow-up, the patient remained disease-free [23].

Conversely, if a pregnant patient in their second trimester is diagnosed with high grade disease, definitive treatment should not be delayed and termination of the pregnancy should be considered. In a Japanese case study, a patient diagnosed with PMP at 27 weeks gestation underwent cesarean section at 34 weeks gestation in consultation with the family, neonatologists and obstetricians. Although the patient was still alive 6 months postoperatively, her cancer had continued to progress [20].

## Conclusion

An index of suspicion should be maintained with all lesions identified during pregnancy. Serial sonography is appropriate. CT scanning and surgical exploration may be necessary in rare cases. This can be delayed to later in the pregnancy in most forms of PMP but should not be delayed in patients with rapid progression of disease. Surgical cytoreduction, intraperitoneal chemotherapy and EPIC appear to be the most effective course of management. Assisted reproduction strategies should be offered as it may be a necessity in achieving future pregnancies.

## Conflicts of Interest

All the authors declare no conflicts of interest.

## Author Note

The PCI grades peritoneal disease based on the extent of peritoneal surface involvement. The abdominal-pelvic region is divided into 13 regions, each of which is given a score out of 3

depending on disease involvement. The PCI is hence out of 39. In typically non-invasive diseases such as PMP, the PCI bears little prognostic value but serves to score the completeness of cytoreduction.

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