

A clustering of breast, lung, and fallopian tube cancers

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PPrimary fallopian tube carcinoma (PFTC) is a rare malignancy. The authors present what may be the first case of PFTC occurring in a woman with a history of both breast and lung cancers. This clustering of lung, breast, and fallopian tube cancers may suggest that they have a common risk factor. Regular tumor surveillance in patients with a diagnosed malignancy may increase the rate of detection of other primary tumors.

PFTC is a rare malignancy, accounting for about 1% of all malignancies of the female genital tract.¹ The average annual incidence of PFTC in the United States was 0.41 per 100,000 women from 1998 to 2003.² About 15% of patients with PFTC have another malignancy before the diagnosis of PFTC.³ Presented here is what may be the first case of PFTC occurring in a woman with a history of both breast and lung cancers.

Case report

A 76-year-old Caucasian woman with a 75 pack/year history of smoking was diagnosed with metastatic adenocarcinoma of the lungs in 2005. She had a complete response with chemotherapy and was being followed with regular imaging for tumor recurrence. Her medical history included a hysterectomy without salpingo-oophorectomy for uterine fibroids in 1982. In 1985, she was diagnosed with ductal carcinoma in situ of the left breast, which was treated with a lumpectomy followed by chemotherapy and radiotherapy. Her family history was negative for colon and ovarian cancers but positive for breast cancer (her mother at 92 years of age). The patient's tumor surveillance for lung cancer consisted of CT scans every 6 months.

In May 2007, she was asymptomatic, but a CT scan of the chest, abdomen, and pelvis showed a new 30-mm abnormal solid and cystic right adnexal mass without any associated hydronephrosis. Stable bilateral pleural parenchymal scarring

was also present. Two pleura-based irregular parenchymal opacities were seen; the larger one (14 mm) was in the left upper lobe, and the smaller one (7 mm) was in the right lower lung.

In November 2007, she reported having some vague intermittent abdominal pain, which resolved spontaneously. No mass was palpable during abdominal or pelvic examination. A scheduled CT scan of the chest, abdomen, and pelvis showed an interval increase in the right adnexal mass to 37 mm, with mild dilatation of the right renal collecting system suggestive of obstructive uropathy due to mass effect. New small cystic changes were also observed in the left adnexal region. The interval size of the larger lung opacity decreased from 14 mm to 12 mm, and the interval size of the smaller lung opacity increased from 7 mm to 10 mm. A new 6-mm ill-defined noncalcified density in the anterior left lung base was also noticed. These findings raised the suspicion of tumor recurrence.

In December 2007, the patient underwent PET/CT, which showed a 42-mm right solid and cystic adnexal mass suspicious of a neoplasm due to the increased uptake of 7.0 SUV_{max} (maximum standardized uptake value). Mild cystic changes were also seen in the left adnexa, with the larger cyst measuring 25 mm but without increased uptake of fluorodeoxyglucose (FDG). Neither of the pulmonary nodules demonstrated an increased uptake of FDG (Figure 1). A pelvic ultrasonogram showed bilateral complex adnexal masses, which were thought to be ovarian in origin. No uterus was seen.

An exploratory laparotomy with bilateral salpingo-oophorectomy was performed. The pathology

