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Primary fallopian tube carcinoma – the experience of a UK cancer centre and a review of the literature

N. L. CLAYTON[1], K. S. JAABACK[2], & L. HIRSCHOWITZ[3]

[1]*Department of Obstetrics and Gynaecology, University of Bristol,* [2]*Department of Obstetrics and Gynaecology and* [3]*Department of Histopathology, Royal United Hospital, Bath, UK*

Summary
Primary fallopian tube carcinoma (PFTC) is rare but may be under-diagnosed. We have analysed the incidence, clinical findings and outcome in patients with PFTC at the RUH Gynaecological Cancer Centre in Bath between 1999 and 2004, and compared the incidence with that of advanced ovarian carcinoma (OC). Eight patients had PFTC, seven of whom were diagnosed after 2001, and 55 patients had advanced OC. Our data suggest a relative increase in the number of patients with PFTC over the study period. PFTC patients had a mean age of 69.6 years, most presented with postmenopausal bleeding, two had a second carcinoma, three were nulliparous and none were diagnosed pre-operatively. All were treated surgically and received platinum-based chemotherapy. Although PFTC patients had better outcomes than those with advanced OC, the difference was not statistically significant ($p = 0.088$). Accurate diagnosis and differentiation of PFTC from advanced OC are important for monitoring trends in incidence, for better characterisation of prognostic features and improved management.

Introduction

Primary fallopian tube carcinoma (PFTC) is a rare gynaecological neoplasm. Several population-based studies from the USA indicate an average annual incidence of 3.6 per million women per year (Rosenblatt et al. 1989), although the incidence varies more than two-fold across registries. In Western countries, PFTC is reported to account for 0.3–1.6% of all gynaecological malignancies (Riska et al. 2003; Baekelandt et al. 2000; McMurray et al. 1986). McMurray et al. (1986) maintained that the true incidence is probably underestimated because advanced cases may be incorrectly diagnosed clinically and histologically as primary ovarian carcinoma. A correct diagnosis of PFTC requires a high index of clinical suspicion and close attention by pathologists to the macroscopic and histological findings in resection specimens. The pathologist has to determine where the bulk of the tumour is located, and methodically sample the fallopian tubes, ovaries, omentum and other resected tissues to ascertain the site of origin.

The criteria of Hu et al. (1950) for differentiating PFTC from ovarian and other gynaecological malignancies were:

1 Grossly, the main tumour is in the tube.
2 Microscopically, chiefly the mucosa should be involved, and the tumour should have a papillary pattern.
3 If the wall of the tube is extensively involved, the transition between benign and malignant tubal epithelium should be demonstrable.

These criteria were later modified by Sedlis (1961, 1978), whose widely accepted proposals for diagnosis of PFTC were:

1 The main tumour arises from the endosalpinx.
2 The histological pattern reproduces the epithelium of tubal mucosa.
3 Transition from benign to malignant tubal epithelium is demonstrable.
4 The ovaries or endometrium are either normal or contain tumour smaller than the tumour in the tube.

A system for staging PFTC was endorsed by the International Federation for Obstetrics and Gynaecology (FIGO) in 1991 (Pettersson 1992).

Woolas et al. (1997) reported the occurrence of three cases of PFTC in the Sheffield area over a 15-month period during which 36 primary ovarian carcinomas were diagnosed and commented that the ratio of primary tubal to primary ovarian carcinoma was approximately ten-fold greater than that expected from national incidence figures. In another study, the ratio was even higher (6:1) (Woolas et al. 1994). In the present study we have analysed the incidence, clinical data and outcome in patients with PFTC in the catchment area of The Royal United Hospital (RUH) in Bath. We have also compared the incidence figures with those for ovarian carcinoma, and with regional and national data over a 70-month period.

Correspondence: Lynn Hirschowitz, Department of Histopathology, Royal United Hospital, Bath BA1 3NG. Tel: +44 (0) 1225 824722. Fax: +44 (0) 1225 824503. E-mail: lynn.love@doctors.org.uk

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Methods

Patients with PFTCs and ovarian carcinoma were identified by reviewing the multidisciplinary team meeting (MDTM) records from 1 January 1999 to 31 October 2004. To confirm that no cases had been missed, a Systematized Nomenclature of Medicine (SNOMED) search of the histopathology database at the RUH was also carried out over the same period, by use of the topographical codes for ovary and fallopian tube. The cases include both secondary and tertiary referral cases to the Gynaecological Cancer Centre at RUH. Patient notes were reviewed to gather relevant clinical data: age, presenting symptoms, past medical history, family history, preoperative investigations (including CA125 levels), details of the surgical procedure, treatment and follow-up information to the end of October 2004. Although the initial dissection and reporting had been performed by all of histopathologists at the RUH, all of the cases of PFTC and ovarian carcinoma were reviewed by LH, who is lead gynaecological pathologist.

