Original Articles

Primary fallopian tube carcinoma: a retrospective clinicopathologic study

P. Singhal[1], *M.D.*; **K. Odunsi**[1], *M.D., Ph.D.*; **K. Rodabaugh**[1], *M.D.*; **D. Driscoll**[2], *B.A.*; **S. Lele**[1], *M.D.*

Department of Gynecologic Oncology[1] *and Department of Biostatics*[2], *Roswell Park Cancer Institute, Buffalo, NY (USA)*

Summary

Introduction: Primary fallopian tube carcinoma is a rare tumor. The aim of this study was to evaluate clinical characteristics and management of fallopian tube malignancies at a large tertiary care cancer institute.

Methods: A retrospective review of the Tumor Registry was conducted to identify all primary fallopian tube carcinomas between 1980 and 2001. Medical charts were retrospectively reviewed. Primary endpoints were overall survival and disease recurrence.

Results: Thirty-five patients had histology consistent with fallopian tube carcinoma. The median age at diagnosis was 56 years. The most common signs or symptoms were abnormal vaginal bleeding (29%) and abdominal/pelvic mass (26%). The most common histology was adenocarcinoma in 16 (46%) patients. Five patients (14%) were Stage I, seven patients (20%) Stage II, 17 patients (49%) Stage III and six patients (17%) Stage IV. Thirty-two (91%) patients received adjuvant chemotherapy and 77% received platinum-based chemotherapy. Twenty-seven (77%) patients underwent second-look surgery, of which 17 patients (63%) were positive for disease. The 5-year survival rate was 64% for Stage I, 42% for Stage II, 32% for Stage III, and 17% for Stage IV.

Conclusions: Fallopian tube malignancies are rare and carry a poor prognosis. More extensive research needs to be performed to have definitive etiologic, diagnostic and treatment guidelines.

Key words: Fallopian tube cancer; Second-look surgery; Chemotherapy.

Introduction

Primary fallopian tube carcinoma is a rare gynecological malignancy with distinct similarities to epithelial ovarian carcinoma. Its incidence ranges between 0.15% and 1.8% of all primary female genital tract tumors [1-6]. Primary fallopian tube carcinoma has been treated with the same surgical and chemotherapeutic approach as ovarian carcinoma [7-9]. The relative rarity and low incidence of fallopian tube carcinoma has made it difficult to study factors influencing clinical outcome, management and long-term survival of women diagnosed with this rare malignancy.

We elected to retrospectively study the prognostic factors, treatment and long-term survival of women diagnosed with fallopian tube carcinoma at a tertiary care referral center.

Materials and Methods

Patients and Samples

Institutional Review Board approval was obtained and patients diagnosed and treated with primary fallopian tube carcinoma between 1980 and 2001 were identified from the Roswell Park Cancer Institute (RPCI) Tumor Registry, Buffalo, NY. Clinical and pathological data were collected retrospectively. Seventy-seven patients were identified with a diagnosis of carcinoma of the fallopian tube. A gynecologic pathologist at RPCI reviewed all pathologic specimens. Cases were included in this study if they met the pathological criteria first suggested by Hu *et al.* [10] and modified by Sedlis [2]. These pathologic criteria include 1) the main tumor is in the fallopian tube and arises from the endosalpinx, 2) the histologic pattern shows a papillary pattern and reproduces epithelium of the fallopian tube mucosa, 3) the transition between benign and malignant fallopian tube epithelium should be demonstrable, and 4) the ovaries and endometrium are either free or contain less tumor than the fallopian tubes. This led to exclusion of 42 patients from the study for the following reasons. Thirty-one patients were reclassified as probable primary ovarian adenocarcinoma, eight cases were reclassified as endometrial adenocarcinoma and three were reclassified as adenocarcinoma of uncertain origin. The remaining 35 patients were staged retrospectively according to the American Joint Committee on Cancer/International Union Against Cancer/FIGO staging system [11, 12]. Medical charts were reviewed retrospectively and clinical data including history, signs and symptoms, diagnosis, treatment and follow-up were collected. Follow-up information was available for all patients until August 2001.

Statistical Methods

Overall survival and disease recurrence were the primary endpoints. Survival estimates were calculated by the method of Kaplan-Meier [13]. Survival distributions were compared using the log-rank test. Patients with Stage I disease were excluded when estimating survival outcomes based on presence/absence of ascites and disease at the end of the primary staging procedure.

