Management of advanced-stage primary carcinoma of the fallopian tube: case report and literature review

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Summary

Primary carcinoma of the fallopian tube is a very unusual gynecologic malignancy that accounts for less than 1% of all malignancies of the female genitalia. A 55-year-old, gravida 7, para 3 woman presented with no gynecologic complaints other than backache. TVS demonstrated a 35 x 25 mm heterogeneous mass that was not clearly separated from the left ovary, and another 31 x 14 mm cystic septated lesion in the left ovary region. Pelvic MRI demonstrated a 35 x 35 x 20 mm left adnexal mass that enhanced with contrast and a neighboring tubular-cystic mass. Upper and lower gastrointestinal endoscopy revealed no malignancy. Serum CA 125-level was merkedly elevated at 369 U/ml (normal < 35 U/ml). Laparotomy revealed left hydrosalpinx and a papillary-fimbrial mass. Pelvic lymph node metastases were observed. Frozen-section analysis identified the mass as a serous adenocarcinoma. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy, omentectomy, pelvic and para-aortic lymph node dissection, and peritoneal washing were performed. The definitive histopathological diagnosis was primary serous adenocarcinoma of the fallopian tube with six of 25 lymph node biopsies showing metastasis. Six cycles of paclitaxel (175 mg/m^2) plus cisplatin (75 mg/m^2) combinatin chemotherapy were administered with 3-week intervals between cycles. Second-look laparotomy was performed; there was no evidence of disease. At the time of writing 12 months after the second-look laparotomy, she was still disease-free.

Key words: Fallopian tube carcinoma; Advanced stage; Debulking surgery; Chemotherapy; Paclitaxel; Platinum-based chemotherapy.

Introduction

Primary fallopian tube carcinomas are rare neoplasms that account for less than 1% of all malignancies of the female genitalia. Approximately 2,000 cases have been reported in the literature to date. The reported range in age at diagnosis with this tumor is 18 to 87 years, and the median age at diagnosis ranges from 54 to 66 years. Papillary serous adenocarcinoma is the most common primary malignant neoplasm of the fallopian tube, and this tumor is characterized by poor differentiation [1-3].

History of pelvic inflammatory disease and a family history of breast-ovarian cancer with mutations in germlines BRCA1 and/or BRCA2 play a role in the etiology of fallopian tube carcinoma [4-7]. This form of cancer is rarely suspected before surgery due to lack of specific signs and symptoms. The most common presenting complaint in these cases is metrorrhagia, and next most frequent are colicky-type pain and vaginal discharge. The most common physical sign is pelvic mass. Unlike ovarian carcinoma, in which two-thirds of patients present with advanced disease, the majority of women with tubal cancer are diagnosed at an earlier stage. Many different modalities for detecting fallopian-tube cancers are currently under investigation, including color and pulsed Doppler transvaginal sonography (TVS), computed tomography (CT), magnetic resonance imaging (MRI), nuclear scan imaging, and expression of tumor markers, particularly cancer antigen (CA)-125 [8-13].

The primary treatment for adenocarcinoma of the fallopian tube is surgical resection at the time of initial diagnosis. In early-stage disease, the patient should undergo peritoneal washing, bilateral salpingo-oophorectomy, total hysterectomy, multiple peritoneal biopsies, and pelvic and para-aortic lymph node dissection. In patients with advanced disease, paclitaxel plus platinum-based chemotherapy followed by aggressive cytoreductive surgery is warranted [14-16]. In this article, we describe a case of primary carcinoma of the fallopian tube that was diagnosed at advanced stage, and also discuss the relevant literature.