The number of cases of PFTC and ovarian carcinoma that were registered for the whole of the south-west of England was obtained from the South West Cancer Intelligence Service (SWCIS) database. The SWCIS data include borderline ovarian tumours. Because the data are collected retrospectively, 2 years in arrears, figures were available for 1999, 2000 and 2001 only; the figures for 2002 were not yet been confirmed and have therefore not been included in this study. National data for PFTC and ovarian carcinoma during 2000 were obtained from the Office for Cancer Statistics, and the number of females in south-west England for the year 2000 from the SWCIS. The number of females in the catchment area of RUH was estimated as being half of the total RUH catchment population as recorded by SWCIS. The incidence of PFTC and the ratio of ovarian:PFTC in south-west England were calculated and compared with national and international data.

Since PFTC may be confused both clinically and histologically with advanced ovarian carcinoma, the survival figures of RUH patients with FIGO Stages III or IV ovarian carcinoma were extracted. Kaplan – Meier survival curves were then constructed for patients with PFTC and advanced ovarian carcinoma and compared using a log-rank test.

Results

Over the 70-month period, 10 patients had been diagnosed as having fallopian tube neoplasia (*in-situ* and invasive). On review, two of these patients were found to have disseminated intra-abdominal papillary serous carcinoma associated with *in-situ* carcinoma of the fallopian tube lining epithelium but without a mass lesion in the endosalpinx. These two patients were excluded from the study because they did not meet Sedlis's criteria for PFTC (Sedlis 1978). Eight patients were confirmed as having PFTC. They ranged in age from 53 to 81 years (mean 69.6; SD 9.0) (Table I).

Clinical presentation

The most common presenting symptom (6/8 patients) was postmenopausal vaginal bleeding (PMB) (Table I), that

Table I. Clinical profiles of patients with PFTC

Patient	Age	Symptoms	Investigations	History	Parity	CA125 U/ml
1	67	2-month history of PMB	Right adnexal fullness on examination. Transvaginal USS – right-sided cystic pelvic mass	Breast carcinoma 4 years earlier.	G3 P1	45
2	53	3-week history of abdominal pain and swelling; weight loss	Transvaginal USS – gross ascites, 3cm solid mass in pelvis, thought to be ovarian on CT	DVT in pregnancy	G2	348
3	69	3-month history of PMB.	Transvaginal USS – large right hydrosalpinx; thickened endometrium	Nil	G1	35
4	74	4 month history of PMB	Transvaginal USS – bilateral ovarian cysts; abdominal X-ray – normal	Maternal history of ovarian carcinoma	Nulliparous (virgo intacta)	9
5	81	2 month history of shortness of breath	Malignant cells in pleural fluid; consistent with origin from a primary Müllerian adenocarcinoma.	Nil significant	Nulliparous	4500
6	65	4 months of LIF pain, bleeding PV + PR, yellow serous discharge, weight loss	CT- pelvic mass	Nil	Nulliparous	276
7	68	One-week history of PMB and vaginal discharge	Transvaginal USS – uterus enlarged.	Fibroid, previous PMB	G2	29
8	80	4 months' intermittent PMB, abdominal pain, weight loss	Transvaginal USS – thickened endometrium; right tubal cystic mass, no free fluid in abdomen	Vulval carcinoma 3 years earlier	G1	34

CT = computerised tomography; LIF = left iliac fossa; PMB = post-menopausal bleeding; PR = per rectum; PV = per vaginum; USS = ultrasound scan.

had been present for 1 week to 4 months (mean = 11.5 weeks). Only two patients described a vaginal discharge, in both cases in association with PMB. At presentation, three patients had weight loss, two abdominal pain and two abdominal swelling/fullness. One patient (the only one with FIGO Stage IV disease) presented with shortness of breath and was found to have malignant cells in her pleural fluid.