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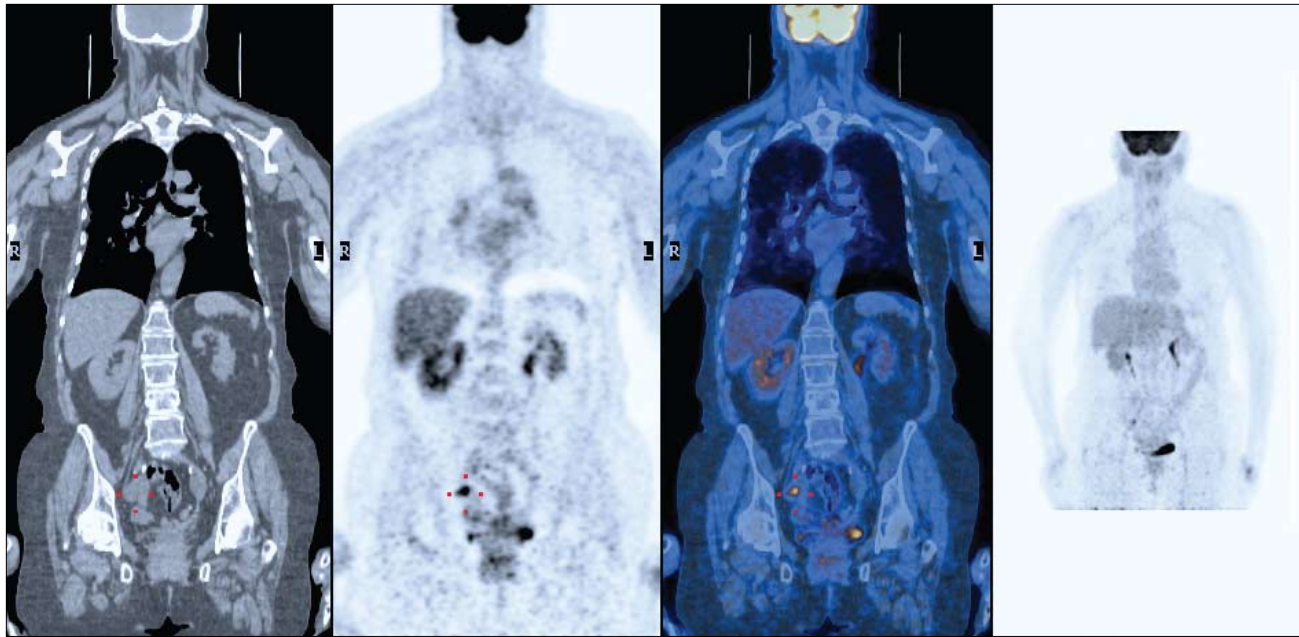


FIGURE 1 Axial and coronal CT, PET, and fusion PET/CT images, as well as coronal maximum-intensity profile images, demonstrate a right adnexal cystic and solid mass on CT, which shows an increased focal activity of fluorodeoxyglucose in the solid component anteriorly.

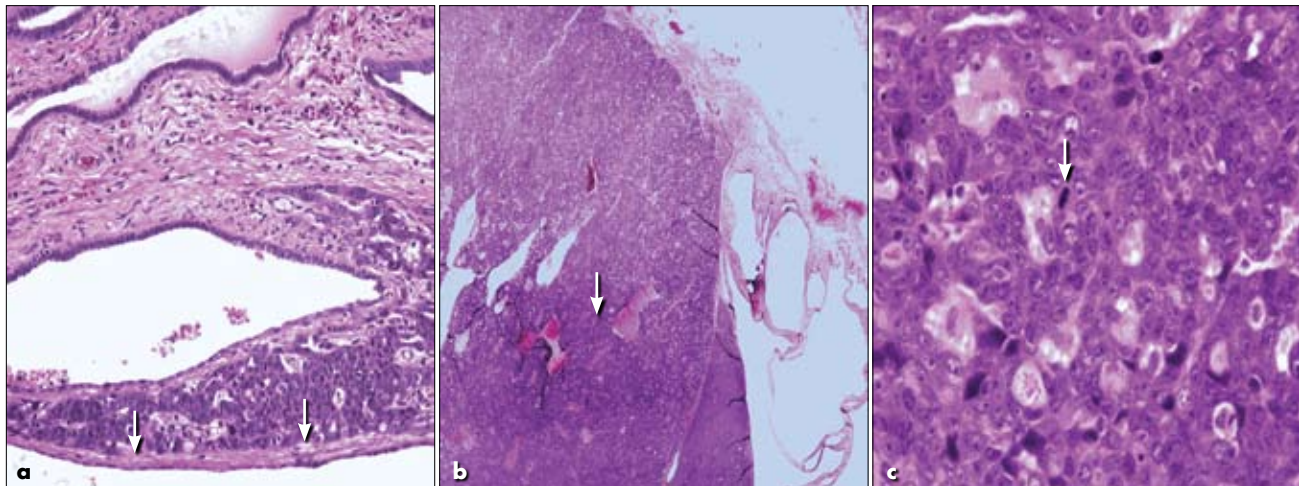


FIGURE 2 (a) Hematoxylin and eosin (H&E) staining of the surgically resected right fallopian tube showing a tumor invading the stroma but not beyond the muscularis mucosa (arrows). (b) H&E staining of the surgically resected right fallopian tube showing adenocarcinoma of the fallopian tube (arrow) adjacent to the lumen of the fallopian tube. (c) A high-powered view of H&E staining of the adenocarcinoma of the fallopian tube showing mitotic figures suggestive of a high-grade tumor (arrow).

report revealed a 23-mm benign serous cystadenoma of the left fallopian tube and an 18-mm grade 3 adenocarcinoma of the right fallopian tube, which invaded the muscularis propria but did not extend beyond it. These cells were negative for TTF1 (thyroid transcription factor 1) making metastasis from the prior lung cancer

unlikely (Figure 2).