Results

A total of 35 patients were included in this study. Age at diagnosis ranged from 32 to 82 years with median age of 56 years. The most common signs and symptoms were abnormal vaginal bleeding (29%), abdominal/pelvic mass (26%) and abdominal pain (17%). The classical pathognomonic symptom complex, hydrops tubae profluens (intermittent colicky pain relieved by sudden watery discharge from the vagina), was not encountered in this study. Adenocarcinoma or atypical cells were detected in

Revised manuscript accepted for publication October 20, 2005

the cervical smears of only two patients (Table 1). Five patients (14%) had been previously treated for another carcinoma in the past. Of these five patients, two patients had prior breast cancers, two had prior cervical cancers and one had prior carcinoid in a rectal polyp. Eight patients (23%) reported a family history of carcinoma, the 2 most common being breast carcinoma (n = 7 relatives) and colon carcinoma (n = 2 relatives).

Table 1. — *Most common signs and symptoms in patient diagnosed with primary fallopian tube carcinoma.*

Symptom/Sign	N	%
Abnormal vaginal bleeding	10	29
Abdominal/pelvic mass	9	26
Abdominal pain	6	17
Abdominal distention	4	11
Abnormal pap smear	2	6
Clear vaginal discharge	2	6
Acute abdomen	1	3
Hernia	1	3

After retrospectively staging all 35 patients, five patients (14%) were Stage I, seven patients (20%) were Stage II, 17 patients (49%) were Stage III and six patients (17%) were Stage IV.

Median survival was 71, 58, 43 and nine months for Stage I, II, III and IV, respectively, (p value 0.0009; Table 3). Estimated 5-year survival rate for Stage I, II, III and Stage IV patient were 64%, 42%, 32% and 17%, respectively (p value 0.002; Table 2).

Table 2. — *Estimated 5-year survival in percentage for Stage I-IV.*

	No. of patients (%)	Estimated 5-year survival in %	p value
Stage			0.002
I	5 (14)	64	
II	7 (20)	42	
III	17 (49)	32	
IV	6 (17)	17	

The most common histological diagnoses were adenocarcinoma in 16 patients (46%) and papillary serous adenocarcinoma in 16 patients (46%). Endometrioid carcinoma, adenosquamous and carcinosarcoma were found in one patient (3%) each. There was no significant difference in estimated survival between serous and nonserous histology (p value 0.78).

Twenty (57%) of the patients had no residual disease at the end of the initial procedure while, 12 (34%) of the patients did have residual disease at completion of primary surgery. Information about three patients (9%) was not available. Stage I patients were excluded when comparing estimated survivals between groups of patients with residual disease present or absent at the end of the staging procedure. Median survival of patients with no residual disease at completion of the staging procedure was 67.57 months compared to 14.64 months for patients with residual disease (p = 0.0005). Estimated 5-year survival for patients with no residual disease was 62% compared to 0% for patients with residual disease present at completion of the initial procedure (p = 0.0001; Figure 1).

Ascites was present in nine (26%) patients. There was no significant difference in median survival between patients with or without ascites (60 months and 59 months, respectively; p value 0.49). Stage I patients were also excluded when comparing estimated survivals between the group of patients with or without ascites (Table 3).

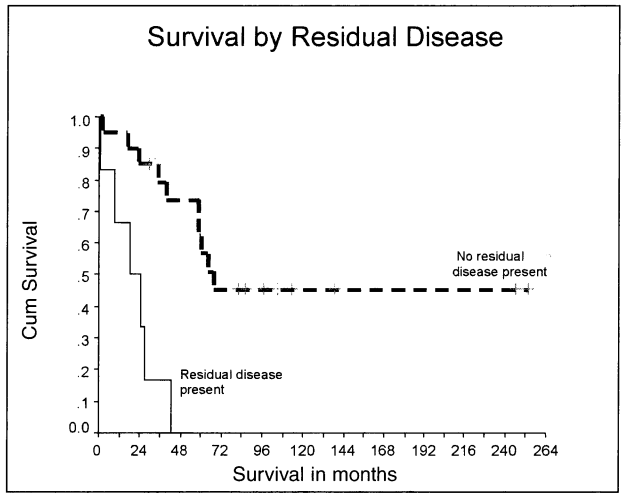

Figure 1. — Kaplan-Meier curve for patients with residual disease present or absent after completion of initial surgery (Stage I patients were excluded from this analysis).

Twenty-seven (77%) patients underwent second-look surgery and 17 (63%) of these patients were found to have disease present. Median survival for patients with disease at second-look surgery was 34 months compared to 59 months for patients with no disease at second-look surgery (p = 0.061).

