Primary fallopian tube carcinoma: a case report and mini-review of the literature

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Summary

Primary fallopian tube carcinoma (PFTC) is an uncommon gynecologic tumor, responsible for 0.14% to 1.8% of genital malignancies, with a mean incidence of 3.6 per million women per annum. The factors that contribute to its appearance are not well-known. Overall survival percentages for patients with PFTC are generally low. Although the preoperative diagnosis rarely occurs and it is usually first confirmed by the pathologist, an earlier diagnosis occurs with early clinical manifestation and prompt investigation leading to better prognosis. Both PFTC and epithelial ovarian cancer (EOC) are treated with similar surgical and chemotherapy methods. The authors report a case of a patient with bilateral high grade serous carcinoma of the fallopian tube, whose initial presentation was bilateral cystic adnexal masses and serosanguinous discharge, with no other pelvic involvement. This article also reviews in brief and presents updates of this rare gynecological malignancy.

Key words: Fallopian tube carcinoma; High-grade serous carcinoma; Risk factors; Treatment.

Introduction

Primary fallopian tube carcinoma (PFTC) is an uncommon gynecologic malignancy which constitutes 0.14% to 1.8% of genital malignancies [1-3], first described by Reynaud in 1847 [4]. It most frequently occurs in women aged between 18-88 years, with the most common age of occurrence being between 40-65, with a mean age of 55 years [5].

Population studies show that the mean incidence of PFTC is 3.6 per million women per annum [5]. The true incidence of PFTC is perhaps underestimated [1, 5] because some of the cases have been wrongly diagnosed as ovarian tumors during initial surgery and/or microscopic examination due to the indistinguishable histological appearance of these neoplasms [1]. PFTC is associated with chronic tubal inflammation, infertility, tuberculous salpingitis, and tubal endometriosis [6]. High parity seems to have a protective effect [2]. Overall survival percentages for patients with PFTC are generally low and mostly ranging between 22% to 57% [7, 8]. The authors report a case of a patient with bilateral high grade serous carcinoma of the fallopian tube, whose initial presentation was serosanguinous discharge and abnormal vaginal bleeding.

Case Report

A 44-year-old, gravida 3, para 2, premenopausal woman with referred two to three months duration episodes of abnormal menstrual cycle/vaginal bleeding was admitted to the department of Obstetrics and Gynecology in Thriasio Hospital, Eleusis, Greece. There was no significant past medical and gynecological history apart from two previous dilatations and curettages (D+C), for treating cervical polyps and bleeding. A D+C was performed as a result of an increased endometrial thickness and the presence of serosanguinous vaginal discharge.

During the gynecologic examination, bilateral cystic masses were detected and transvaginal ultrasonography confirmed this finding, confirming the presence of these masses (size: approximately three cm each). A culture of the vaginal discharge was sent and antibiotics were given. All other laboratory tests -including tumor markers- were normal.

After a two-month period, due to continuous vaginal serosanguinous discharge, transvaginal ultrasonography and pelvic computed tomography examination were performed, showing a complex cystic adnexal mass measuring 12.5×4.9×4.2 cm in the right parametrium and another complex cystic adnexal mass measuring 7.4×7.5×4.6 cm in the left parametrium. The patient's complete blood count showed hemoglobin 13.5 g/dl, total leukocyte count 5,900 /ml, platelet count 298,000/ml. The serum concentration of carbohydrate antigen (CA) 125 was 12.2 U/ml, CA 19-9 9.81 U/ml, CA 15-3 5.5 U/ml, carcinoembryonic antigen (CEA) 0.71 ng/ml, and alpha-fetoprotein (AFP) 5.89 ng/ml. She had a normal chest X-ray and pap smear test.

The present authors' preoperative diagnosis was ovarian masses and a laparotomy was carried out. The appearance of the uterus was normal (Figure 1). However, the adnexa were both enlarged with complex cystic/papillary appearance; total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, bilateral pelvic lymphadenectomy, peritoneal washing, and multiple biopsies of the peritoneum were carried out.

Histologic examination was positive for cancer in both fallopian tubes and the one on the right was invasive into the wall/serosa of the fallopian tube (Figure 1). The tumor featured papillary structures, lined by cells with high-grade nuclei and numerous mitotic figures. One small polyp was found in the endometrium and endocervitis was also present. Uterus, ovaries, abdomen, and adjacent structures were free of cancer. The final result of the histopathologic examination arrived four days later and reported: bilateral high grade serous carcinoma of the fallopian tubes.