The specimen of the regional lymph nodes, the ovaries, and the peritoneum was also assessed and showed no tumor involvement. The patient was then started on adjuvant chemotherapy with carboplatin and docetaxel (Taxotere). She was advised to consult with a clinical geneticist regarding the pos-

sibility of a *BRCA1* or *BRCA2* germline mutation. However, she refused the test due to financial reasons.

Discussion

The highest incidence of PFTC has been reported in non-Hispanic white women and women between the ages of 60 and 79 years,² as was the

case with our patient. There appears to be no difference in the frequency of PFTCs of the right and left tubes.²

Around 15% of patients with PFTC are found to have another malignancy before the diagnosis of PFTC.⁴ In a study by Riska et al, previous breast cancer was a risk factor for PFTC.⁵ Our patient had breast cancer (ductal carcinoma in situ) and lung cancer. Approximately 16%–43% of patients with PFTC have a *BRCA* mutation, mainly *BRCA1*.⁶ PFTC has been typically associated with low parity; our patient was gravida 2 and para 2. Although our patient had had a hysterectomy many years before, a previous hysterectomy has not been found to be protective against PFTC.⁵

Adenocarcinoma accounts for about 90% of all fallopian tube tumors. About 50% are poorly differentiated, whereas only less than 5% are well differentiated. Some of the less frequent types of fallopian tube tumors include squamous cell carcinoma, endometrioid, adenosquamous carcinoma, clear cell carcinoma, and even malignant teratoma.²

Nearly 89% of patients with PFTC present with at least one or more of the following signs and/or symptoms: abnormal vaginal bleeding, abdominal pain, abnormal watery discharge, a palpable abdominopelvic mass, and ascites.¹ Our patient complained of some vague intermittent abdominal pain. Only 4% of patients with PFTC are diagnosed preoperatively.³ In our case, PET/CT first confirmed the suspicion of a neoplasm. The rate of detection of a second primary tumor during PET/CT imaging is 0.31%.⁷

Many authors have speculated that fallopian tube cancers present at an earlier stage than do epithelial ovarian cancers because of abdominal pain secondary to tubal distension.⁸ However, no studies could be found to confirm this hypothesis. Our case was diagnosed at an early stage due to the incidental detection of the adnexal mass through imaging performed for tumor

surveillance as well as for the patient's vague clinical symptoms. These tumors can be highly aggressive; positive lymph nodes can be found, even in disease limited to the fallopian tubes.⁹

It is interesting that our patient had no tumor involvement of the regional lymph nodes, the ovaries, or the peritoneum. Because the tumor extended into the submucosa but did not penetrate to the serosal surface of the fallopian tubes, our case was Schiller stage 1 and International Federation of Gynecology and Obstetrics (FIGO) stage 1A. According to Schiller and Silverberg,¹⁰ the overall 5-year survival for patients with stage I disease is 53%, compared with 85% for patients with stage 1A disease per FIGO statistics.¹¹

Even after complete surgical resection, the risk of tumor recurrence and distant metastasis is high, even among patients with early-stage disease. In the review article by Baekelandt et al, 39% of patients with stage 1 cancer recurred, and about 75% of these patients were found to have at least one extraperitoneal tumor.¹ Considering this high rate of recurrence and the good functional status of our patient, she was treated with intravenous carboplatin and docetaxel. Unfortunately, she tolerated this chemotherapy poorly, requiring hospitalization for nausea, vomiting, and dehydration, so adjuvant treatment was discontinued after one course. Recommendations for adjuvant treatment are generally similar to those for ovarian cancer. Because 75% of these patients have been found to have a complete response to cisplatin-containing combination chemotherapy, the standard therapy now involves a platinum (cisplatin or carboplatin) and a taxane (paclitaxel or docetaxel).¹²

Conclusion

The clustering of lung, breast, and fallopian tube cancers may suggest that they have a common risk factor, perhaps smoking. The most likely association, however, may be a germline *BRCA1* or

BRCA2 mutation. Regular tumor surveillance in patients with a diagnosed malignancy may increase the rate of detection of other primary tumors.

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