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Original Article

Primary fallopian tube carcinoma: Clinicopathological analysis of 12 cases

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Abstract

Objective: Primary fallopian tube carcinoma is one of the least common gynecological cancers and is difficult to diagnose preoperatively. We aimed to analyze the clinicopathological characteristics of this rare disease and to identify the prognostic factors predicting prognosis.

Materials and Methods: Twelve cases of primary fallopian tube carcinoma that had been diagnosed and treated in Kaohsiung Chang Gung Memorial Hospital between July 1986 and December 2005 were retrospectively reviewed. Factors, including age, gravidity, parity, stage, surgical intervention, pathological findings, relapse, and survival, were analyzed.

Results: The median age of the 12 cases was 54 years (range, 32–67 years), whereas the median follow-up time was 38 months. None of the 12 cases were diagnosed preoperatively. Preoperative diagnoses were adnexal mass of unknown nature in six (50%), tubo-ovarian abscess in three (25%), ovarian carcinoma in two (16.7%), and endometrioma in one (8.3%) cases. Two patients (16.7%) had experienced the typical symptom of watery vaginal discharge. Three patients (25%) were in Stage I, three (25%) in Stage II, four (33.3%) in Stage III, and two (16.7%) were unstaged. Nine patients had received postoperative platinum-based adjuvant chemotherapy. The 5-year disease-free survival rate was 64%. On evaluating the correlation between clinicopathological parameters and survival, only the Federation of Gynecology and Obstetrics stage ($p = 0.017$) was a significant prognostic factor.

Conclusion: Although preoperative diagnosis of fallopian tube carcinoma is difficult, still 16.7% of our patients experienced the typical symptom suggestive of tubal carcinoma. Prognostic factors associated with fallopian tube cancer were similar to those of epithelial ovarian cancer.

Keywords: Adnexal mass; Primary fallopian tube carcinoma (PFTC)

Introduction

Primary fallopian tube carcinoma (PFTC) is one of the least common gynecological cancers and is difficult to diagnose preoperatively. Fewer than 5% of patients are accurately diagnosed before surgical exploration [1]. Although the symptom complex of "hydrops tubae profluence" is considered pathognomonic for PFTC, it is rarely encountered. Rarely, patients with PFTC are diagnosed preoperatively by a positive Papanicolaou smear, negative endometrial/endocervical curettage, and the presence of a pelvic mass on ultrasonography [2,3]. This rare disease has traditionally been treated in the same manner as epithelial ovarian cancer; however, the prognosis for PFTC is variable. Some investigators report that the prognosis with PFTC is better than that with ovarian cancer, whereas other investigators claim that it is worse for PFTC [4,5]. The purpose of this study was to review the experience of managing PFTC in Kaohsiung Chang Gung Memorial Hospital and to identify the prognostic factors.

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Materials and methods

Patients with fallopian tube carcinoma treated between July 1986 and December 2005 were identified in the cancer registry databases at Kaohsiung Chang Gung Memorial Hospital. In total, 15 patients were identified over this period. The pathology slides from these 15 patients were retrieved and retrospectively reviewed by one of the study authors (C.-C. Huang) to confirm the diagnosis of PFTC based on the criteria proposed by Hu et al [6]. Epithelial ovarian cancer with tubal metastasis was diagnosed in three patients instead of PFTC. Medical records for the remaining 12 patients were then evaluated for information regarding age, gravidity and parity, clinical presentation, preoperative diagnosis, stage of disease, surgical intervention, pathological findings, relapse, and survival. International Federation of Gynecology and Obstetrics (FIGO) staging for fallopian tube cancer was completed whenever possible using surgical and pathological findings extracted from the patients' surgical records.

Univariate and multivariate analyses of possible prognostic factors (age, gravidity, parity, FIGO stage, histological type, tumor differentiation, and residual tumor) were performed. Kaplan–Meier life table analysis was used to generate survival curves. Survival based on categorical variables was compared using the log-rank test (univariate analysis), whereas multivariate analysis was performed using the Cox proportional hazards regression model. All statistical analyses were performed with the SPSS for Windows version 11.5 program (SPSS Asia Pacific Pte. Ltd., Singapore). A p value less than 0.05 was considered significant.

Results

The median age at the time of diagnosis was 54 years (range, 32–67 years). Only one of the 12 patients diagnosed with PFTC was nulliparous. None of the included patients had either hysterectomies or tubal sterilization. Six (50%) of the included patients were postmenopausal (i.e. cessation of menstruation for at least 1 year) and no patient had a family history of breast, uterine, colon, and/or ovarian cancer in a first-degree relative.

The most common presenting symptoms were abdominal pain (50.0%), watery vaginal discharge (16.7%), vaginal bleeding (16.7%), leukorrhea (8.3%), and flank pain (8.3%). None of the 12 patients was correctly diagnosed preoperatively. Instead, preoperative diagnoses included adnexal mass of unknown nature ($n = 6$, 50.0%); tubo-ovarian abscess ($n = 3$, 25.0%); ovarian carcinoma ($n = 2$, 16.7%); and ovarian endometrioma ($n = 1$, 8.3%).