The patient was staged according to International Federation of Obstetrics and Gynecology (FIGO) staging for fallopian tube carcinoma, and allocated as high grade serous carcinoma Ic.

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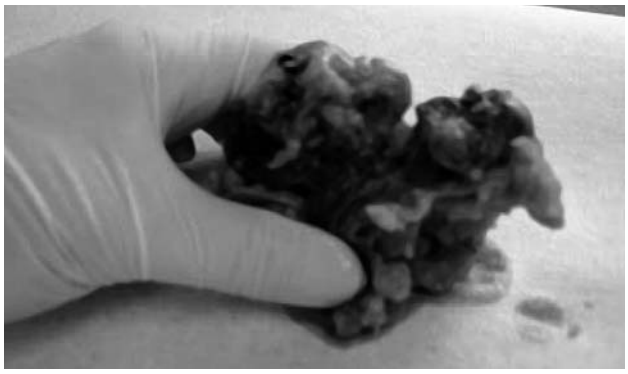

Figure 1. — Pathological specimen of the right fallopian tube, revealing a complex cystic papillary adnexal mass.

Discussion

PFTC is a rare but aggressive gynecological malignancy accounting for <1% of all genital cancers. Serous carcinomas originating in the fallopian tube are asymptomatic in their early stages until their spread to other pelvic sites [9].

Although it shares common characteristics with epithelial ovarian cancer (EOC) (such as surgical FIGO staging and surgical management, epidemiological characteristics, correlation residual tumor size with prognosis, better response with platinum-based chemotherapy, there also seems to be a great difference between them: PFTC is diagnosed at an earlier stage, despite the fact that in many cases, diagnosis may occur only postoperatively by the pathologist [10]. That may be a result of abdominal pain, resulting from tubal dilatation, and/or bloody-watery vaginal discharge [10].

Preoperative tumor markers, such as CA-125, vary. Other authors report high CA-125 levels [11], while others state that CA-125 is always elevated in advanced disease but not in earlier stages of the disease [12].

The first line of therapy for PFTC consists of total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, bilateral pelvic lymphadenectomy, and adjuvant chemotherapy [13].

Peritoneal washings should be taken at the time of surgery because positive washings are an adverse prognostic indicator suggesting extratubal spread and are associated with an increased risk of lymph node metastasis [14]; these washings have been found to contain malignant cells, in up to 20% of cases [14].

In most previous studies, PFTC has been graded subjectively and not according to the more objective Silverberg criteria. Rosen *et al.* [14] found no correlation between tumor grade and patient outcome; a correlation found by Hellstrom *et al.*, even with marginal statistical significance [15].

The survival rates of patients with PFTC are reported to be poor. Moreover, it seems to be worse than that of patients with equivalent stages of EOC; survival is found to be worse than other early-stage gynecological malignancies [14, 15].

Recently, it has become apparent that PFTC is a multietiological disease with different clinical and morphological aspects. It seems to have an increased incidence and its accurate diagnosis and differentiation from EOC is important for better prognosis and management. Improvements in treatment and, therefore, outcome can only materialize if preceded by an early and accurate diagnosis.

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Normal-sized ovary carcinoma syndrome (NOCS) detected with FDG-PET/CT

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Summary

Background: Normal-sized ovary carcinoma syndrome (NOCS) is an ovarian cancer with ovaries being of normal size, accompanied by diffuse metastatic disease of the peritoneal cavity. *Case:* A 39-year-old woman presented with lower abdominal pains. The computed tomopraphy (CT) of the chest, esophagogastroduodenography, and colonoscopy showed no remarkable findings. A magnetic resonance imaging (MRI) displayed a slightly enlarged right ovary, thickening of the peritoneum, and massive ascites. The right ovary showed high intensity on T2 images and scattered low intensity spots on diffusion-weighted images. The cytology of ascites suspected adenocarcinoma cells. A positron emission tomography (PET) and CT using 18F-fluorodeoxyglucose (FDG) demonstrated markedly increased FDG uptake at the right ovary and peritoneum. The presumptive diagnosis of normal-sized ovary carcinoma syndrome was made. She underwent a total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy, and partial omentectomy. The pathological examination revealed serous cystadenocarcinoma of the right ovary. *Conclusion:* FDG-PET/CT is useful for the detection of NOCS.

Key words: Normal-sized ovary carcinoma syndrome; FDG-PET/CT; Primary tumor detection.

