

# Primary peritoneal cancer in pregnancy: case report and review of the literature

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## Summary

**Introduction:** As this is the second only published report of primary peritoneal cancer (PPC) in pregnancy, it aims to bring awareness and reviews the current information of this exceptionally rare condition. **Case Report:** The case report outlines the clinical presentation of a 31-year-old pregnant woman and how she was diagnosed with the condition. **Discussion:** PPC can be difficult to diagnose with similar characteristics to ovarian cancer. From studying the literature, this paper addresses the histological and immunohistochemical distinguishing features. It also addresses some of the issues with diagnosing cancer in pregnancy or for women in their reproductive years. **Conclusion:** As this condition is so rare in young women, this overview is a useful addition to the medical literature.

**Key words:** Chemotherapy in pregnancy; Neoplasia in pregnancy; Serous carcinoma; Ovarian cancer; Primary peritoneal cancer.

## Introduction

This is a case report and review of the literature into primary peritoneal cancer (PPC) in pregnancy. The aim is to highlight and bring awareness to the clinical manifestations of this exceptionally rare condition.

Malignant neoplasia in pregnancy is rare with an incidence of one in 1,000 pregnancies [1]. The most common gynaecological cancers in pregnancy are of cervical and ovarian origin [2]. PPC arises from the abdominal and pelvic peritoneum and can disseminate to the omentum. Usually there is no other primary tumour and the ovaries appear normal [3]. The most prevalent histological type is serous adenocarcinoma [4].

There has been only one other reported case of PPC in pregnancy in the literature. This involved a 28-year-old multigravida Taiwanese woman who presented with gastro-intestinal symptoms late in her pregnancy. She was found to have PPC with metastases to her colon. At caesarean section bilateral peritoneal tumours measuring 7 and 8 cm were noted; both ovaries appeared normal. The histology of the tumours showed serous papillary adenocarcinoma. A follow-up CT scan revealed neoplastic change in the descending colon and the patient subsequently underwent a left hemicolectomy. This histology showed metastatic serous adenocarcinoma, confirming PPC [5].

This is the second reported case of PPC to be diagnosed in pregnancy.

## Case Report

A 31-year-old Caucasian woman presented at 36 weeks gestation to the present Hospital with a history of constant back pain, lethargy, and reduced appetite. She previously had an uncomplicated pregnancy resulting in a normal delivery of a healthy, average sized baby. Her past medical history was unremarkable and she had no family history of note. Initial clinical examination did not reveal any significant obstetric or medical pathologies and she was treated for mechanical back pain with simple analgesia. However, during the admission she developed night sweats, vomiting and abdominal distension.

An obstetric growth ultrasound scan indicated normal fetal growth, liquor volume, and umbilical artery Dopplers, and significant maternal ascites were also detected.

Blood serology revealed normal liver and renal function but a low albumin of 18 g/L. A chest X-ray showed a small right pleural effusion and a transthoracic echocardiography showed a small pericardial effusion. Tumour markers revealed an elevated Ca125 (1180 kU/L) and AFP (81 kU/L) but a normal CEA (<0.5 ug/L) and Ca19-9 (24 kU/L).

In view of the markedly raised Ca125 and the significant amount of peritoneal fluid, it was deemed necessary to induce labour and arrange further investigations post-delivery. The patient underwent induction of labour two days after her admission and delivered a healthy baby vaginally without any obstetric complications.

A postnatal CT of the abdomen and pelvis confirmed large ascites and right side pleural effusion with normal pelvic organs. Cytology from the ascitic fluid showed numerous clumps of adenocarcinoma cells. The immuno-profile was CK7+, EMA+, NFE+, GCDPF15-, Napsin-, TTF1, and CK20-. The ascites were subsequently drained for symptomatic relief (Figure 1).

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Figure 1. — A CT image demonstrating the patient's ascites.

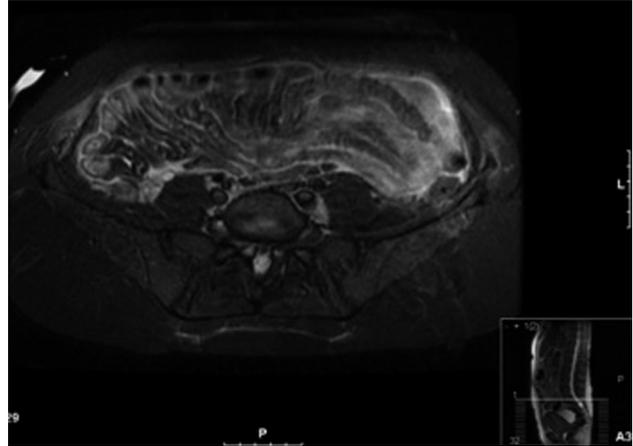


Figure 2. — The patient's MRI image showing the extensive omental disease.

