Primary fallopian tube cancer - a ten year review. Clinicopathological study of 12 cases

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Summary

Primary fallopian tube cancer is the rarest of all gynecologic cancers, presenting as benign pelvic disease or more often as ovarian cancer and almost all cases are diagnosed at operation or autopsy. Primary adenocarcinoma is the most common histological type of primary tube cancer which has traditionally been managed and treated in the same manner as epithelial ovarian cancer. However, unlike ovarian cancer, fallopian tube cancer is not routinely suspected and treatment may be delayed and also seems to have a worst prognosis than ovarian cancer. We present a retrospective study involving 12 patients with primary fallopian tube cancer treated in our department. The clinicopathologic characteristics and treatment are reviewed.

Key words: Primary; Fallopian tube; Adenocarcinoma.

Introduction

Primary fallopian tube carcinoma is a very uncommon cancer that appears between 40 and 65 years old and comprises only 0.2-1% of all gynecologic malignancies [1]. The differential diagnosis between primary malignant tumors of the fallopian tube and metastatic tumor masses is often difficult because of widespread disease at the time of surgical exploration. Tumor masses in the fallopian tube are generally metastatic from the ipsilateral ovary [1-4].

Primary fallopian tube cancer is rarely diagnosed pre- or peri-operatively and is often mistaken for benign pelvic disease or ovarian cancer. Primary adenocarcinoma of the fallopian tube with papillary features is the most common histological type of primary tubal cancer (> 90%).

Compared with ovarian carcinoma, fallopian tube cancer more often presents in early stage but seems to have a worst prognosis, stage for stage. Primary tube cancer is treated like ovarian cancer: surgical debulking followed by multi-chemotherapy (taxol and cisplatinum-combined treatement) [1-3].

We present a retrospective study of 12 patients with primary fallopian tube cancer that were treated in our department from 1993 to 2003.

Materials and Methods

This retrospective study was undertaken at the Gynecology-Oncology Unit of the 2nd Department of Obstetrics and Gynecology of the University of Athens in Aretaieion Hospital between January 1993 and January 2003. During this period 12 patients with primary fallopian tube cancer were diagnosed and treated in our department. All cases were diagnosed at operation or after intraoperative histological examination. Preoperatively most of these tumors presented as benign pelvic disease or (most often) as primary ovarian neoplasms. The median age of the patients was 59 years (range 42-78).

For the histological part of this study, all specimens received in the Pathology Department were fixed in buffered formalin solution. Multiple sections were examined after routine procession and hematoxylin-eosin (H-E) staining. The morphology of the cancer, the degree of differentation and the local extension were described.

Primary tumors were classified as tumors lying mainly in the tube, arising from the endosalpinx. This was confirmed by the presence of intraepithelian development of the tumor. The ovaries were normal or involved partially, but the neoplasm was focal in the cortex.

Patients were studied for clinical stage, parity, symptomatology, histology, kind of treatment and five-year relative survival.

Results

The distribution by stage at the time of diagnosis – according to the classification of fallopian tube cancer by the FIGO Committee of Gynecologic Oncology – was as follows:

- four patients had Stage I tumor (33.3%)
- four patients had Stage II tumor (33.3%)
- three patients had Stage III tumor (25%) and
- one patient had Stage IV tumor (8.3%).

Eight out of 12 patients (66%) were diagnosed with Stage I or II disease. Most women with this stage were treated with surgery alone and did not undergo surgical evaluation of the lymph nodes, while most women with Stage III or IV disease were treated with surgery (debulking operations) and chemotherapy.

The mean age of the women at presentation was 59; four patients (33.3%) were 50 or younger.

All cases with primary fallopian tube cancer were unrecorgnized pre-operatively. The most common clinical symptoms at admission were metrorrhagia in eight patients (66%), slight pelvic pain in nine patients (75%) and leukorrhea in four patients (33%). In 11 out of the 12

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cases (92%), after appraisal of these symptoms an ultrasound scan was performed which revealed a pelvic mass at the anatomic position of the adnexal region. In all these cases the mass was suspected to originate from the ovary and thus the first suspicion was an ovarian tumor. In the remaining case, the patient was found to have fibromyomas of the uterus without other symptoms and with a normal ultrasound scan but during laparotomy the intraoperative biopsy of a suspicious adnexal region was positive for cancer.

Although infertility, low parity or nulliparity have been incriminated as risk factors for the cause of tubal carcinoma, in our study only one patient was nulliparus and all the other women had two children or more.

The assessment of serum CA-125 preoperatively was positive in eight patients (58-850 IU/ml). In the other four patients the measurement of serum CA-125 levels showed a value below 30 IU/ml – all these cases were diagnosed with Stage I or II disease. Values of serum CA-125 in cases with Stage III or IV disease were significantly higher compared with levels of cases with Stage I or II disease. There is a trend for a positive correlation between levels of CA-125 and FIGO stage. Values before surgery were significantly higher compared with postoperative levels and CA-125 antigen should therefore be used in patient follow-up.

In all the cases of our study the initial therapy consisted of surgery followed, in some cases, by pelvic irradiation or adjuvant chemotherapy. In nine patients the tumor could be radically removed. The surgical method applied in 11 patients was removal of the uterus and the adnexa, and removal of the omentum or lymph nodes if necessary. In one case where the patient had undergone surgical treatment in another hospital a second operation for completion was performed (surgical debulking). After oncologic consultation four patients (all with Stage I disease) received no further treatment but remain under close oncological observation. Combined postoperative treatment with radiation and multi-chemotherapy (taxol and cisplatinum) was implemented in two cases. Postoperative treatment in six cases was poly-chemotherapy alone. Only one second-look procedure (secondary debulking) has been performed until now.