Four (36.7%) tumors were adenocarcinoma of serous type, whereas seven (63.6%) were non-serous (4 poorly differentiated, 3 endometrioid type, and 1 mucinous type) tumors and one was a mixed-type tumor. Seven patients had preoperative serum CA125 (enzyme immunoradiometric assay) levels evaluated. Antigen levels were greater than 35 U/mL in four patients: three patients in Stage III disease and one patient in Stage I/II disease.

Complete surgical staging (including lymphadenectomy) was achieved in 10 patients. Of these, three were in Stage I, three were in Stage II, and four were in Stage III. All 12 patients had surgical removal of their tumor as primary therapy. Furthermore, nine patients received platinum-based chemotherapy [7 with cisplatin (Kemoplat, India) and cyclophosphamide (Endoxan, Germany) and 2 with paclitaxel (Phyxol, Taiwan) and cisplatin].

The median follow-up time was 38 months (range, 18–210 months). Eight patients had no recurrence in the follow-up period, whereas the remaining four patients did have disease recurrence and finally succumbed to the disease. The overall 5-year disease-free survival rate was 64% (Fig. 1). By log-rank univariate analysis, survival was significantly related to the FIGO stage (Stage I or II *vs.* Stage III, $p = 0.017$; Fig. 2). The clinicopathological factors associated with 5-year disease-free survival have been summarized in Table 1. In the Cox regression model, the FIGO stage had only a marginal level of significance. It is likely that this analysis was affected by the small number of cases included in this study.

Discussion

PFTC is a very rare disease, accounting for less than 1% of all gynecological malignancies [7]. Therefore, unlike ovarian cancer, fallopian tube cancer is not routinely suspected in a patient with a complex pelvic mass. Preoperative diagnosis of tubo-ovarian abscess was made in 25% of the 12 patients included in this study, similar to previously published studies [8–10]. Although accurate preoperative diagnosis is difficult, PFTC reportedly is most often diagnosed in an earlier stage of disease than its ovarian carcinoma counterpart [11,12]. This might be because of many PFTC patients experiencing lower abdominal pain as a result of tubal dilatation and because of the development of an abnormal watery vaginal discharge.

With modern advances in medical imaging technologies, the successful preoperative diagnosis of PFTC using transvaginal color and pulsed Doppler ultrasound has been reported

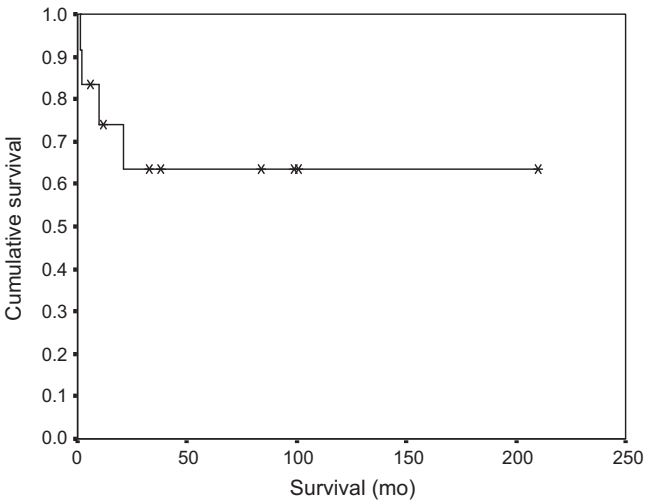

Fig. 1. Five-year disease-free survival.

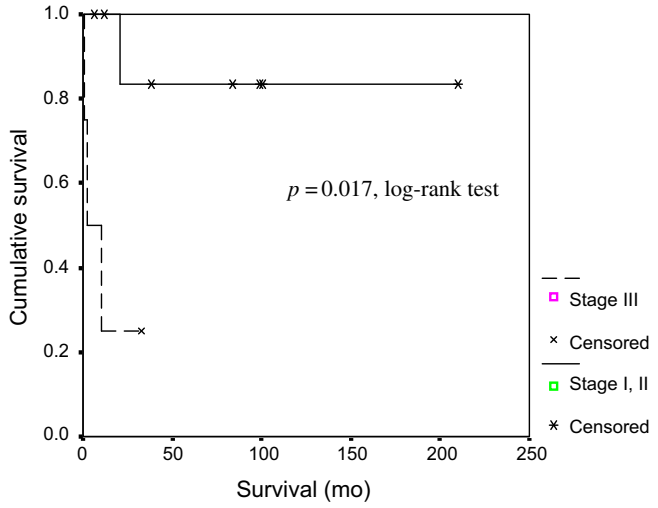

Fig. 2. Five-year disease-free survival according to the Federation of Gynecology and Obstetrics stage.

recently. According to one group, identification of a typical cystic lesion of the fallopian tube with papillary projections, distinct from the ovary and uterus, in association with a low vascular impedance, might lead to a suspicion of tubal malignancy [13].

