Fallopian tube primary cancer: report of five cases and review of the literature

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Summary

Objective: The aim of this retrospective study was to analyze the clinical characteristics, management and prognosis of five patients with fallopian tube primary cancer (FTPC) who were diagnosed and treated in our departments. A review of the current literature is also presented. *Materials and Methods:* Between January 2000 and August 2009, five cases with histologically confirmed FTPC were diagnosed in our departments and were then evaluated retrospectively. All patients underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and total omentectomy. *Results:* We had two patients in Stage IA (40%), two patients in Stage IC (40%) and one patient in Stage IIIA (20%). All patients received adjuvant chemotherapy with platinum-based combinations and two of them received additional radiotherapy. *Conclusion:* FTPC, compared with ovarian primary cancer (OPC), is more likely to present at an early stage and have an overall more favourable outcome. More extensive clinical research must be performed to have definite aetiologic, diagnostic and management modalities.

Key words: Fallopian tube cancer; Treatment; Chemotherapy; Prognosis.

Introduction

Fallopian tube primary cancer (FTPC) is a very rare disease, accounting for approximately of 0.14-1.8% of all female genital tract malignancies [1, 2]. The true incidence is probably underestimated because advanced cases may be incorrectly diagnosed as ovarian primary cancer [3]. Carcinomas are more than 95% of all FTPC, whereas malignant mixed mullerian tumours are exceptional [4, 5].

The aetiology of FTPC is largely unknown, but may be similar to the aetiology of ovarian primary cancer (OPC) [2, 6]. Hormonal, reproductive and possibly genetic factors might increase the risk for FTPC [7]. History of pregnancy, high parity and use of oral contraceptives significantly decreases the risk for FTPC [2, 7].

FTPC most commonly occurs in postmenopausal women, with a mean age of 55 years [8, 9]. The most common symptoms and signs in women with FTPC are abdominal pain (30-49%), vaginal bleeding or discharge (50-60%) and palpable pelvic mass (12-61%) [6, 10]. The rate of preoperative diagnosis is low and even the intraoperative diagnosis is missed in up to 50% of patients [11, 12]. Even when such disease is resected, it is often impossible on histopathological examination to determine the origin of the tumour [7, 13].

The aim of this retrospective study was to analyze the clinical characteristics, management and prognosis of five patients with FTPC who were diagnosed and treated in our departments, together with a review of the current literature.

Material and Methods

Between January 2000 and August 2009, five cases with histologically confirmed FTPC were diagnosed in the Department of Obstetrics and Gynaecology of the University of Patras Medical School and the 2nd Department of Gynecology of St. Savvas Anticancer - Oncologic Hospital of Athens. These cases were evaluated retrospectively.

All patients underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and total omentectomy. Lymph node sampling of pelvic and paraortic lymph nodes was performed in one case. A cytologic test of the peritoneal fluid was performed in all patients. Staging procedures were performed by a gynaecologic oncologist.

Tissue specimens were stained with haematoxylin-eosin. Cases were identified according to FTPC diagnostic criteria established by Hu *et al*. and modified by Sedlis [9, 14]. Staging was determined using the surgical staging system for FTPC established by the International Federation of Obstetrics and Gynecology (FIGO) [15]. Tumour histologic classification was performed using the criteria of the World Health Organization (WHO).

Results

The median age at diagnosis of FTPC was 64.6 years (range 54-77 years). The median follow-up was 49 months (range 22-70 months).

The most common symptoms and signs were abdominal pain (60%), vaginal bleeding or discharge (40%) and palpable pelvic mass (40%). None of the women with FTPC were diagnosed preoperatively. The median preoperative serum CA-125 level was 370.1 (range 9.4-1534.8). It was elevated in three patients (60%) and normal in two patients (40%) (Table 1).

In our study, we had two patients had fallopian tube adenocarcinoma, one patient fallopian tube malignant mixed mullerian tumour, one patient synchronous fallop-

Revised manuscript accepted for publication February 8, 2010

Table 1. — *Clinical features*.

		Patients	Percentage (%)
Age at diagnosis	< 60	2	40%
	≥ 60	3	60%
Symptoms & signs	Abdominal pain	3	60%
	Vaginal bleeding or discharge	2	40%
	Palpable pelvic mass	2	40%
Preoperative CA-125 levels	≤ 35	2	40%
	> 35	3	60%

Table 2. — *Histopathologic findings - treatment*.

		Patients	Percentage (%)
Stage	I	4	80%
	II		0%
	III	1	20%
	IV		0%
Histological type	Adenocarcinoma	4	80%
	Other	1	20%
Grade	Grade 1	1	20%
	Grade 2	1	20%
	Grade 3	3	60%
Surgery	Yes	5	100%
	No	0	0%
Chemotherapy	Yes	5	100%
	No	0	0%
Radiotherapy	Yes	2	40%
	No	3	60%

ian tube adenocarcinoma and endometrioid endometrial cancer and one patient with synchronous fallopian tube adenocarcinoma and ovarian cancer.

According to the FIGO classification, two patients were in Stage IA (40%), two patients in Stage IC (40%) and one patient was in Stage IIIA (20%). All patients received adjuvant chemotherapy with platinum-based combinations and two patients received additional radiotherapy. These data are shown in Table 2.

During a mean follow-up of 49 months, one patient with Stage IC disease died 36 months after surgery and four patients are well with no evidence of relapse.