Introduction

A positron emission tomography (PET) and computed tomography (CT) using 18F-fluorodeoxyglucose (FDG) has been shown to increase the diagnostic accuracy of pre-treatment stage of ovarian cancer patients in comparison with contrast enhanced CT [1] and to have a high diagnostic value in differentiating between malignant and benign ovarian tumors [2]. In addition, FDG-PET/CT is reported to be useful for predicting the diagnosis and restaging of suspected recurrent ovarian carcinoma [3-5], the detection of recurrence of ovarian cancer and predicting patients' survival [6], and early prediction of response to neoadjuvant chemotherapy [7].

In 1989, normal-sized ovarian carcinoma syndrome (NOCS) was defined as a clinical situation in which diffuse metastatic disease of the peritoneal cavity is noted, but the ovaries are of normal size, with or without a fine granularity on their external surface [8]. The histology of NOCS was reported to be the same as common epithelial ovarian cancer with variable degrees of differentiation, but has a great tendency to spread externally [9]. The preoperative diagnosis of NOCS remains a diagnostic challenge. When the patients with peritoneal carcinomatosis with unknown origin are encountered, preoperative radiologic assessment and surgical exploration are warranted to discern the site of origin. A recent report has demonstrated that the use of FDG-PET/CT detected the site of NOCS despite the failure with magnetic resonance imaging (MRI) and CT [10]. Nonetheless, little information is available regarding the usefulness of FDG-PET/CT for the diagnosis of NOCS.

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Herein, the authors describe a case of NOCS that could be correctly diagnosed with FDG-PET/CT, although the imaging results of CT and MRI were negative or inconclusive.

Case Report

A patient was a 39-year-old nulliparous woman with no medical history of malignancy. She presented with persistent left lower abdominal pains. Series of examinations including a CT of the chest, esophagogastroduodenography, and colonoscopy showed no remarkable findings. A MRI of the pelvis displayed the slightly enlarged right ovary, thickened peritoneum, and massive ascites. The right ovary showed the high intensity at the solid parts (Figure 1A), and the peritoneum anterior to the rectum was thickened with showing low intensity on T2 images (Figure 1A). The scattered low intensity spots were noted in the solid components of the right ovary on diffusion-weighted images (Figure 1B). A CT of the pelvis failed to detect any apparent tumors in the pelvis (Figure 1C). The cytology of ascites suspected adenocarcinoma cells. Serum CA125 levels were elevated at 248 IU/ml. She was diagnosed as having peritoneal carcinomatosis. However, the site of origin remained undetermined.

Subsequently, in order to detect a possible site of primary malignancy, she underwent FDG-PET/CT at one and two hours after intravenous injection of 2.23 MBq/kg body weight of ^{18}F-FDG. FDG-PET/CT demonstrated markedly increased FDG uptake at the solid components of the right ovary (the maximum standard uptake value (max SUV) = 9.3) (Figure 2A, B) and the irregularly thickened peritoneum at the cul-de-sac (max SUV = 4.8) (Figure 2A, B). The left ovary had the solid components, but showed no FDG accumulation. Besides these findings, no abnormal FDG accumulation was noted in the whole body scanning.

Based on the imaging studies in addition to the cytological malignancy of ascites and elevated serum CA125 levels, a presumptive diagnosis of NOCS was made. On laparotomy, the bladder was adherent to the anterior wall of the uterus, and the sigmoid and rectum were adherent to the peritoneum of the cul-

