

Rare primary fallopian tube carcinoma; a gynaecologist's dilemma

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Abstract

Primary fallopian tube carcinoma is rare and accounts for 0.14-1.8% of all malignancies of the female genital tract. It has been found to be associated with nulliparity and subfertility, as well as with pelvic inflammatory disease. High parity has been reported to be protective but not in our 3 cases. History of pregnancy and the use of oral contraceptives decrease the PFTC risk significantly in literature. PFTC has been described in high-risk breast-ovarian cancer families with germ-line BRCA-1 and BRCA-2 mutations. Symptoms are nonspecific and include abdominal pelvic pain, vaginal bleeding and watery discharge. However, diagnosis is rarely achieved pre-operative because of misleading imaging. In many cases, the diagnosis is made incidentally on histopathology after surgery for an unrelated condition commonly being an ovarian carcinoma.

Keywords: PFTC (Primary fallopian tube carcinoma), CA-125 levels, EOC (Epithelial ovarian cancer), BRCA-1 and BRCA-2 mutations.

Introduction

Primary fallopian tube carcinoma is rare and accounts for 0.14-1.8% of all malignancies of the female genital tract. Secondary malignant lesions arise usually from the adjacent ovary or from the uterus, sometimes from the gastrointestinal tract and on a rare occasion from the breast or peritoneal carcinomatosis.¹ It is seen to arise in post-menopausal women. Symptoms are nonspecific and include abdominal pelvic pain, vaginal bleeding and watery discharge.² However; diagnosis is rarely achieved pre-operative because of misleading imaging.¹ Diagnosis of PFTC may be suspected in cases of postmenopausal bleeding or spotting with negative diagnostic curettage.⁵ In many cases, the diagnosis is made incidentally after surgery for an un-related condition commonly being an ovarian carcinoma. There have been a little over 2000 case reports, since its first description in 1847.¹

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Case Series

Three cases are presented. The data of case 1 and 2 was retrieved from the records after fulfilling the requirements and informed consent was taken from case 3 for publishing the findings.

Case-1

A 65 year old female para 5+2, presented with a lower abdominal mass, in August 2002. All five of her deliveries were spontaneous vaginal deliveries, and she had been post-menopausal since the past 15 years. She also gave a history of having had paraumbilical hernia around 10 years back.

On abdominal examination a firm mobile mass, about the size of a tennis ball was found to be palpable below the umbilicus. Moderate ascites was also present. Per vaginal examination revealed a smooth and firm cervix, the uterus could not be demarcated and no mass was felt.

CA 125 was 1120i.u/ml. Ultrasound abdomen showed a mixed echogenic mass, measuring 5.8 × 4.5cm, a little on the right side of abdomen and mild to moderate ascitic fluid was found to be present. Ultrasound pelvis showed a small uterus, measuring 5.8 × 4.5cm, floating in the fluid and a complex irregular mass in the right adnexa surrounded by fluid. Massive fluid was seen in the pelvis and the left ovary was not visualized.

Based on the investigations a staging laparotomy keeping diagnosis of ovarian cancer, was planned and performed which showed an anteverted uterus, covered with multiple small pinhead sized nodules. Both the ovaries were found to be atrophic and the entire peritoneal cavity was studded with tiny metastatic nodules. The omentum was thick and adherent to the anterior abdominal wall and the appendix was also thickened and studded with deposits. A Total abdominal hysterectomy with bilateral salpingo-oophorectomy and omentectomy was performed and the specimens, along with the ascitic fluid (about 3 liters), were sent for a histopathological and cytological assessment respectively. She was staged as FIGO stage IIIB.

Histopathology demonstrated adenomyosis, with a leiomyoma in the uterus and the outer wall of the right fallopian tube showed a poorly differentiated primary

fallopian tube adenocarcinoma. The omentum showed metastatic adenocarcinoma and the ascitic fluid cytology showed malignant cells, also consistent with metastatic adenocarcinoma. She was referred for chemotherapy.

Case-2

A 50 year old, para 12+1, came in with complaints of abdominal distension, constipation and urinary retention since the past 1 week, in 2009.

She was married for the past 35 years and had her last delivery was 7 years back. All her deliveries were vaginal.