Case report

A 55-year-old, gravida 7, para 3 woman presented with no gynecologic complaints other than backache. The woman's menstrual cycle was regular, and a gynecologic examination performed one year earlier had revealed no abnormal findings. Her family history included treatment for ovarian carcinoma in a sister. There were no pathologic findings on pelvic examination, but TVS demonstrated a 35 x 25 mm heterogeneous mass that was not clearly separated from the left ovary, and another 31 x 14 mm cystic septated lesion in the left ovary region. The endometrial thickness was 11 mm, and the other genital sonograms were normal. Pelvic MRI demonstrated a 35 x 35 x 20 mm left adnexal mass that enhanced with contrast and a neighboring tubular-cystic mass. We suspected that these lesions might represent left hydrosalpinx secondary to a distal fallopian

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mass. The images also showed conglomeration of the right para-iliac lymph nodes. Upper and lower gastrointestinal endoscopy revealed no malignancy. A cervico-vaginal smear was assessed as chronic cervicitis. The patient's serum CA 125-level was markedly elevated at 369 U/ml (normal < 35 U/ml).

Laparotomy revealed left hydrosalpinx and a papillary-fimbrial mass. The uterus, right fallopian tube and both ovaries appeared normal. Pelvic lymph node metastases were observed. Frozen-section analysis identified the mass as a serous adenocarcinoma. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy, omentectomy, pelvic and para-aortic lymph node dissection, and peritoneal washing were performed.

The definitive histopathological diagnosis was primary serous adenocarcinoma of the fallopian tube with six of 25 lymph node biopsies showing metastasis (Figures 1-2). The condition was classified as Stage IIIc surgical staging according to the guidelines of the International Federation of Gynecology and Obstetrics. Six cycles of paclitaxel (175 mg/m^2) plus cisplatin (75 mg/m^2) combination chemotherapy were administered with 3-week intervals between cycles. During the treatment period, tumor status was monitored by physical examination and serial serum CA-125 measurements. After chemotherapy was completed, testing showed that the patient's CA-125 level had fallen to within normal range (8.4 U/ml) and abdomino-pelvic CT revealed no signs of tumor. Second-look laparotomy was performed, and multiple peritoneal biopsies and peritoneal washes were examined. There was no evidence of disease, and the patient continued to undergo rechecks at 3-month intervals. At the time of writing 12 months after the second-look laparotomy, she was still disease-free.

Discussion

Primary carcinoma of the fallopian tube is a very unusual gynecologic malignancy that carries an unfavorable prognosis. One meta-analysis of 577 affected women revealed a mean age of 56.7 years at time of diagnosis and relatively low parity [16]. In our case, the patient was 55 years old and para 3.

The etiology of fallopian tube carcinoma is unclear; however, the literature indicates possible associations

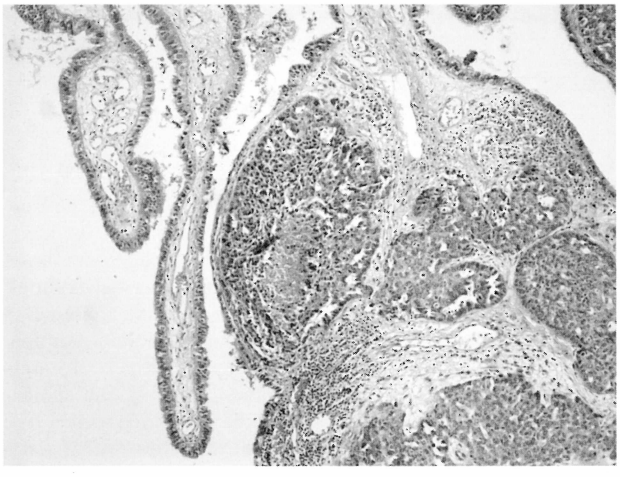

Figure 1. — Serous adenocarcinoma of the fallopian tube. On the section, normal tubal epithelium with continuity of neoplasia is evident (H&E x 10).