One patient had a history of maternal ovarian carcinoma, another had had recent vulval carcinoma and a third had had breast carcinoma 4 years previously. None of the other patients had past medical or family histories of significance. Three of the eight were nulliparous; the remaining five each had between one and three children.

Clinical investigations

Initial investigations included ultrasound scans (USS) in six patients: five had transvaginal scans and one had an abdominal scan. In two patients, adnexal masses had been identified in CT scans. None of the PFTCs had confidently been diagnosed as such on imaging.

Pre-operative CA125 ranged from 9 – 4500 U/ml. In five cases, levels were <50. In two patients, the levels were between 200 and 400 U/ml, and in only one (the patient with FIGO Stage IV disease) was CA125 elevated into the thousands (4500 U/ml). Malignant cells were identified in ascitic fluid taps in three patients and one of these also had malignant cells in a pleural fluid sample. Suspicious cells were identified in one patient, no malignant cells were identified in one, and in three patients, an ascitic fluid sample was not submitted as part of the pre-operative investigations.

The FIGO stages were: IC (two cases), IIA (one case), IIB (one case), IIIB (one case), IIIC (two cases) and IV (one case).

Pathology

The carcinoma arose in the right fallopian tube in six cases; one case involved the left tube and one patient had bilateral tumours. In all but one case there was dysplasia in the lining of the adjacent fallopian tube (Figure 1), and the case without dysplasia had a mass lesion confined to the fallopian tube and no evidence of primary ovarian, endometrial or peritoneal disease at surgery. The omentum appeared macroscopically normal and was not resected. Bilateral tubal epithelial dysplasia was identified in one patient with a right-sided tubal carcinoma.

Seven of the eight cases were carcinomas of serous type; five had a papillary architecture, one was solid and one was of mixed solid and papillary type. The eighth case was a transitional cell carcinoma. All of the tumours were graded according to the Silverberg method (Silverberg 2000) as high grade (Silverberg grade 3).

Treatment

All patients were treated surgically although the procedures varied (Table II), and all were treated with three or six cycles of platinum-based chemotherapy; three also received pelvic radiotherapy. Chemotherapy was administered prior to surgery in one patient (the patient with FIGO Stage IV disease), but the remaining seven had chemotherapy after surgery. Further chemotherapy was given when recurrent

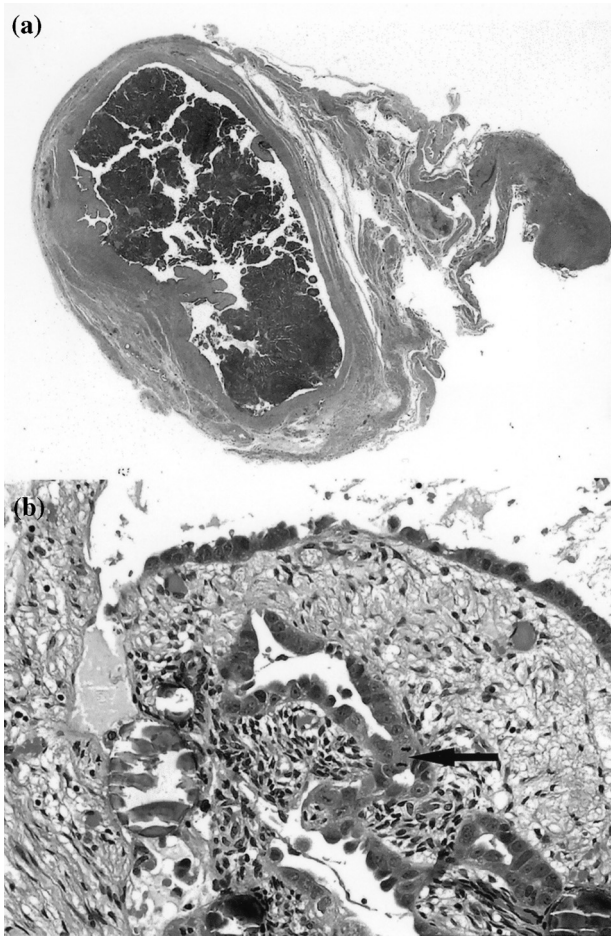

Figure 1. Histological findings in PFTC. (a) Transverse section through fallopian tube, with papillary carcinoma filling the lumen. (b) Tubal epithelial dysplasia adjacent to PFTC. Note the presence of a mitotic figure (arrow) in the dysplastic epithelium.

disease was detected in two patients, 8 and 18 months after the original diagnosis of PFTC, and further surgery was performed for tumour recurrence and bowel obstruction in one patient who also received additional radiotherapy.