An MRI of the abdomen and pelvis followed and revealed extensive omental disease, ascites, a possible metastatic subcapsular lesion of the liver, and normal ovaries and uterus (Figure 2).

The histology from a CT guided omental biopsy was consistent with a serous papillary carcinoma of unknown origin (WT1 +ve, P53 +ve, CK7 +ve, CK20 -ve, and proliferation index 50%) (Figure 3).

The patient underwent neoadjuvant chemotherapy after a mammogram and BRCA gene testing. She was BRCA positive. The patient subsequently had a debulking laparotomy that involved a total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, appendicectomy, peritoneal biopsies, and plasma-jet ablation of peritoneal nodules. The histology confirmed Stage 3c high-grade serous carcinoma of the peritoneum.

She recovered well after the surgery and at the time of writing is currently undergoing further cycles of carboplatin and paclitaxel chemotherapy.

## Discussion

PPC in pregnancy is an extremely rare pathology as it predominantly affects peri-menopausal or post-menopausal women with a median age range of 63-67 years of age [6,7].

PPC or serous extra-ovarian carcinomas have similar clinical presentations, histological appearances, and immunohistochemical features to ovarian carcinomas. However, the incidence of PPC is significantly lower than that of epithelial ovarian cancer (6.78 vs. 120.5 cases per million) [8]. This figure has increased substantially over the past 30 years. This could be due to a true increase or improvements in the available diagnostic modalities [7].

Preoperative diagnosis can be difficult. PPC typically presents with abdominal pain, abdominal distension, nausea, vomiting or change in bowel habits. Those can also be common pregnancy-related symptoms or symptoms of ovarian carcinoma. Radiological evidence usually includes normal-sized ovaries, ascites, omental caking or peritoneal

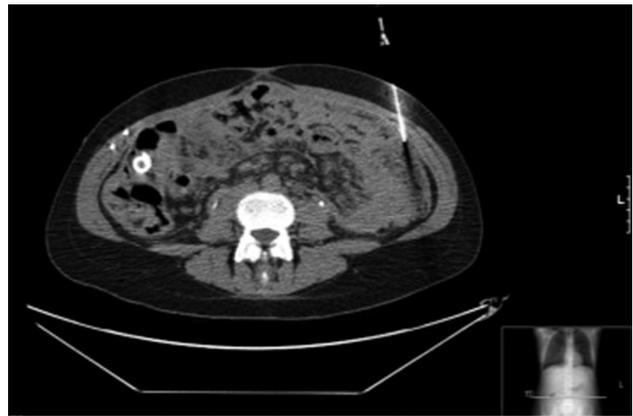


Figure 3. — An image of the patient's CT guided omental biopsy.

nodules [9]. The Gynecological Oncology Group (GOG) has developed specific criteria to improve the definition and diagnosis of PPCs. The criteria include: 1) ovaries are of normal size (<4.0 cm largest diameter); 2) extra-ovarian site involvement exceeds that of the ovarian surface; 3) ovaries not involved or there is only superficial or cortical involvement of <5mm in depth; 4) predominant serous histology [10].

Histopathology is mandatory to confirm primary peritoneal serous carcinoma. However, it cannot reliably differentiate from primary ovarian carcinoma due to its histological similarities [9]. Almost 10% of epithelial ovarian carcinomas are reclassified as primary peritoneal serous carcinomas [11]. One theory for their similarity proposes that PPC arises directly from neoplastic changes of the müllerian epithelium, commonly found in the para-tubal and ovarian area. Another theory suggests a metaplastic change from distant coelomic epithelium to Müllerian, followed

by neoplasia due to oncogenic stimuli [12]. These hypotheses suggest an identical embryological heritage and explain why primary peritoneal serous carcinomas and epithelial ovarian carcinomas are difficult to distinguish.

Despite their similarities, there are some differences. In both conditions CA-125 is markedly elevated and can be used for monitoring disease progression, efficacy of treatment, and recurrence [6]. However Choi *et al.* stated that primary peritoneal serous carcinoma presents with higher levels of CA-125 in comparison to epithelial ovarian cancer. The omentum is involved to a greater extent and PPC is less responsive to platinum-based chemotherapy [13].