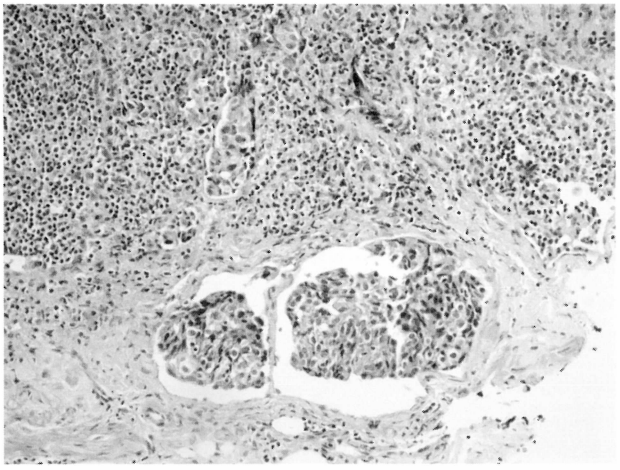

Figure 2. — Lymph node involvement of serous adenocarcinoma of the fallopian tube (H&E x 20).

with tuberculous salpingitis and history of pelvic inflammatory disease [3, 4, 17]. Family history of breast-ovarian cancer with germline BRCA1 and BRCA2 mutations has also been linked with fallopian tube cancer. Several reports have described the detection of occult primary fallopian tube carcinoma during prophylactic salpingo-oophorectomy in carriers of the BRCA1 mutation [5-7, 18, 19]. Molecular studies have documented high p53 overexpression and high mutation rates in patients with fallopian tube carcinomas [20, 21]. Our patient's sister was treated for ovarian carcinoma; however, we were unable to test for BRCA mutations

Only 11% of patients with tubal carcinoma present with the classic combination of pelvic pain, pelvic mass, leukorrhea or vaginal bleeding, vaginal discharge and lower abdominal pain [22]. Another sign is hydrops tubae profluens, and a meta-analysis of 122 patients revealed a 9% frequency of this feature [23]. Surprisingly, our patient had undergone a gynecologic examination one year prior to diagnosis and nothing abnormal was found during that assessment. Also unusual was her presenting symptom of generalized backache.

The differential diagnosis for fallopian tube cancer includes salpingitis, ovarian abscess or tumor, and ectopic pregnancy; however, most cases are not diagnosed prior to surgical exploration. Some authors have advocated Papanicolaou smears (Pap test) as a preoperative screening tool for patients with non-specific symptoms, and these reports have noted wide-ranging frequencies of positive results (0% to 60% of cases tested) [24]. Attempts at identifying cases by endometrial sampling have also been discouraging [25].

The radiodiagnostic tools used for detecting fallopian tube carcinomas include TVS, CT, MRI; color and pulsed doppler TVS are highly sensitive methods for pinpointing areas of neovascularization within the tube. Three-dimensional Doppler sonography accurately depicts irregularities of the tubal wall and shows vascular architecture that

is typical of a malignant growth pattern [8, 9]. Magnetic resonance imaging is better than TVS and CT for differentiating the fallopian tube from other pelvic organs, and reports suggest that MRI is superior to TVS and CT for diagnosing fallopian tube carcinoma [12, 26]. In our case, the MRI findings were suspicious but were not conclusive. One group of authors identified CA-125 levels above 65 U/ml as a possible indicator of fallopian-tube malignancy, with a specificity of 98% and a sensitivity of 75% [11]. However, serum antigen levels can also be elevated in benign conditions such as endometriosis, pelvic inflammatory disease and early pregnancy. Our patient's CA-125 level was extremely high at the time of diagnosis (369 U/ml).

The most common histological type of fallopian tube carcinoma is serous carcinoma, and endometrioid, clear cell and transitional cell carcinoma are less frequent forms. The most important prognostic factor in all these types is disease extension, and reported 5-year survival rates range from 32% to 80% in Stage I cases, 16% to 58% in Stage II disease, and 0% to 29% in Stage III-IV cases [14, 15, 27]. Other reported prognostic variables are tumor grade (still controversial), residual disease after initial surgery (better prognosis if residual tumor < 1 cm diameter), depth of tubal wall infiltration, and vascular space invasion. Other reported predictors of poor prognosis in these cases are advanced age, ascites, elevated serum CA-125 before treatment, and p53 alterations [10, 11, 13, 14, 15, 20, 21].