Outcome

One patient with FIGO Stage IC disease died 15 months after the diagnosis, and two patients (FIGO Stage IIB and IIIC) are terminally ill with progressive disease at 24 and 32 months, respectively (Table II). Of the remaining, follow-up to date has ranged from 4 to 27 months. One patient (FIGO Stage IC) is alive without recurrence at 27 months; another (FIGO Stage IIB) is alive without apparent disease at 5 months, and two patients (FIGO Stage IV and IIIC, respectively) are alive with disease after 19 and 24 months. One patient with residual tumour after surgery, who has been followed for only 4 months, has declined further treatment.

Epidemiological data

For 2000, the female population in England as a whole was 25,162,540, the south-west of England 2,524,004, and the catchment area of RUH Bath 252,500. The calculated incidence of PFTC and ovarian carcinoma is shown in Table III.

Table II. Histological findings, treatment and follow-up of patients with PFTC

Patient	Age	Surgery	Histological findings	FIGO stage	Ascitic fluid cytology	Chemotherapy	Period of follow-up and status as of 31/10/04
1	67	BSO; omental biopsy	Grade 3 papillary serous carcinoma right fallopian tube; tubal epithelial dysplasia	IC	Suspicious cells	3 cycles platinum based chemotherapy	15 months, dead of disease
2	53	TAH, BSO omentectomy, splenectomy	Bilateral grade 3 papillary serous fallopian tube carcinomas with tubal epithelial dysplasia	IIIC	Malignant cells	6 cycles platinum based chemotherapy	32 months, now terminally ill Recurrence at 8 months - etoposide resistant; calyx; DVT; treosulfan
3	69	TAH, BSO	Grade 3 serous carcinoma, solid type left tube; no in-situ component	IC	No malignant cells	3 cycles platinum based chemotherapy; adjuvant pelvic radiotherapy for enlarged para-aortic nodes	27 months, alive without evidence of disease.
4	74	TAH, BSO, omental and peritoneal biopsies	Grade 3 papillary and solid serous carcinoma right fallopian tube with bilateral tubal epithelial dysplasia	IIIB	Malignant cells	3 cycles platinum based chemotherapy + pelvic radiotherapy	24 months, now terminally ill Recurrence at 18 months; colostomy for infiltration of bowel; pulmonary and liver metastases
5	81	BSO, omentectomy	Grade 3 papillary serous carcinoma right tube with tubal epithelial dysplasia	IV	Malignant cells in ascitic and pleural fluid	3 cycles of platinum-based chemotherapy prior to surgery, followed by a further 3 cycles	24 months CA125 rise to 3121; further chemotherapy, followed by fall and then rise of CA125 (909 to 995IU/ml); etoposide
6	65	TAH, LSO, peritoneal biopsies, node sample, sigmoid colectomy	Grade 3 transitional carcinoma left fallopian tube with tubal epithelial dysplasia	IIIC	Not sent	6 cycles of platinum based chemotherapy	19 months CA125 = 11 at 15 months; CT shows good response to treatment
7	68	Laparoscopic BSO; debulking with TAH, omentectomy and peritoneal biopsies 4 months later	Grade 3 papillary serous carcinoma right fallopian tube	IIB	Not sent	3 cycles of platinum based chemotherapy	5 months Further adjuvant carboplatin after debulking
8	80	TAH, BSO, para-aortic and pelvic node sampling, omentectomy	Grade 3 papillary serous carcinoma right tube with tubal epithelial dysplasia	IIA	Not sent	Platinum based chemotherapy and pelvic radiotherapy	4 months Residual disease; declined further chemotherapy

BSO = bilateral salpingo-oophorectomy; DVT = deep vein thrombosis; LSO = left salpingo-oophorectomy; TAH = total abdominal hysterectomy.

