Fallopian Tube Carcinoma—A Review

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Abstract

Although a common site of metastases, primary fallopian tube carcinoma comprises only 0.3% of all gynaecological malignancies. Presenting symptoms are variable and non-specific, with preoperative diagnosis rarely entertained. The FIGO system assigns nearly twothirds of patients to stage I or II and is based on surgical staging criteria similar to those for ovarian cancer.

Likewise, management is based on that for ovarian cancer-radical debulking followed by platinum-based combination chemotherapy. Five-year survival for patients with disease confined to the tube at diagnosis (stage I) is only about 60% and only 10% of patients with advanced disease will be cured.

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Introduction

Fallopian tube cancer is the least common of gynaecological malignancies. It was first described by Renaud in 1847.¹ Since then, there have been over 1500 cases documented in the literature. It comprises 0.3% of all gynaecological cancers. The incidence of this condition is about 3.6 /million women per year from USA figures.

The rarity of this condition has meant that most of the cases reported have been on isolated case reports and on retrospective studies often comprising of fewer than 100 cases over a long period of time. The period of retrospective analysis is also subject to question where staging criteria and treatment modalities may have changed as newer evidence becomes available over the years.

The International Federation of Gynaecology and Obstetrics (FIGO) Oncology committee published an updated staging classification in Singapore in 1991² which now serves to allow for standardisation of classification and comparison of results from recent studies.

Histopathology

It is important to distinguish between primary malignant tumours of the fallopian tube from lesions that are secondary from the ovary, uterus or the gastrointestinal tract which are by far the commonest malignant lesion found in the fallopian tube.¹ The most common primary cancer is the ipsilateral ovary which has spread by direct invasion or from a contralateral ovary via transcoelomic spread.

Primary adenocarcinoma of the fallopian tube with papillary features is the most common histological type forming more than 90% of malignant tumours. Other less common histological types include clear cell carcinoma, squamous cell carcinoma, mixed carcinoma, endometrioid carcinoma and sarcoma.³

It is also important to distinguish invasive tube cancer from atypical epithelial hyperplasia of the fallopian tube.

The common mullerian origin of fallopian tube and ovarian cancer could explain the cytological and histological similarities between them.

Difficulties in diagnosis exist due to the similarities shared between fallopian tube carcinoma and epithelial ovarian carcinoma. Hu et al,⁴ established diagnostic criteria to distinguish fallopian tube carcinoma from other primary tumours in 1950. This classification was modified in 1978 by Sedlis⁵ which stands as:

- The tumour arises from the endosalpinx
- The histological pattern reproduces the epithelium of tubal mucosa
- Transition from benign to malignant epithelium is found
- The ovaries are either normal or with smaller tumour

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than that in the tube

Hu also produced grading for fallopian tube cancer based on the histological appearance of the tumour which follows that of endometrial adenocarcinoma:

- Grade I: papillary
- Grade II: papillary-alveolar
- Grade III: alveolar medullary

Grading can also be based on that for ovarian cancer, that is, well, moderately and poorly differentiated.

Grading at present has not been shown to affect prognosis up to five years but may influence prognosis beyond that. 6

Clinical Features

The mean age of presentation is quoted as 56 years with most cases presenting in the fourth, fifth and sixth decades. Cases have been reported in women from the ages of 17 to above 80 years. There appears to be a higher incidence in Whites over Blacks.⁷ It is more common in post menopausal women.

The classical triad of symptoms: a serosanguinous discharge, pain and an adnexal mass, and *hydrops lubae profluens* as described by Latzko in 1916 is rarely reported.¹

The presenting symptoms are non-specific which often result in misdiagnosis. The most common symptoms are abnormal vaginal bleeding or discharge and abdominal pain. A measure of the frequency of these symptoms in 5 studies is shown in Table I.

The clinical symptoms of fallopian tube cancer and ovarian cancer are similar with the exception of abdominal pain, which is a frequent complaint and may lead to earlier presentation. The pain is colicky and lower abdominal in nature which may be related to distension of a partially blocked fallopian tube by fluid which is then relieved by passage of blood or discharge.

The presence of a pelvic mass often leads to further investigations such as an ultrasound scan. Although the presence of the mass can thus be confirmed, its origin is not always determined.

The presence of abnormal glandular cytology in the

 TABLE I:
 PROPORTION OF SYMPTOMS PRESENT AT DIAGNOSIS

 OF FALLOPIAN TUBE CANCER

Symptom	%	
Vaginal bleeding	34	
Vaginal discharge	20	
Pain	23	
Abdominal distension	9	
Others	8	
Urinary frequency	3	
None	3	

absence of any cervical or endometrial pathology should raise the possibility of an ovarian or fallopian tube malignancy.