Another area of distinction is the tumorigenesis of these two cancers. PPC will often include the involvement of cytokeratin 7 (CK7), HER-2/neu, p53, estrogen (ER), Wilm's tumor suppressor protein (WT1), CA 125, bcl-2, nm23- H1, Ber-EP4, MOC31, and mesothelin [14-16]. Teng-Hou *et al.* also isolated potential molecular markers. They found three Wnt intracellular signalling proteins important in PPC; beta-catenin, E-cadherin, and Wnt5a. Wnt5a was negative in all of the PPC cases, whereas all three were positive in the ovarian carcinomas [17]. This could be a possible immunological distinguishing marker.

Studies have shown that 30% of patients with PPC Stage III or above were positive for BRCA 1 or 2 [18]. Women who were positive for BRCA 1 /2 and had undergone a prophylactic bilateral salpingo-oophorectomy still had a subsequent substantial risk of developing peritoneal cancer [19].

In the present case the immunohistochemical staining from the omental biopsy was positive for WT1, p53, Ca125, and CK7 and negative for CK20. The majority of noncolonic carcinomas likely to metastasize to the ovary are CK7+/CK20- [20]. These results are consistent with PPC. The other differential diagnosis could include peritoneal tumour metastasized from the ovaries [14]. However, the present authors considered the lesion to be a PPC due to the presence of normal ovaries on radiological imaging and on histological examination.

Clinical and histopathological similarities between PPC and epithelial ovarian carcinoma have led to the suggestion that the management should be identical. The primary management is maximum cytoreduction. The treatment consists of debulking surgery, including a total abdominal hysterectomy with bilateral oophorectomy and omentectomy, followed by cisplatin-based chemotherapy. Improved prognosis and higher response rate has been achieved in patients who have undergone optimal cytoreduction surgery [21]. Cisplatin-based chemotherapy is the most common first-line regimen. However, combination regimens using paclitaxel as well showed better responses [21, 22]. The present patient received a combination of carboplatin and paclitaxel. Interestingly, the grade of the serous adenocarcinoma does not seem to affect chemotherapy response [21].

Although there is no data available for the best regimens

Table 1. — Potential effects of chemotherapy at varying gestations [23].

Gestational age (weeks)	Development stage	Effects on embryo/fetus
0-2	Multicellular	Spontaneous abortion
3-12	Organogenesis	Spontaneous abortion; major congenital abnormalities
>12	Intrauterine growth and development inc. CNS; palate; gonads; eyes; ears	Functional defects; stillbirth; Intrauterine growth restriction; premature labour; myelosuppression

Table 2. — Demonstrating survival and severe disability percentages in preterm babies [24-27].

Gestational age (weeks)	22	23-25	26-28	29-32	34
(%) Survival to discharge home	2	20-66	77-90	95	99
(%) Severe disability	No data	20-35	10-25	10-15	Same as term

regarding PPC during pregnancy, the overall prognosis is poor with a median survival ranging between 7-28 months and a five-year survival rate varying between 0-26.5% [9].

Peritoneal cancer in pregnancy poses unique issues involving the timing of delivery and the commencement of chemotherapy treatment. Surgical management is the mainstay of treatment often with adjuvant or neoadjuvant chemotherapy. Cytotoxic chemotherapy treatments can be administered in the second and third trimesters but the fetus is at an increased risk of intrauterine growth restriction and altered development of the central nervous system. Table 1 shows these potential effects. It can also cause minor anomalies of late-forming tissues, premature labour, myelosuppression, and even stillbirth. This emphasises the importance of a multidisciplinary approach, especially in pregnancy in order to evaluate the risks and benefits of delivering the baby prematurely versus commencing treatment while in utero [23]. Table 2 shows the survival rates and morbidity for varying preterm deliveries.

Women of reproductive age, who have not started or completed their families at the time of diagnosis, could undergo treatment to preserve their fertility first. This could include oocyte vitrification and cryopreservation of ovarian tissue before the surgery and chemotherapy [28].

## Conclusion

Since there is only one similar reported case, the present authors consider this report a useful addition to the medical literature. This case illustrates that common pregnancy symptoms could be related to an underlying life-threatening aetiology. The present authors suggest that PPC should

be included in the differential diagnosis for non-specific gastrointestinal symptoms in the antenatal period. Timely diagnosis as result of the awareness of this entity could contribute to immediate treatment and improved prognosis.

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