Table III. Incidence of PFTC and primay ovarian carcinomas in the south-west of England and at RUH Bath

	South-West					RUH Bath				
	Ovary		Fallopian tube (FT)			Ovary		Fallopian tube (FT)		
Year	New cases	†Incidence	New cases	†Incidence	FT:ovary	New cases	†Incidence	New cases	†Incidence	FT:ovary
1999	444	175.91	8	3.17	0.0180	36	142.57	0.00	0.00	0.0000
2000	441	174.72	2	0.79	0.0045	51	201.98	1.00	3.96	0.0196
2001	439	173.93	2	0.79	0.0046	49	194.06	0.00	0.00	0.0000
2002	449	177.89	N/A	N/A	N/A	41	162.38	4.00	15.84	0.0976
2003	N/A	N/A	N/A	N/A	N/A	60	237.62	1.00	3.96	0.0167
2004 (10 months)	N/A	N/A	N/A	N/A	N/A	47	223.37	2.00	9.50	0.0426
Mean 1999–Oct 2004	443	175.61	4	1.58	0.0090	49	199.20	1.37	5.70	0.0286

†new cases/million population/year.
N/A = figures not available.

The average number of new cases of PFTC/year at RUH over the 70-month study period was 1.37 and the incidence 5.7 per million women/year, as compared with an average number of 49 new cases of ovarian carcinoma/year and an incidence of 199.20 per million women/year.

In the south-west region, the number of new cases of PFTC registered between 1999 and 2001 was four and the incidence 1.58 per million women/year. In 2000, the incidence of PFTC for the whole of England was 2.19 per million women/year (55 cases in total). The mean number of cases of ovarian carcinoma for England as a whole during the year 2001 was 214.6 per million women/year (5,400 cases). The ratio of PFTC:ovarian carcinoma for the RUH and the south-west of England was 0.0286, 0.0090, and in 2000 the ratio for England as a whole was 0.010.

Survival data

As the main differential diagnosis of PFTC is advanced ovarian carcinoma, we compared the survival of our PFTC patients with that of 55 patients with FIGO Stage III (52 patients) or IV (three patients) ovarian carcinoma with comprehensive follow-up data, diagnosed between January 1999 and December 2003. During the same period, the total number of patients whom we diagnosed as having ovarian carcinoma was 237. The patients with advanced ovarian carcinoma ranged in age from 38 to 99 years (mean = 64 years, SD = 16) had a follow-up of 326 – 1,979 days, and a median survival of 641 days. Thirty-three of the 55 patients died (60%) within 30 – 985 days of follow-up. Although survival curves at 3 years suggest a difference in outcome for patients with PFTC and ovarian carcinoma, the number of PFTC patients is small and log-rank comparison shows that this is not statistically significant ($p = 0.088$) (Figure 2).

Discussion

Although numbers are small, our data suggest that there has been a relative increase in the number of PFTC at the RUH Gynaecological Cancer Centre in Bath. Although

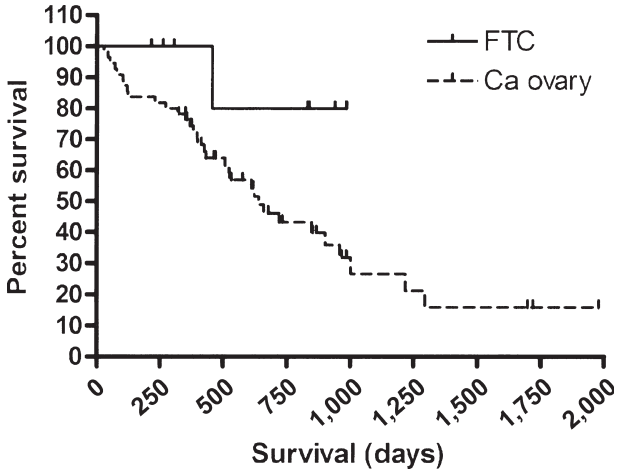

Figure 2. Kaplan – Meier survival curves for PFTC (solid line) and advanced ovarian carcinoma (dashed line). At 1,000 days, 80% of patients with PFTC are still alive, compared with fewer than 40% of patients with advanced ovarian carcinoma.

the incidence of ovarian carcinoma has also increased, the latter change has been much smaller. There are several possible explanations. As PFTC is uncommon, small chance variations from year to year can produce large changes in incidence. An increase in clinical and histological awareness of this type of neoplasm could also be a factor; although all of the present cases were reviewed by the same pathologist for this study, changes in practice by the various pathologists responsible for the initial dissections may have influenced the likelihood of, for example, sampling critical segments of the fallopian tube. A similar increase in incidence of PFTC was documented over a 45-year period at the Finnish Cancer Registry (Riska et al. 2003), although in that study the diagnosis was not confirmed by pathological review. The incidence of registered PFTC in Finland rose 4.5-fold from 1.2/million female population between 1953 and 1957, to 5.4/million between 1993 and 1997. Lastly, it is possible that our data and the findings of others (Woolas et al. 1997, 1994; Riska et al. 2003) reflect a genuine increase in the incidence of PFTC; it will be of interest to see whether more recent regional and national figures mirror this trend.