Etiological factors for the development of PFTC have not been clearly defined. Although some investigators have suggested that primary carcinoma of the fallopian tube shares several biological and clinical features with ovarian carcinoma [14,15], we did not find an increased number of nulliparous women among our patient cohort. Another etiological factor that probably relates to fallopian tube carcinoma is chronic tubal inflammation [16]. Several previous reports and ours found a higher incidence of tubo-ovarian abscess in fallopian tubes, concurrent with carcinoma; however, the exact causal relationship between the abscess and carcinoma is unknown. It is unclear whether PFTC and epithelial ovarian carcinomas share the same etiological factors. One recent publication reported that pelvic serous carcinoma could follow a defined precursor of the distal fallopian tube that has been present for some time [17].

Table 1
Predictors for survival in univariate analysis

Factor	*n* (%)	5-yr survival (%)	*p* (log rank)
Age (yr)			
<50	4 (33.3)	50	0.658
>50	8 (67.7)	75	
Gravida			
≤2	6 (50)	42.9	0.079
>2	6 (50)	100	
Parity			
≤2	8 (66.7)	57.4	0.226
>2	4 (33.3)	100	
Federation of Gynecology and Obstetrics stage			
I, II	6 (60)	83.3	0.017
III	4 (40)	25.0	
Histology			
Serous	4 (36.7)	75.0	0.869
Non-serous	7 (63.6)	68.6	
Differentiation			
Grade I/II	7 (58.3)	57.1	0.536
Grade III	5 (41.7)	75.0	
Residual tumor			
No	9 (75)	74.1	0.178
Yes	3 (25)	33.3	

Significant if $p < 0.05$.

Initial management of PFTC is surgical, and the FIGO staging system requires a surgical extirpation similar to that mandated for ovarian carcinoma. Postoperative chemotherapy with a platinum-based regimen is usually recommended in patients, except in those diagnosed with well-differentiated Stage IA and B disease. In the study reported herein, two patients did not receive standard surgical staging procedures owing to the undiagnosed tubal carcinoma during surgery. The need for adjuvant chemotherapy in such apparent early-stage disease was therefore very difficult to assess. Nonetheless, patients are advised to undergo chemotherapy because there may be up to a 33% incidence of upstaging [18].

With the introduction of cisplatin-containing chemotherapy regimens, an objective response rate of about 80% can be achieved in patients with advanced disease [19,20]. In the patients included in this study, three Stage III patients had residual disease after surgical treatment. Of these, two had measurable disease, and both achieved complete clinical response after six courses of chemotherapy. Unfortunately, the response duration was quite short: only 2 months and 10 months. Both patients finally succumbed to the disease.

The 5-year disease-free survival rate for all stages of PFTC varies, ranging from a low of 22% to a high of 57% [14,15]. Differences in stage distribution could contribute to this large discrepancy, because FIGO stage is the most consistent prognostic factor associated with survival [11,12,14,15,21,22]. In the patients included in this series, eight of the patients' cancers (66.7%) were confined to the pelvis, which likely explains the relatively high survival rate. Other useful prognostic factors, although less consistent than FIGO stage, include patient age at time of diagnosis, residual tumor after initial surgery, and histological grading [5,12,15]. Although the current study failed to demonstrate that patient age was an independent prognostic factor for survival, the median age at time of diagnosis in the 12 patients was 54 years, which was much lesser than that in the largest report by Rosen et al [12]. In their study, the mean age of 143 patients was 62.5 years. The lesser patient age in our series might also help explain the better survival rate in the present study.

Despite the application of appropriate statistical techniques regarding the risk factors for tubal cancers, multivariate analysis is not adequate for the analysis of small numbers of cases. In the study presented earlier, only the stage was a significant prognostic factor predicting survival. Histology, differentiation, and residual tumor were not significant prognostic factors; however, these three factors are widely considered by oncologists to be effective factors in the prognosis of ovarian cancers. As mentioned earlier, tubal cancer

reportedly is often diagnosed in an earlier stage than ovarian carcinoma. Nonetheless, tubal cancers are still commonly diagnosed with intraperitoneal dissemination. Prognosis of tubal cancers seems to be better than that of ovarian cancers at each stage because the histology of this malignancy is usually of the serous type that is sensitive to chemotherapy [4]. Because only four cases of serous-type tumors were included in this study, this small inclusion would explain the lack of significance for prognostic factors. Tubal cancer is a rare type of gynecological malignancy, and a large multicenter study will help establish the prognostic risk factors.

In conclusion, the presence of abdominal pain in a patient with PFTC is highly significant because cancers of the ovary, endometrium, and cervix do not typically cause abdominal pain until their diagnosis is all too obvious. A diagnosis of PFTC should be considered in patients complaining of lower abdominal pain in association with vaginal bleeding/watery discharge or with a tubo-ovarian abscess. The etiology of fallopian tube and epithelial ovarian carcinomas is not well established, but both cancers should be managed in the same manner. The clinicopathological prognostic factors of PFTC are almost identical to those of epithelial ovarian carcinoma.

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