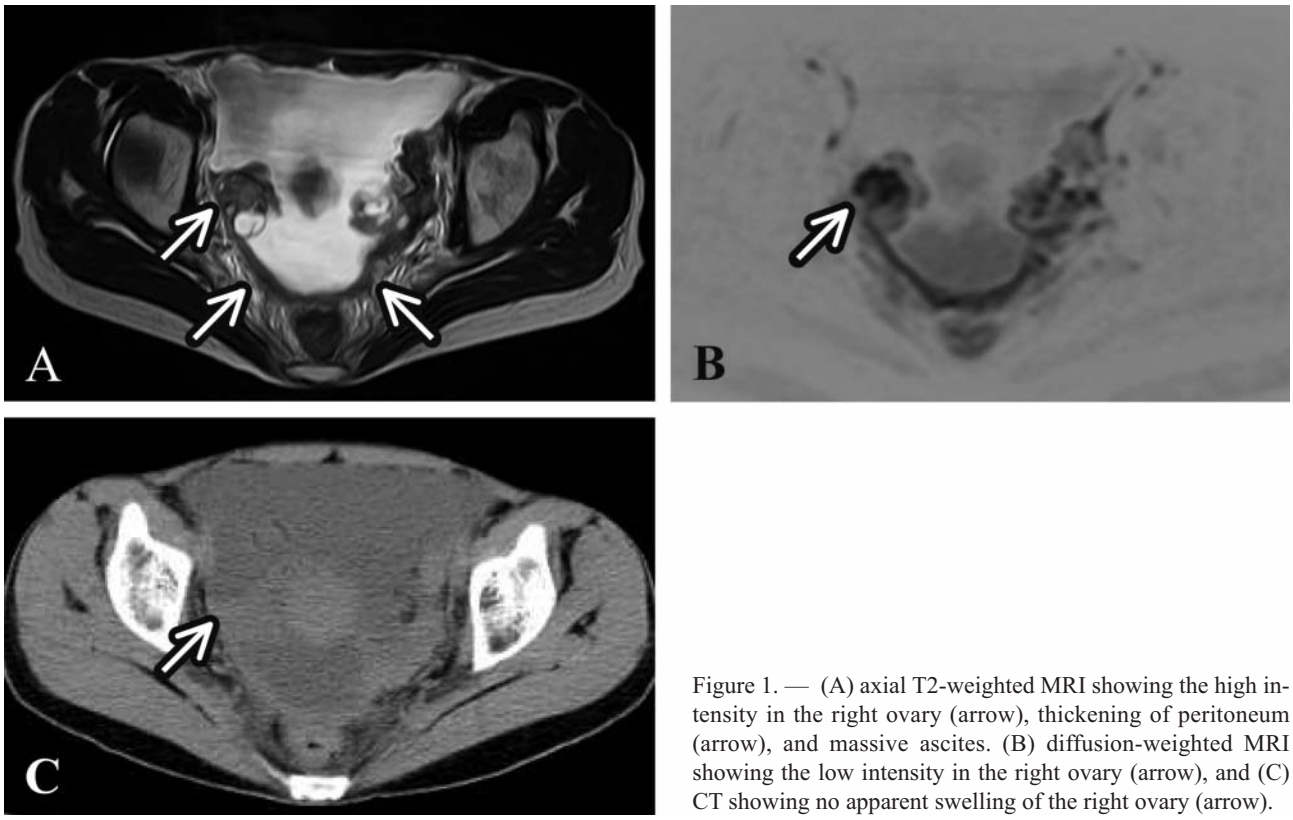

Figure 1. — (A) axial T2-weighted MRI showing the high intensity in the right ovary (arrow), thickening of peritoneum (arrow), and massive ascites. (B) diffusion-weighted MRI showing the low intensity in the right ovary (arrow), and (C) CT showing no apparent swelling of the right ovary (arrow).

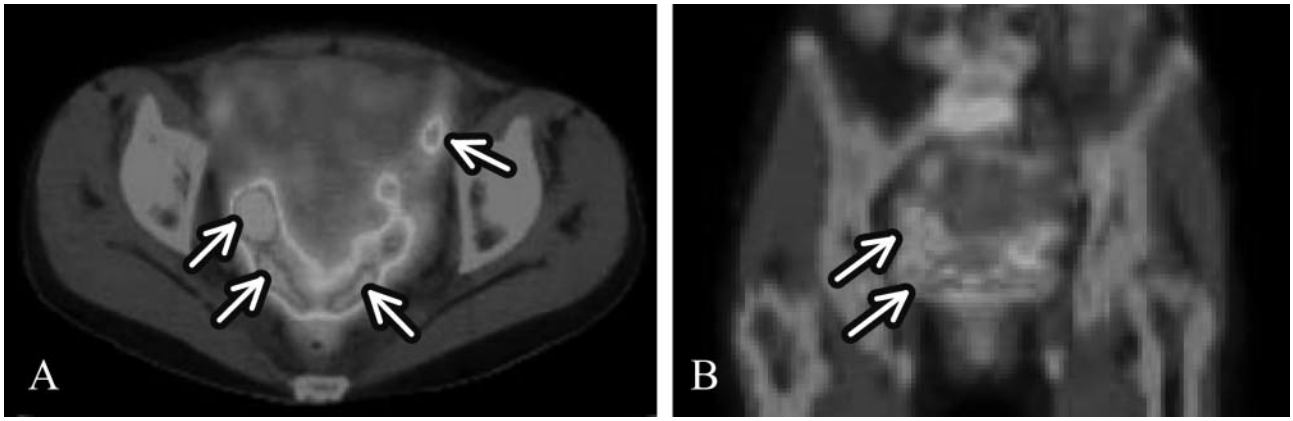

Figure 2. — (A) axial FDG-PET/CT showing markedly increased FDG accumulation in the right ovary (arrow) and peritoneum (arrow) and (B) coronal FDG-PET/CT showing the increased metabolic activity in the right ovary (arrow) and peritoneum (arrow).