Patients in our cohort tended to be older, on average 69.6 years, than those in previously published series, in which the mean age has ranged from 55 to 61 years (Ng and Lawton 1998; Baekelandt et al. 1993b, 2000; Alvarado-Cabrero et al. 1999; Wolfson et al. 1998). The youngest patient reported to have PFTC was 14 years old, and the oldest 85 (Nordin 1994). The most common signs and symptoms at presentation are pelvic pain, a pelvic mass and serosanguineous discharge (so-called 'Latzko's triad'), or vaginal bleeding, discharge and lower abdominal pain (Nordin 1994). In our series, the most common presenting symptom (in 6/8 patients) was postmenopausal bleeding, and this was of relatively short duration (a mean of 11.5 weeks prior to presentation). In an earlier study of patients with PFTC, 38% of patients had been symptomatic for more than 6 months and 13% for more than 1 year (Eddy et al. 1984). Other studies have found up to 14% of patients to be asymptomatic at the time of diagnosis (Peters et al. 1988). Weight loss was the second most common symptom in our patients. Abdominal pain or swelling/fullness were uncommon manifestations.

A pelvic mass is the most common finding on physical examination in approximately 65% of patients; however, ascites is reported in only 15% (Nordin 1994). This may explain why ascitic fluid was not submitted as one of the initial pre-operative investigations in three of our cases. The ascitic fluid from four of the remaining five patients in this series contained suspicious or malignant cells. Peritoneal washings should be taken at the time of surgery because positive washings are an adverse prognostic indicator – they suggest extratubal spread and are associated with an increased risk of lymph node metastasis (Gadducci 2002). Peritoneal washings have been reported to contain malignant cells in up to 20% of cases (Wolfson et al. 1998).

Because PFTC is uncommon and the symptoms are relatively non-specific, pre-operative diagnosis is rare (Baekelandt et al. 1993b). Only 4.6% of cases were diagnosed pre-operatively in one study (Alvarado-Cabrero et al. 1999). Our own experience mirrors that of others in that CT, MR and ultrasonographic imaging are of limited value for diagnosis of PFTC. Three-dimensional static and power Doppler sonography has recently been reported to be more successful in distinguishing tubal from ovarian pathology (Kurjak et al. 2000).

Serum CA125 levels are increased in approximately 85% of cases (Knapp et al. 1996). Ng and Lawton (1998) state that CA125 is always elevated in advanced disease but fewer than half of the patients in this study had elevated levels. In a study of 151 cases, CA125 was measured in 40 patients (26%) (Baekelandt et al. 2000) of whom 26 had levels >35 U/ml (range 43 – 19,021 U/ml; mean 1,799; median 250 U/ml). In our study, pre-operative CA125 levels were significantly raised into the thousands in only one patient, who had FIGO Stage IV disease, and up to 348 U/ml in two cases. Since serum CA125 levels may also be elevated in patients with ovarian or primary peritoneal serous carcinomas, this marker lacks specificity for PFTC. Significantly raised levels of serum CA125 may also be found in a range of benign conditions including pelvic inflammatory disease, endometriosis, functional ovarian cysts, menstruation and early pregnancy. Nevertheless, raised levels in the presence of an adnexal mass, particularly in a postmenopausal woman, should prompt additional clinical and radiological investigations to exclude underlying malignancy. Serum CA125 levels are also a useful means for monitoring disease progression (Rosen et al. 1994a; Hellstrom 1998).

Alvarado-Cabrero et al. (1999) reported that 95% of the 103 PFTCs in their study were unilateral and 3% bilateral. Of the unilateral cases, 58% involved the right fallopian tube and 42% the left. The laterality of PFTCs is not mentioned in most of the large, multicentre reviews but our study confirms a right-sided predominance (6/8 cases) (Baekelandt et al. 2000). Baekelandt et al. (2000) reported a 12.5% bilaterality rate, identical to that in the present study. A higher incidence of bilaterality (26%) was reported by Sedlis (1961) and a later review by Rose et al. (1990) claimed bilaterality of 10 – 26%.