The primary treatment for adenocarcinoma of the fallopian tube is surgical resection at the time of diagnosis. In early-stage disease, cytologic assessments should be done on ascitic fluid and/or peritoneal washes, and on peritoneal sampling of the diaphragm, bladder, and bowel. The patient should also undergo hysterectomy, omentectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymph node dissection. Systemic pelvic and para-aortic lymphadenectomy is preferred because of the strong and early tendency for lymphatic spread of these tumors [14, 15, 28, 29]. In our case, we performed aggressive debulking surgery and surgical staging.

The risk of fallopian tube carcinoma recurrence is relatively high, even in cases with complete surgical resection; thus, adjuvant therapy is often suggested for women with early disease. Currently, radiotherapy is considered strictly palliative for fallopian tube carcinoma. Intraperitoneal instillation of radioisotopes does not appear to reduce the risk of recurrence in early disease [3, 30]. Platinum-based chemotherapy, which is reportedly associated with an objective response in 53% to 92% of cases, is currently the most widely used adjuvant treatment for these patients [14, 15, 31-34]. After comprehensive surgical staging and systematic pelvic and para-aortic lymphadenectomy is completed, patients with carcinoma confined to the tube, with no tumor penetration of the serosal surface, and with no problems of intraoperative tumor rupture are not deemed to require adjuvant treatment. Individuals with early-stage disease should receive chemotherapy if the tumor has infiltrated the serosa, or if it ruptured pre-or intraoperatively. Serum CA-125 assay is often used to evaluate response to chemotherapy, and may also be useful for early detection of recurrent disease in patients with fallopian tube carcinoma [10]. Recent data have indicated good response rates with cisplatin-based combination chemotherapy in both early- and advanced-stage fallopian tube carcinomas [31-34]. Little is known about the activity of paclitaxel as first-line chemotherapy in patients with this malignancy. Reports have noted that this agent is active in patients with this fallopian tube carcinoma who are platinum-pretreated [15, 35]. Other authors observed a 23% response rate with docetaxel in 30 patients with ovarian, fallopian tube and primary peritoneal cancer in whom paclitaxel-based chemotherapy failed [36]. Combination chemotherapy with docetaxel and carboplatin is highly active in the treatment of ovarian and fallopian carcinoma [37]. In patients who are resistant to platinum-based treatments, non-platinum agents such as topotecan or liposomal doxorubicin should achieve response [38]. It appears that surgical reassessment offers no clinical benefit for patients with stage III-IV fallopian tube carcinomas; however, randomized studies are needed to confirm this. Based on current data, second-look laparotomy should be reserved for patients enrolled in clinical trials.

Anecdotal evidence suggests that, complete secondary surgical cytoreduction is associated with a survival advantage in patients with late recurrent disease. This procedure should only be performed in select cases that feature good performance status, a long disease-free interval, and no extra-abdominal or intraparenchymal hepatic metastases [39, 40].

In our case, six cycles of paclitaxel-plus-cisplatin chemotherapy were administered after the surgery, and a second-look laparotomy showed that the patient was free of disease. The patient's CA-125 level was dramatically reduced by chemotherapy.

Conclusion

The management of fallopian tube carcinoma is similar to that for ovarian carcinoma. In cases of advanced fallopian tube carcinoma, the primary treatment is bilateral salpingo-oophorectomy, total abdominal hysterectomy, comprehensive surgical staging and aggressive debulking. Paclitaxel plus platinum-based combination chemotherapy should be administered to patients with Stage IIb-IV disease. If complete response is achieved, the patient should be followed closely or should be entered in a trial of consolidation treatment, as is done in patients with ovarian cancer. Second-line chemotherapy for patients with persistent/recurrent fallopian tube carcinoma should be mainly based on the platinum-based regimes. Concerning recurrent disease, secondary surgical cytoreduction should only be considered in very select cases with localized late relapse.

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