de-sac, forming a frozen pelvis. The ascites amounted to 1,650 ml. Numerous peritoneal implants less than five mm in diameter were noted on the serosa of the intestines and omentum. A frozen section analysis of the right ovary revealed serous cystadenocarcinoma. She underwent a total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy, and partial resection of the omentum. Macroscopically, the tumor was 20 x 30 x 20 mm in size. The microscopic examination confirmed serous cystadenocarcinoma of the right ovary. She has been treated with adjuvant chemotherapy consisting of paclitaxel and carboplatin.

Discussion

The authors presented a case of NOCS that was correctly diagnosed with FDG-PET/CT preoperatively. Wu *et al.* described that normal-sized ovarian serous surface papillary carcinomas should be kept in mind as an origin of disease in patients who have peritoneal carcinomatosis [11]. Nevertheless, the diagnosis of NOCS still remains a diagnostic challenge. In the present case, a CT of the pelvis failed to detect any pelvic mass and localize peritoneal involvement. MRI

displayed the slight swelling of the right ovary and thickened peritoneum on T2-weighed images and low intensity of the right ovary on DW images, but these findings were inconclusive for determining the site of primary malignancy. However, FDG-PET/CT clearly demonstrated markedly increased FDG accumulation in the sites corresponding to the right ovary and peritoneum, indicating the right ovarian cancer with peritoneal dissemination.

A recent report has also demonstrated that the use of FDG-PET/CT detected the site of origin in a case of ovarian serous surface papillary carcinoma with manifestation of NOCS [10]. They reported that PET/CT confirmed the intense FDG uptake in both the right and left ovaries with max SUV of 5.0 and 6.0, respectively, and abnormal FDG uptake in the nodular/irregular thickening of the mesentery and peritoneum with max SUV of 2.5 to 4.6 [10]. The origin of the peritoneal carcinomatosis was thought to be the left ovary with the right ovary being involved by tumor implant. They suggested that FDG-PET/CT seems to be advantageous in evaluating peritoneal carcinomatosis in NOCS.

With FDG-PET/CT, peritoneal implants were shown to appear as nodular soft-tissue masses, often with a variable degree of increased metabolic activity, and omental thickening and nodularity with diffuse FDG uptake were indicative of omental involvement [5]. The present patient had numerous military peritoneal implants on the intestines and omentum, but these lesions were not displayed with FDG-PET/CT. This may be due to the inability of FDG-PET/CT to depict small volume lesions. However, Sanli *et al.* evaluated the diagnostic value of FDG-PET/CT in comparison with MRI for the detection of recurrent ovarian cancer, and demonstrated that although PET/CT was similar to MRI for the detection of recurrent ovarian cancer, PET/CT had greater accuracy in the detection of small-to-medium-sized (< two cm) peritoneal implants compared with MRI [12]. Furthermore, Kim *et al.* demonstrated that in ovarian cancer patients with peritoneal carcinomatosis, the sensitivity and the specificity for the diagnosis of peritoneal carcinomatosis were 96.2% and 90% for PET/CT and 88.5% and 65% for enhanced abdominal CT and that the accuracy of PET/CT was statistically higher compared with enhanced CT [13]. They suggested that FDG-PET/CT imaging is efficient in the diagnosis of peritoneal carcinomatosis and that its performance is superior to that of enhanced CT [13].

Recent study has demonstrated that FDG-PET/CT is a useful method for the detection of cancer of unknown primary (CUP), which represents a heterogeneous group of metastatic tumors for which no primary site can be detected following a thorough medical history, careful clinical examination, and extensive diagnostic workup [14]. A meta-analysis showed that FDG-PET/CT could detect 37% of primary tumors in patients of CUP with high sensitivity and specificity of 84% [14]. In three cases (1.9%) among patients with CUP, the ovary was found to be the location of primary tumors detected with FDG-PET/CT [14]. This fact may reinforce the usefulness of FDG-PET/CT for the detection of NCOS.

Collectively, this case emphasizes that FDG-PET/CT is useful for the diagnosis of NOCS in combination with the evidence of malignant ascites and elevated serum CA125 levels, even when imaging results of CT or MRI are negative or inconclusive.

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