Carcinomas of all of the types described in ovarian surface epithelial tumours can also occur in the fallopian tube. As in most series, most of our patients had papillary serous adenocarcinomas, although in one study Alvarado-Cabrero et al. (1999) found only 50% to be of serous type and 25% to be of endometrioid type. Transitional cell carcinoma (as in one of our cases) is generally rarer (Chin et al. 1998; Alvarado-Cabrero et al. 1999) but accounted for 43% of cases in a Japanese study (Uehira et al. 1993).

In most previous series, PFTC has been graded subjectively rather than according to the more objective Silverberg criteria that we used. Rosen et al. (1994b) showed no correlation between tumour grade and outcome, but a marginally significant correlation was found by Hellstrom et al. (1994).

Aetiological factors have not been clearly defined. Chronic inflammation has been implicated (Hellstrom et al. 1994; Gungor et al. 2003) but there was no history of pelvic inflammatory disease in our patients. Infertility and nulliparity have also been implicated as risk factors. In the present study, three out of eight patients were nulliparous; other studies have reported nulliparity rates between 13 and 45% (Alvarado-Cabrero et al. 1999; Baekelandt et al. 2000; Hellstrom et al. 1994) and infertility in up to 71% (Hellstrom 1998). Surprisingly, one study found that nulliparous women with PFTC had a better prognosis (Hanton et al. 1966). The incidence of PFTC is higher among Caucasian women (including Hispanics) than in African Americans (Rosenblatt et al.

1989). Age is considered the most significant risk factor: 95% of all cases occur in women over 35 years.

The management of PFTC is primarily surgical and based on the management of ovarian carcinoma (Baekelandt et al. 1993b, 2000; Gadducci, 2002), i.e. total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and lymphadenectomy (>30% of patients with disease limited to the fallopian tube have nodal metastases) (Di Re et al. 1996; Wolfson et al. 1998). The frequency of early lymphatic spread is emphasised in several reviews (Baekelandt et al. 1993b) and is reported in patients with high-grade carcinomas (Alvarado-Cabrero et al. 1999). Comprehensive staging is important (Gadducci 2002). Platinum-based therapy significantly improves survival, especially of patients with high-risk (e.g. after intraoperative rupture) early-stage ovarian cancer (Hellstrom et al. 1994; Gadducci 2002). Overall a 70% response rate has been reported with platinum based chemotherapy, with a median response of 12.5 months (Baekelandt et al. 2000). In those patients with advanced disease, paclitaxel and carboplatin-based chemotherapy are advised. Second-line treatment for persistent or recurrent disease should be based on the platinum-free interval, and secondary cytoreduction should be considered only for highly selected patients with localised, late relapse (Gadducci 2002). It is recommended that peritoneal washings should be taken at the time of surgery because positive washings suggest extratubal spread and increased risk of lymph node metastasis and thereby affect the prognosis. Optimal tumour debulking similar to that for ovarian carcinoma is advised; residual disease of >2 cm is associated with a poor prognosis (Baekelandt et al. 2000; Peters et al. 1988; Obermair et al. 2001). Serosal involvement is also an adverse prognostic indicator (Hellstrom 1998).

Although older studies advocated either pelvic or whole abdominal radiotherapy, this should no longer be used except for palliation of specific symptoms (Gadducci 2002; Baekelandt et al. 2000), because of low efficacy and a high rate of serious complications. The role of progestational agents in the treatment of PFTC is uncertain; there are no known randomised studies.

The outcome of patients with PFTC is reported to be poor, and worse than that of patients with equivalent stages of ovarian carcinoma or other early-stage gynaecological malignancies. (Vaughan et al. 1998; Obermair et al. 2001) However, the accuracy of histological diagnosis in many series and wide variation in treatment have resulted in data that are difficult to compare. Schneider et al. (2000) report an overall 5-year survival rate for all FIGO stages of 22%, and 80% for Stage I; none of the patients with FIGO Stage III and IV disease survived for 5 years. In a more recent study by Kosary and Trimble (2002), in which half of the patients with Stage I/II disease did not have lymphadenectomy and most with Stage III/IV disease were treated with surgery and chemotherapy, the 5-year relative survival of patients according to FIGO stage was: Stage I 95%; Stage II 75%; Stage III 69% and Stage IV 45%. The stage-by-stage survival rates in this study were better than for women with ovarian epithelial carcinoma. Although we too found survival at 3 years to be better than that of women with advanced ovarian carcinoma (the group with which patients with PFTC are most likely to be confused), the difference was not significant.