On examination the patient looked anxious and her vitals were normal. Abdominal examination revealed distention and an ill-defined mass up to 14-16 weeks in size. Per vaginal examination the cervix was found to be firm and pushed posteriorly, the uterus was anteverted, bulky and adnexal fullness and tenderness were present.

CA 125 was 729i.u/ml. The ultrasound of abdomen and pelvis showed ascites and a cystic mass in the right adnexa, measuring 11.9×7.9cm. A CT scan was done which showed evidence of a solid (12×6cm) cum cystic (13×12cm) mass in the pelvis, probably ovarian in origin. A large amount of free fluid was also seen in the abdomen, pelvis and peri-hepatic region but liver was unremarkable. Infiltration was also seen in the mesentery beneath the abdominal wall as well as the lower pelvic region, and was invading the pelvic bowel loops. Ascitic fluid was taken for cytology, which showed giant malignant cells.

The patient was advised a staging laparotomy, which was performed with the patient's consent. Considering ovarian carcinoma on examination and investigations

staging laparotomy was planned but due to extensive metastasis it was not possible to debulk the disease. During the procedure about 5 liters of ascitic fluid was drained, bilateral ovarian tumours, with mucinous fluid and ruptured capsules, were removed. The uterus could not be removed as it was fixed and adherent to the bladder. The omentum was studded with deposits and was removed. Metastatic nodules were present all over the peritoneum, bowel loops and under surface of the liver. She was staged as FIGO stage III C as parenchyma of liver was not involved on CT scan.

The bilateral ovarian masses, fallopian tubes and omentum were sent for histopathological analysis, which showed primary serous cyst adenocarcinoma of the fallopian tube. The tumour involved one fallopian tube and bilateral ovarian surfaces; the residual ovaries showed no abnormalities. The omentum showed extensive tumour involvement.

The patient was referred to an oncologist for chemotherapy.

Case-3

A 45 year old female, Para 2+1, was admitted in 2014 with complains of heavy menstrual bleeding since the past 8 years, with the provisional diagnosis of endometriosis and adenomyosis. She had a painful regular menstrual cycle, with a heavy flow for she had to change 15-16 times a day. She had already tried conservative treatment, which had not improved her symptoms.

Her routine investigations were normal. Ultrasound revealed a 5×3.5cm cyst in the left ovary with internal echoes. Her serum Ca-125 level was 77.3U/ml

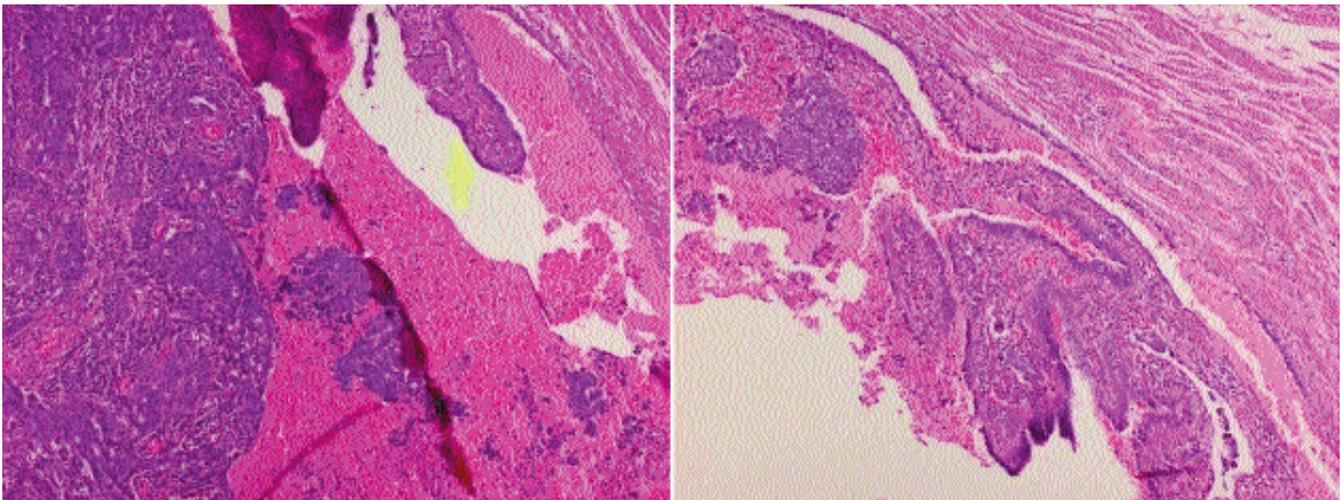


Figure-1: Primary Serous Cyst Adenocarcinoma of the Fallopian Tube.