The lack of specificity of symptoms can lead to delays in presentation and diagnosis. In Eddy's series, 38% of patients had been symptomatic for more than 6 months with 13% of patients being symptomatic for more than 1 year.⁸ Peters et al⁹ in their series of 115 patients, found that 14% were asymptomatic at the time of diagnosis.

Tumour markers such as CA125 are proving to be of help in the diagnosis of fallopian tube cancer. Levels of CA125 rise with advancing stages of disease and are always positive at advanced stages. The use of CA125 in conjunction with endometrial aspiration cytology has been described where positive measures of these 2 factors in the absence of endometrial invasion would increase the index of suspicion of a fallopian tube or ovarian malignancy.¹⁰

The role of transvaginal ultrasonography is becoming more established where the presence of a pelvic mass possibly distinct from the ovary with abnormal Doppler flow indices could raise the index of suspicion of a malignant lesion especially in conjunction with an elevated CA125 level. A cogwheel-like appearance with polyploid tissue growing from the inner surface of the fallopian tube has been described suggestive of fallopian tube pathology.¹¹

Nevertheless, due to the insiduous nature of its symptomatology, a significant proportion of patients will still present with late disease where the presumed diagnosis of fallopian tube cancer will be made for the first time at laparotomy.

Staging and Prognosis

The staging of fallopian tube cancer is surgical and based on that for ovarian cancer. The latest update by the FIGO was produced in 1991 (Table II). This incorporates Schiller and Silverberg's classification and the prognostic features of peritoneal washings, tumour nodule size, and node metastases.

It has been shown that the 5-year survival was 80% when tubal wall penetration was taken into consideration. The 5-year survival fell to 60% if there was less than 50% penetration and to less than 20% if there was deeper invasion.⁹

Most series at present, however, tend to classify staging broadly into I, II, III and IV without providing information regarding subgroups within each group. Survival may be potentially altered within each subgroup depending on how staging is determined.

Management

The management of fallopian tube carcinoma has been based on the management of epithelial ovarian cancer.

TABLEII: WHO STAGING SYSTEM FOR FALLOPIAN TUBE CANCER

	CANCER					
	Definition					
0	Carcinoma in situ (limited to tubal mucosa)					
I	Growth limited to fallopian tubes					
Ia	Growth limited to one tube with extension into the submucosa or muscularis, or both, but not penetrating the serosal surface; no ascites					
Ib	As Ia but growth limited to both tubes					
Ic	Tumour stage Ia or Ib with extension to serosa or ascites or peritoneal washings containing malignant cells					
II	Growth involving one or both fallopian tubes with pelvic extension					
IIa	Extension or metastasis, or both, to the uterus or ovaries, or both					
IIb	Extension to other pelvic tissue					
IIc	Stage IIa or IIb with ascites containing malignant cells or positive peritoneal washings					
ш	Tumour involves one or both fallopian tubes with extrapelvic peritoneal implants or retroperitoneal or inguinal nodes containing tumour					
IIIa	Tumour seems limited to true pelvis but histologically proven malignant extension to the small bowel or omentum					
IIIb	Tumour grossly limited to the true pelvis with negative nodes with histologically confirmed microscopic seeding of the abdominal peritoneal surfaces					
IIIc	Tumour involving one or both tubes with histological confirmed implants of abdominal peritoneal surfaces, none exceeding 2 cm in diameter					
IV	Abdominal implants greater than 2cm in diameter or retroperitoneal or inguinal nodes or both, containing tumour Growth involving one or both fallopian tubes with distant metastases Pleural effusion cytology must show malignant cells to be					
	stage IV Parenchymal liver metastases equals stage IV					

The current recommendation for surgery is to carry out a total abdominal hysterectomy, bilateral salpingooophorectomy, omentectomy and lymphadenectomy. Peritoneal washings should be taken at the time of surgery as positive peritoneal washings suggestive of extratubal spread increase the risk of lymph node metastases with an adverse effect on prognosis.¹²

Tumour debulking applies in a similar way to that of ovarian cancer where Peters et al⁹ showed that residual disease of more than 2 cm was found to be a poor prognostic factor.

Lymph node metastases were noted to have occurred in a significant proportion of patients seen in a series by Tamimi and Figge.¹³ In their series, lymph node spread was seen in 53% of cases with paraaortic node metastases in 33%. Cormio et al¹¹ demonstrated that the incidence of positive lymph nodes at laparotomy in patients with surgical stage I and II disease was 30% and 68% in those with stage III and IV disease. A series by Di Re et al¹⁴ found that 33% of patients with disease limited to the fallopian tube had positive nodes.

Lymphadenectomy should therefore be performed where disease is clinically confined to the tubes. Lymph node sampling will not improve survival but will provide an indication of long-term survival.

Conservative surgery has been described in the literature in disease limited to the fallopian tube where a pregnancy was desired by in vitro fertilisation.³

The 5-year survival was reported to have improved with adjuvant treatment for stage I disease compared to non treatment.⁹ Current opinion dictates that post surgery, treatment should be given following guidelines for epithelial ovarian cancer. Radiotherapy was the treatment of choice up to the early eighties but has now been superseded by chemotherapy.