Discussion

FTPC is a rare entity. More than 90% of FTPC is papillary serous adenocarcinoma [4, 8]. Other cell types include endometrioid and clear cell carcinoma. Rare types include sarcoma, germ cell tumours and lymphoma [4, 5, 8]. In our study four patients had adenocarcinoma and one patient malignant mixed mullerian tumour.

FTPC is usually diagnosed in early stages [8, 16]. The nonspecific nature of the signs and symptoms in patients with FTPC still makes preoperative diagnosis exceptional [12, 16]. The relatively early occurrence is probably the principal explanation for the typical stage distribution seen in patients with FTPC, with an overrepresentation of early-stage patients compared with ovarian carcinoma [16]. In our study two patients were in Stage IA, two patients Stage IC and one patient Stage IIIA.

The ultrasound (US) appearance of FTPC can be nonspecific, mimicking other pelvic diseases such as tuboovarian abscess, ovarian tumour and ectopic pregnancy [8]. The distinction between FTPC and OPC by transvaginal colour and pulsed Doppler depends on the stage and spread of the tumour [17]. In early stages it is usually possible to distinguish them, but in advanced stages the distinction is not possible [17, 18]. The diagnostic accuracy may be improved by the introduction of 3D power Doppler sonography [18]. Magnetic resonance imaging (MRI) is superior to computed tomography (CT) and US in detecting local tumour infiltration of the bladder, pelvic fat, vagina, pelvic sidewalls and bowel [8, 19]. None of our study women with FTPC were diagnosed preoperatively.

Serum CA-125 is a useful tumour marker for diagnosis, assessment of response to treatment and detection of tumour recurrence during follow-up [20]. Although CA-125 is not diagnostic of FTPC, more than 80% patients have elevated preoperative serum CA-125 levels and 87% of tumour tissues stain positively for CA-125 [20, 21]. Preoperative serum CA-125 level is an independent prognostic factor of disease-free and overall survival in patients with FTPC [20]. Postoperative serum CA-125 levels have been associated with response to chemotherapy [20]. Postoperative serum CA-125 level is an early and sensitive marker for tumour progression during follow-up of patients with FTPC [20]. In our study we had preoperative serum CA-125 levels elevated in three patients (60%).

FTPC is an aggressive malignancy with a tendency to metastasize even in apparently early stages of the disease. The pattern of spread of FTPC is similar to that of OPC, principally by the transcelomic exfoliation of cells that implant throughout the peritoneal cavity [22]. In approximately 80% of patients with advanced disease, metastases are confined to the peritoneal cavity [22]. Tumour spread may also occur by means of contiguous invasion, transluminal migration, haematogenous dissemination and through lymphatic spread [23]. Metastases to the pelvic and paraortic lymph nodes have been documented in at least 33% of the patients with all stages of disease [24].

Surgery is the treatment of choice for FTPC. Surgical principles are the same as those used for OPC. Patients with FTPC should undergo total abdominal hysterectomy with bilateral salpingo-oophorectomy and comprehensive surgical staging including peritoneal washing, omentectomy, peritoneal biopsies, pelvic and paraaortic lymph node sampling [3, 16, 25, 26, 27]. Considering the strong tendency for lymphatic spread of the tumour, a systematic pelvic and paraortic lymphadenectomy should be preferred to lymph node sampling [27]. Aggressive cytoreductive surgery, with removal of as much tumour as possible, is warranted in patients with advanced disease [26, 27]. In our study all patients underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and total omentectomy. Lymph node sam-

pling of pelvic and paraortic lymph nodes was performed in only one case.

Because of its rarity, the optimal therapeutic strategy for FTPC has not been well defined [26]. Based on the propensity for microscopic distant spread and the relatively high risk of recurrence despite complete surgical resection, chemotherapy seems to have a strong rationale as adjuvant treatment for patients with early stage FTPC [7, 26]. Single agent chemotherapy does not seem to be effective, while platinum-based combination chemotherapy is the most commonly used adjuvant therapy for FTPC patients [7, 26, 27]. Patients with Stage IA and IB may not require adjuvant chemotherapy, as for patients with OPC [7]. All other patients must be treated with platinum-based combinations [7, 26, 27]. However, very few data are currently available regarding chemotherapy for advanced stage FTPC [7, 26, 27]. Pelvic radiotherapy in FTPC has not been shown to improve survival and the role of whole abdomen radiotherapy is still uncertain [7, 28, 29]. In view of its low efficacy and high rate of serious complications, the use of postoperative radiotherapy in the treatment of patients with PFTC is no longer recommended [7]. In our study five patients received adjuvant chemotherapy with platinum-based combinations and two patients received additional radiotherapy.

Stage of FTPC at the time of diagnosis and residual disease after initial surgery, are the most important prognostic factors [25, 30]. FTPC compared with OPC is more likely to present at an early stage and have an overall more favourable outcome [31]. The reported 5-year survival rate for patients with Stage I is about 95%, for patients with Stage II about 75%, while for patients with Stage III it is about 69% and for patients with Stage IV about 45% [32]. The improved survival for FTPC compared with OPC is most pronounced for patients with advanced stage disease [31]. More extensive clinical research must be performed to have definite etiologic, diagnostic and management modalities.

To conclude, FTPC, compared with OPC, is more likely to present at an early stage and have an overall more favorable outcome. More extensive clinical research must be performed in order to have definite etiologic, diagnostic and management modalities.

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