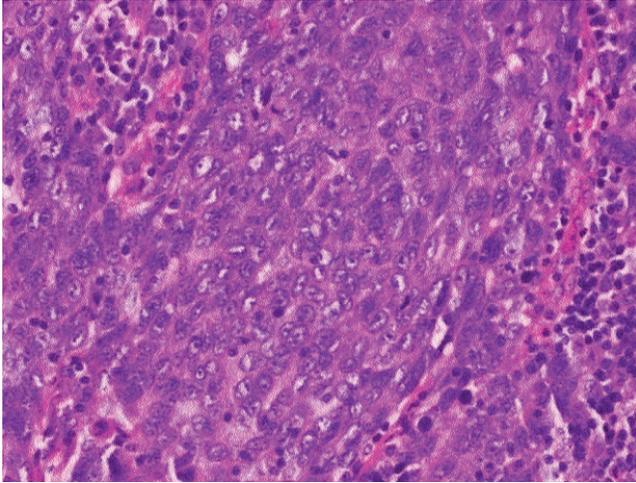


Figure-2: Higher magnification view: Primary Serous Cyst Adenocarcinoma arising from the lumen of right fallopian tube.

Considering endometriosis on history examination & ultrasound a total abdominal hysterectomy with bilateral salpingo-oophorectomy was planned and performed. On inspection of the pelvic cavity adhesions between the gut, the left adnexa and uterus were seen. The uterus was anteverted with restricted mobility, 8-10 weeks in size. The right ovary with a chocolate cyst and nodular fallopian tube was adherent to posterior ovarian fossa and gut. The rectum was adherent to the posterior uterine wall. Left fallopian tube and ovary were both normal.

The uterus, both ovaries and both fallopian tubes were sent for histopathological analysis, which revealed primary serous cyst adenocarcinoma of the fallopian tube confined to right tube only (Figure-1,2) The right ovary showed endometriosis. Moderate nonspecific endocervicitis was also present. She was staged as FIGO stage 1a of Primary fallopian tube carcinoma. In this case the pre-operative diagnosis was incorrect. This is indicative of the fact that Fallopian tube carcinomas are almost difficult to diagnose pre operatively and diagnosis is made usually after histopathology.

The patient was discharged, 4 days after the procedure and was referred to an oncologist who advised her 6 cycles of chemotherapy. She is doing well uptill now and in follow up with C.T scan and serum CA 125

Discussion

Primary Fallopian Tube Carcinoma (PFTC) is a malignancy of the tubal epithelium; first discovered in 1847.¹ These are one of the rarest carcinomas, accounting for about 0.14-1.8% of all gynaecological malignancies, and are

mostly adenocarcinomas on histological findings. The peak incidence is between the ages 60 and 64 years, with the mean age of incidence being 55 years (age range: 17~88 years).² Our 2 patients were postmenopausal and 1 patient was premenopausal. There are no known predisposing factors, but it has been found to be associated with pelvic inflammatory disease as well as with nulliparity and subfertility.⁴ This was not the case in all 3 patients. High parity has been reported to be protective which was again not present in our case. History of pregnancy and the use of oral contraceptives decrease the PFTC risk significantly. PFTC has been described in high-risk breast-ovarian cancer families with germ-line BRCA-1 and BRCA-2 mutations. Some studies suggested that the frequency and structure of the chromosomal changes (BRCA-1 or BRCA-2 mutations) observed in PFTC had similarities with those found in breast, serous ovarian, and uterine carcinomas, and consequently, a common molecular pathogenesis was claimed.⁵

Patients usually present with a palpable pelvic/abdominal mass (61%), abnormal vaginal bleeding (47.5%), lower abdominal pain (39%), and abnormal watery vaginal discharge (20%),^{1,2} Rarely episodes of profuse watery discharge or hydrops tubae profluentis are seen.