Radiotherapy

Radiotherapy has been given in the form of external beam pelvic and abdominal radiotherapy while brachytherapy has also been used. It has been felt that radiotherapy did not improve survival rates when given adjuvant treatment and was associated with severe side effects.³ This may be because most patients receiving radiotherapy may already have had abdominal disease which would have conferred a poorer prognosis.

Analysis of results has been difficult due to the small numbers in reported series and differences in radiotherapy doses and fields, which make comparisons difficult. Klein et al¹⁵ evaluated adjuvant therapy however, and found that the 5-year survival rate for stage I and II disease was better with radiotherapy (53%) compared to chemotherapy (27%) in equally matched groups of patients. Adding abdominal irradiation to the pelvic field conferred no benefit and was associated with more side effects. Jerecek et al¹⁶ also implied that radiotherapy may give better control for local disease in their series.

The difference in the survival of these studies could be explained by difference in staging of disease, where patients classified as stage I and II may have actually had more advanced disease depending on whether lymph node sampling was carried out.

Although the current consensus is that radiotherapy should not be used as adjuvant treatment, these results suggest that there may still be a role of postoperative pelvic radiotherapy in patients who are staged accurately.

Chemotherapy

The use of chemotherapy in fallopian tube cancers is again based on that for epithelial ovarian cancer. Tumour responsiveness using platinum based therapy and responses of up to 90% were reported.^{17,18} Survival rates appear to be increased and the use of adjuvant chemotherapy is now recommended for all but the earliest tumours.

It appears that chemotherapy is most useful in advanced disease. The regimen used is usually cyclophosphamide, doxorubicin and ciplatinum (CAP).

There have been anecdotal cases reports describing the use of Taxol in the management of recurrent fallopian tube cancer with complete responses noted. Tresukol et al¹⁹ described a patient with fallopian tube cancer which recurred late following surgery and adjuvant chemotherapy. An attempt at secondary cytoreduction and treatment with repeat platinum for a recurrent pelvic mass was unsuccessful. Taxol was used which resulted in complete resolution of the pelvic mass.

The role of taxol may have a role as a second line agent but this has yet to be determined in clinical trials.

Second Look Laparotomy

This procedure has been used to assess the response of disease to chemotherapy. A second look laparotomy would be completed four to six weeks after cessation of chemotherapy usually after 6 cycles of CAP (cyclophosphamide, doxorubicin and cisplatinum) given at three weekly intervals.

In a recent series by Cormio et al,²⁰ stage and grade of tumour were not seen to be predictive of disease status at second look laparotomy. CA125 measurements positively predicted patients with persistent disease. Patients found to have disease at second look had secondary cytoreduction and were given radiotherapy, further chemotherapy or a progestogen. No difference in survival was noted due to small numbers in this group.

Follow up of patients with a negative second look showed that up to 33% of patients had a recurrence with a median survival of 49 months. The median survival of patients with a positive second look was 18 months.

The conclusion from that study was that a second look laparotomy provided useful prognostic information for patients with fallopian tube carcinoma but did not alter long-term survival. The high rate of recurrence in patients with a negative second look and lack of an effective second line treatment was a major criticism of this procedure.

Prognosis

The most important prognostic factor in fallopian carcinoma is stage of disease at laparotomy. Staging should include results of lymph node analysis which would alter staging levels to stage III.

The 5-year survival according to stage of disease in various series is shown in Table III.

Although grading of disease is thought not to be of

TABLEIII: PERCENTAGE 5-YEAR SURVIVAL ACCORDING TO STAGE OF DISEASE

Stage	Tamimi et al ¹³	Denham et al ²²	McMurray et al ²³	Peters et al ⁹	Rosen et al ²⁴	Vaughn et al ²¹
I II	50	68 39	56 27	61 29	50.8	73 33
III IV	33	21 0	14 0	17 0	13.6	0 0

significance to 5-year survival rates, there appeared to be an improvement in survival beyond five to ten years, when comparing grade I and II disease vs grade III.²¹The presence of lymphocytic infiltrate along the edge of the tumour margin was found to improve survival.

The 5-year survival of fallopian tube carcinoma (stage I and II) is poorer at 50.8% than that of ovarian cancer at 77.5%.⁶

Conclusion

Fallopian tube carcinoma is a rare gynaecological malignancy. Despite its similarities with ovarian cancer, it is still associated with a poorer prognosis. Information available on this condition is limited by small series leading to difficulty in performing prospective randomised studies to determine treatment of choice. Management of this condition should be limited to tertiary referral centres which have experience of this condition. There have been calls for multicentre trials to be performed and hopefully, this will be possible in the near future.

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