Table 3. — *Patient characteristics.*

	Number of patients no. = 35 (%)	Median survival in months (95% CI)	p value
Stage			0.0009
I	5 (14)	71 (CI 31, 112)	
II	7 (20)	58 (CI 18, 98)	
III	17 (49)	43 (CI12, 73)	
IV	6 (17)	9 (CI 0, 28)	
Histologic Type			0.78
Non serous/ nonclear cell	19 (54)	60 (CI 35, 83)	
Serous/clear cell	16 (46)	59 (CI 38, 80)	
Grade			0.20
1	3 (8)	64 (CI 38, 89)	
2	8 (23)	60 (CI 35, 84)	
3	22 (63)	52 (CI 29, 76)	
NA	2 (6)		
Residual Disease			0.0005
Absent	20 (57)	68 (CI 18, 117)	
Present	12 (34)	15 (CI 0, 36)	
Information not available	3 (9)		
Ascites			0.49
Present	9 (26)	60 (CI 0, 165)	
Absent	24 (68)	59 (CI 27, 91)	
Information not available		2 (6)	
Presence of disease at second-look			0.06
Positive	17 (63)	34 (CI 10, 59)	–
Negative	10 (37)	59 (CI 12, 105)	–

Over time, treatment modalities for fallopian tube carcinoma have varied, and nine different chemotherapy regimens were utilized in this series. Postoperatively 32 (91%) patients received front-line chemotherapy: of these 27 (71%) patients received platinum or a platinum containing drug combination.

Twenty-three patients (66%) had recurrence of their disease. The most common site for disease recurrence was the upper abdomen (16 patients, 46%), pelvis (9 patients, 26%) and retroperitoneal lymph nodes (6 patients, 17%). Four patients (11%) were also found to have recurrence in the liver, lungs and brain. All 24 patients with recurrence were treated with second-line chemotherapy

Discussion

The rarity of primary fallopian tube carcinoma has prevented the conduction of large prospective trials that could provide information on optimal treatment modalities and prognostic factors. Only large retrospective clinical series have been able to provide information about this rare disease. The most common histological pattern in this study population was adenocarcinoma and serous type [14-16]. Most tumors in this study were poorly differentiated. In our series of patients abnormal uterine bleeding and abdominal/pelvic mass were the most common presenting symptoms [17, 18]. Abnormal pap smears were discovered in only 6% of the patients. This is consistent with previous reports of positive cervicovaginal cytology in 0-23% of cases of fallopian tube carcinoma [14, 19, 20]. Cervicovaginal cytology, therefore has minimal diagnostic relevance for this malignancy.

In this series of patients, univariate analysis showed that early stage of disease and absence of residual tumor at the end of the initial surgical procedure were the strongest predictors of survival. In multivariate analysis however, the absence of residual disease after initial surgery was the only prognostic factor predicting survival, even more so than stage of disease. This highlights the importance of correct staging and maximal surgical effort to render patients with the diagnosis of primary fallopian tube carcinoma optimally debulked.

Second-look surgery (SLL) has been recommended in patients with fallopian tube carcinoma as a guide to further treatment [21-23]. In our series, 27 patients (77%) underwent SLL with 17 (63%) of these patients being positive for disease. There was no significant difference in survival in patients that did or did not undergo SLL. There was also no significant difference in survival between patients that did not have disease compared to patients that had disease at SLL.

Although our study is limited by sample size and its retrospective nature, it emphasizes the need to surgically remove all visible tumor in patients with fallopian tube malignancy. Future studies are warranted to study the biology of this rare disease, to identify other prognostic factors that can identify risk of recurrence, and also to identify patients with advanced disease that will respond favorably to chemotherapy.