Tumour markers like serum Ca-125 may be raised.⁶ Ultrasound is the simplest and usually the initial imaging investigation. Fallopian tube malignancy should be considered where unexplained solid masses, corresponding with the expected location of the tubes, are seen in association with normal ovaries. In addition, Color Doppler can help to detect neo-vascularisation and low resistance indices within solid components. Features on ultrasound that suggest a fallopian tube malignant lesion include neo-vascularization in tube, the presence of an irregular tubal wall, papillary protrusions and pseudosepta.⁶ On CT scan and MRI tumours can be completely solid and others are predominantly cystic and the latter contain papillary projections or solid regions.⁶ Pre-operative diagnosis of PFTC was made in 4.6% of cases in the series of Alvarado-Cabrera et al,⁷ because of it being rare they are found incidentally in patients undergoing exploratory laparotomy.

When compared with EOC, PFTC is often diagnosed at an earlier stage because of abdominal pain secondary to tubal distention but was not so in our cases. However, a diagnosis of PFTC may be suspected in cases of postmenopausal bleeding or spotting with negative diagnostic curettage. Pap smear positivity occurs in 10%-36% of cases. The Pap smear shows abnormal, suspicious,

or poorly differentiated cells or glands alternating with negative smear. Also, psammoma bodies found in the Pap smear are suggestive of gynaecologic malignancy, and more detailed examination is required.⁵

PFTC spreads by local invasion, transluminal migration and via the lymphatics and the bloodstream. 33% of patients with all stages of disease have been reported to have para-aortic lymph nodes metastasis.^{6,8} Data from the literature indicate that patients with PFTC have a higher rate of retroperitoneal and distant metastases than those with EOC as was seen in 2 of our cases. Metastases to the para-aortic lymph nodes have been documented in 33% of the patients with all stages of disease. The PFTC is richly permeated with lymphatic channels that drain into the para-aortic lymph nodes through infundibulopelvic lymphatics.⁵ The stage of disease at the time of diagnosis is the most important factor affecting the prognosis. PFTC carries five-year survival rates of about 68-76% for Stage I disease, 27-42% for Stage II disease and 0-6% for Stage III and IV disease so it is very important to diagnose these neoplasms in the early stages.^{6,8} These tumours are staged surgically according to the updated staging classification by the International Federation of Gynecology and Obstetrics (FIGO) Oncology Committee. In 3 of our cases PFTC was diagnosed histopathologically after surgery was done for different reasons

Surgery is the treatment of choice for PFTC, and the surgical principles are the same as those used for ovarian cancer. The procedure of choice is abdominal total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, selective pelvic and para-aortic lymphadenectomy for any stage for fallopian tube carcinoma. Postoperative adjuvant chemotherapy that's similar to that used for ovarian carcinoma is employed with intravenous Taxol and Cisplatin being today's drug combination of choice.^{9,10}

CA-125 is a useful tumour marker for the diagnosis, assessment of response to treatment, and detection of tumour recurrence during follow-up as it was raised in all our patients. The CA-125 antigen is often expressed by PFTC. Although CA-125 per se is not diagnostic for PFTC, as more than 80% of patients have elevated pre-treatment serum CA-125 levels. Elevated serum CA-125 levels have been detected more frequently in advanced or recurrent disease. Most recurrences are extrapelvic, and half or more of them are extraperitoneal, usually in combination with intraperitoneal recurrence. Most recurrences have been reported in the first 2-3 years but

have also occurred many years later. Because there is no effective second-line or salvage chemotherapy, recurrent disease is associated with a very poor prognosis.⁵

Conclusion

As already mentioned, primary fallopian tube carcinoma is extremely rare. Etiology also remains unclear due to similar reasons. Menopause has been identified as a risk factor; but considering its late clinical presentation, it is possible that diagnosis may be postmenopausal, whereas the disease itself may be present before the onset of menopause and may be found incidentally as reported in one of the case in this series. It has been reported to present clinically, with a variety of non-specific signs and symptoms. On imaging, it is mostly described as a lower abdominal, pelvic or adnexal mass and it is often confused with ovarian malignancies. A definitive diagnosis can only be made on a microscopic analysis. So clinicians should consider fallopian tube carcinoma differential diagnosis while planning for surgery in pre and post-menopausal patients, as early diagnosis can improve the prognosis. Suspicion should be high in atypical cases.

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