The histological type of the primary cancer in all patients of our study was primary adenocarcinoma of the fallopian tube with papillary features.

Discussion

The cause of tubal carcinomas is obscure and only a few risk factors are known. Age is an important factor since 95% of all the cases are over 35 years and 80% are menopausal. Infertility, low parity or nulliparity, chronic inflammation and tubal endometriosis have been incriminated but without conclusive evidence or statistical support (in our study only one patient was nulliparus). The pathogenesis is obscure. Experimental animal models do not provide conclusive data [5-7]. The morphogenesis, growth kinetics and immunology are unknown. It is possible that the model of the known sequence from hyperplasia to invasive carcinoma operates, but no strict criteria for preinvasive cancer have been described [6, 7].

Chronic inflammation and hyperestrogenic states are known to induce simple or atypical hyperplasia of tubal mucosa. In situ carcinoma is usually recognized by cellular and nuclear atypia and mitotic activities. The usual locus of tubal carcinoma is the ampulla, it is uni or bilateral [8].

Nordin described the following gross patterns: nodular, papillary, infiltrate and massive [7]. The cancerous tube grossly may look normal in shape and size or present swelling, induration and a solid or solid-cystic tumorous mass.

Microscopically three types are described that correlate with histological grade:

Grade 1 (papillary);

Grade 2 (papillary- glandular);

Grade 3 (glandular- compact).

Tubal carcinoma resembles an ovarian tumor with the difference that it is often accompanied by abdominal pain which constitutes an early symptom (75% in our study). The result is that tubal cancer is detected in earlier stages than ovarian cancer but for some authors seems to have a worst prognosis, stage for stage [9-11].

In contrast Kosary and Trimble reported 416 cases with fallopian tube cancer and they compared survival to that of 9,032 women with epithelial ovarian cancer. Their findings estimated better survival, stage by stage, for women with fallopian tube cancinoma than for women with epithelial ovarian cancer. They also suggest that women with fallopian tube cancer should be treated in accordance with the same guidelines for surgical staging, debulking and adjuvant chemotherapy as for women with epithelial ovarian cancer [2].

In a review of the literature about treatment of fallopian tube cancer Takeshima and Hasumi estimated that aggressive cytoreductive surgery followed by chemotherapy and negative second-look laparotomy offer a possibility of long-term survival. They also suggested the need of a thorough evaluation of the lymph nodes at the time of surgery and the use of platinum-based chemotherapy for both early and advanced stages [3].

The CA-125 antigen is expressed in fallopian tube cancer and in our study we found a positive correlation between CA-125 levels and Figo stage. CA-125 should therefore be used in the diagnosis and follow-up of women with tubal cancer. The same results were reported by Rosen *et al.* in a study of preoperative and postoperative CA-125 serum levels in primary fallopian tube carcinoma [4].

Conclusion

Neoplasms of the fallopian tube are very uncommon and are often diagnosed at surgery or autopsy. Patients usually present with a pelvic mass but no abdominal or pelvic pain. Primary fallopian tube cancer should be con-

sidered in the differential diagnosis of any case of pelvic mass. Primary adenocarcinoma with papillary features is the most common histological type of primary fallopian tube cancer which has traditionally been managed and treated in the same manner as epithelial ovarian cancer: surgical debulking and adjuvant multichemotherapy (taxol and cisplatinum).

References

[1] Mertens H.J., Nap M., Leers M.P., Salemans T.H.: "Multiparameter flow cytometry in the diagnosis of a gynaecologic double tumor: a case report". *Virchows Arch.,* 2003, *442* (3), 294.

[2] Kosary C., Trimble E.L.: "Treatment and survival for women with Fallopian tube carcinoma: a population based study". *Gynecol. Oncol.*, 2002, *86* (2), 190.

[3] Takeshima N., Hashumi K.: "Treatment of fallopian tube cancer". *Arch. Gynecol. Obstet.,* 2000, *264* (1), 13.

[4] Rosen A.C., Klein M., Rosen H.R., Graf A.H. *et al.*: "Preoperative and postoperative CA-125 serum levels in primary fallopian tube carcinoma". *Arch. Gynecol. Obstet.,* 1994, *255* (2), 65.

[5] Rosen A., Klein M., Lahousen M., Graf A.H., Rainer A., Vavra N.: "Primary carcinoma of the fallopian tube, a retrospective analysis of 115 patients. The Austrial Cooperative study group for fallopian tube carcinoma". *Br. J. Ca.,* 1993, *68,* 605.

[6] Wheeler J.E.: "Diseases of the fallopian tube". In: Kurman R.J. (ed.). Blaustein's Pathology of the Female Genital Tract. 5th ed. New York, Springer, Vergal, 2002, 529.

[7] Nordin A.J.: "Primary carcinoma of the fallopian tube: a 20 year literature review". *Obstet. Gynecol.*, 1984, *148,* 1057.

[8] Cornio G., Maneo A., Gabriele A., Rota S.M., Lissone A., Zanatta G.: "Primary carcinoma of the fallopian tube. A retrospective analysis of 47 patients". *Ann. Oncol.,* 1996, *7,* 271.

[9] Baekelandt M., Kockx M., Wesling F., Gerris J.: "Primary adenocarcinoma of the fallopian tube. Review of the literature". *Int. J. Gynecol. Cancer,* 1993, *3*, 65.

[10] Kosary C.R.: "FIGO stage, histology, histologic grade, age and race as prognostic factors in determining survival for cancers of the female gynecological system". *Semin. Surg. Oncol.,* 1994, *10,* 31.

[11] Scully R.E., Young R.H., Clement P.B.: "Tumors of the ovary, maldeveloped gonads, fallopian tube and broad ligament". AFIP (Atlas of Tumor Pathology) series 3, fasc. 23, Washington DC 1998, 481.

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