References

[1] Brown K.E., Kapp D.S., Schwartz P.E., Merino M.: "Fallopian tube carcinoma". *Int. J. Radiat. Oncol. Biol. Phys.*, 1985, *11,* 583.
[2] Sedlis A.: "Primary carcinoma of the fallopian tube". *Obstet. Gynecol. Surv.*, 1961, *16,* 209.
[3] Eddy G.L., Copeland L.J., Gershenson D.M., Atkinson E.N., Wharton J.T., Rutledge F.N.: "Fallopian tube carcinoma". *Obstet. Gynecol.,* 1984, *64,* 546.
[4] Semrad S.D., Hardee G.E., Hardee M.M., Moore J.N.: "Flunixin meglumine given in small doses: pharmacokinetics and prostaglandin inhibition in healthy horses". *Am. J. Vet. Res.*, 1985, *46,* 2474.
[5] Roberts J.A., Lifshitz S.: "Primary adenocarcinoma of the fallopian tube". *Gynecol. Oncol.*, 1982, *13,* 301.
[6] Raju K.S., Barker G.H., Wiltshaw E.: "Primary carcinoma of the fallopian tube. Report of 22 cases". *Br. J. Obstet. Gynaecol.*, 1981, *88,* 1124.
[7] Ozols R.F., Eifel P.J.: "Ovarian cancer, fallopian tube carcinoma, and peritoneal carcinoma". Principles and Practice of Oncology, 6th editon, Philadelphia, Lippincott Williams & Wilkins, 2001.
[8] McMurray E.H., Jacobs A.J., Perez C.A., Camel H.M., Kao M.S., Galakatos A.: "Carcinoma of the fallopian tube. Management and sites of failure". *Cancer,* 1986, *58,* 2070.
[9] Lacy M.Q., Hartmann L.C., Keeney G.L., Cha S.C., Wieand H.S., Podratz K.C. *et al.*: "c-erbB-2 and p53 expression in fallopian tube carcinoma". *Cancer,* 1995, *75,* 2891.
[10] Hu C.Y., Taymor M.L., Hertig A.T.: "Primary carcinoma of the fallopian tube". *Am. J. Obstet. Gynecol.,* 1950, *59,* 58.
[11] Creasman W.T.: "Revision in classification by International Federation of Gynecology and Obstetrics". *Am. J. Obstet. Gynecol.,* 1992, *167,* 857.
[12] Fleming C.J., Henson D.E., Hutter R.V.P., Kennedy B.J., Murphy G.P.: American Joint Committee on cancer staging. AJCC Cancer Staging Manual, 5th edition, Philadelphia, Lippincott-Raven, 1997.
[13] Kaplan E. L., Meir P.: "Nonparametric estimation from incomplete Observations". *J. Amer. Stat. Assoc.,* 1958, *53,* 457.
[14] Podratz K.C., Podczaski E.S., Gaffey T.A., O'Brien P.C., Schray M.F., Malkasian G.D. Jr.: "Primary carcinoma of the fallopian tube". *Am. J. Obstet. Gynecol.,* 1986, *154,* 1319.
[15] Hellstrom A.C., Silfversward C., Nilsson B., Pettersson F.: "Carcinoma of the fallopian tube. A clinical and histopathologic review. The Radiumhemmet series". *Int. J. Gynecol. Cancer.,* 1994, *6,* 395.
[16] Scully R.E. C.P.: "Tumors of the ovary, maldeveloped gonads, fallopian tube and broad ligament". Washington, DC, Armed Forces Institute of Pathology, 1998.
[17] King A., Seraj I.M., Thrasher T., Slater J., Wagner R.J.: "Fallopian tube carcinoma: a clinicopathological study of 17 cases". *Gynecol. Oncol.*, 1989, *33,* 351.
[18] Maxson W.Z., Stehman F.B., Ulbright T.M., Sutton G.P., Ehrlich C.E.: "Primary carcinoma of the fallopian tube: evidence for activity of cisplatin combination therapy". *Gynecol. Oncol.*, 1987, *26,* 305.
[19] Harrison C.R., Averette H.E., Jarrell M.A., Penalver M.A., Donato D., Sevin B.U.: "Carcinoma of the fallopian tube: clinical management". *Gynecol. Oncol.,* 1989, *32,* 357.
[20] Peters W.A., 3rd, Andersen W.A., Hopkins M.P., Kumar N.B., Morley G.W.: "Prognostic features of carcinoma of the fallopian tube". *Obstet. Gynecol.,* 1988, *71,* 757.
[21] Eddy G.L., Copeland L.J., Gershenson D.M.: "Second-look laparotomy in fallopian tube carcinoma". *Gynecol. Oncol.,* 1984, *19,* 182.
[22] Barakat R.R., Rubin S.C., Saigo P.E., Lewis J.L. Jr., Jones W.B., Curtin J.P.: "Second-look laparotomy in carcinoma of the fallopian tube". *Obstet. Gynecol.,* 1993, *82,* 748.
[23] Cormio G., Gabriele A., Maneo A., Marzola M., Lissoni A., Mangioni C.: "Second-look laparotomy in the management of fallopian tube carcinoma". *Acta. Obstet. Gynecol. Scand.*, 1997, *76,* 369.

Address reprint requests to:
S. LELE, M.D.
Department Surgery
Division of Gynecologic Oncology
Elm and Carlton Street
Buffalo, 14263 NY