Other factors that have been noted to influence survival include the histological type of the PFTC: survival is similar for PFTC of serous and transitional types, and better for tumours with an endometrioid morphology (Alvarado-Cabrero et al. 1999). These authors suggested that depth of invasion into the wall of the fallopian tube be investigated further because of the influence of depth of invasion on prognosis in other viscera that have muscle in their walls, e.g. uterus, bladder, gastrointestinal tract. A better prognosis was also demonstrated for patients whose fallopian tube was occluded at the fimbriated end, giving a hydrosalpinx-like appearance. This was postulated to prevent spread into peritoneal cavity (Baekelandt et al. 1993a). In patients with Stage 0 and I PFTC, depth of invasion into the tube wall and intraoperative rupture were of independent prognostic significance (Baekelandt et al. 2000).

In our cohort, two patients had histories of vulval and breast carcinoma respectively, and one had a maternal history of ovarian carcinoma. There are no published data on the significance of a family history of carcinoma in PFTC but association of this with other carcinomas has been reported. A total of 11% of patients in one series had underlying breast carcinoma (Alvarado-Cabrero et al. 1999). A higher frequency of other gynaecological malignancies and breast carcinomas was reported by Hellstrom (1998), and of 151 patients studied by Baekelandt et al. (2000), eight patients had breast carcinoma, two had colonic carcinoma, 12 had a second gynaecological neoplasm, two later developed chronic myeloid leukaemia and one developed a lung carcinoma. Alvarado-Cabrero suggested that the association between breast and gynaecological malignancies was due to their similar hormone-responsiveness (Alvarado-Cabrero et al. 1999). More recent data have linked PFTC with *BRCA1* and *BRCA2* mutations that are also associated with breast carcinoma. A study of 44 unselected patients with PFTC found germline *BRCA1* mutations in five and *BRCA2* mutations in two (Aziz et al. 2001). The frequency of proliferative lesions of the tubal epithelium is increased in *BRCA1* mutation carriers (Carcangiu et al. 2004). Examination of the whole of the fallopian tube in 30 patients with *BRCA1* or *BRCA2* gene mutations, or a family history indicating susceptibility to ovarian and breast carcinoma, revealed five clinically occult gynaecological malignancies; it is noteworthy that four of these were only identified on review by a pathologist with gynaecological expertise (Leeper et al. 2002). The recommendations of Leeper et al. (2002) and Colgan and colleagues (2001, 2003) in dealing with known *BRCA1* and *BRCA2* mutation carriers and those whose family history indicates that they are at high-risk, can be summarised as follows: (1) the fallopian tubes and ovaries should be processed in their entirety and examined in serial sections by a pathologist with expertise in gynaecological malignancies; (2) laparoscopy and laparotomy should be carried out at the time of prophylactic oophorectomy to allow inspection of the peritoneal surfaces; and (3) peritoneal fluid should be collected for cytological evaluation.

In conclusion, although numbers are small, our findings suggest that PFTC may be increasing in incidence and that its accurate diagnosis and differentiation from advanced ovarian carcinoma are important for prognostication and management. Further clinical and histological studies are still desirable to define more clearly the differences between ovarian and PFTC. Pre-operative investigations should be

refined. Other studies suggest that because of the high risk of lymph node metastases, lymphadenectomy is advisable even in patients with early stage disease. Examination of resected tumours should be carried out by pathologists with expertise in gynaecological pathology, and according to a standard protocol, such as that proposed by the Cancer Committee of the College of American Pathologist (Scully et al. 1999). Thorough histological assessment will help not only to corroborate prognostic indicators such as occlusion of the fimbriated end of the fallopian tube but also to ascertain the significance of infiltration of the myosalpinx, provide refinements in the staging system of PFTC, and clarify diagnostic criteria for tubal epithelial dysplasia. Improvements in treatment and outcome can only properly be evaluated if underpinned by earlier and more accurate diagnosis.

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