RESEARCH COMMUNICATION

Clinicopathological Features and Prognosis of Thai Women with Endometrioisis-Associated Ovarian Carcinoma

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Abstract

This study was undertaken to evaluate the clinical features and survival outcomes of ovarian cancer patients who had associated pelvic endometrioisis. The medical records of 1076 patients with ovarian cancer treated at Chiang Mai University Hospital between 1995 and 2005 were reviewed. Among of these patients, 37 (3.4%) had associated pelvic endometriosis. The mean age of the patients was 44 years (25-62 years). The most common presenting sign and symptom was an abdominal mass (12), followed by abdominal pain (10), abdominal distension (7), abnormal uterine bleeding (2). Twenty-one (56.8%) patients were nulliparous and 14 (37.8%) were single. The stage distribution was stage I (24), stage II (4), stage III (4), and stage IV (1). Four patients had 2 primary carcinomas. The most common histology of the 37 patients was clear cell carcinoma (17) followed by endometrioid carcinoma (11). The estimated 5-year disease - free survival was 55.4%. In conclusion, most patients associated with endometriosis-associated ovarian carcinoma present with abdominal masses and pain. Clear cell CA is the most common histology in ovarian cancer patients who have associated endometriosis. Three fourths of the patients are in stage I and have favorable prognosis.

Key Words: Endomeriosis - ovarian carcinoma - survival - histology

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Introduction

Endometriosis is defined as the implantation of endometrium-like glandular and stromal cells outside the uterine cavity mainly in the pelvis. The prevalence of pelvic endometriosis approached 6-10% in the general female population and more frequent as 35-50% in infertile patients (Sensky et al.,1980, Houston et al., 1984, Cramer et al., 1987). The ovaries are the most common anatomical location for endometriosis (Jenkins et al., 1986). Although this disease is generally benign condition, its demonstrated some characteristics suggestive of malignancy, such as development of local and distant foci and attachment to and invasion of other tissue with subsequent damage of the target organs (Garry R.,2001). There is increasing awareness that malignant transformation of endometriosis is a distinct entity since 1925. Sampson has first proposed the criteria used to identify malignant tumors arising from endometriosis. The criteria included : 1) clear evidence of endometriosis close to the tumor, 2) the carcinoma must be seen to arise in endometriosis, and not to be invading it from some other sources, 3) presence of tissue resembling endometrial stromal surrounding characteristic glands (Sampson et al.,1925). After that time, there was a number of studies that described malignancy arising in both gonadal and extragonadal endometrial implants (Brooks et al., 1977, Heaps et al., 1990, Moll et al.,1990) . The pathogenesis of ovarian cancer related to ovarian endometriosis is not well known and different hypotheses have been put forward. One of these theories includes retrograde menstruation and the development of endometriosis as the origin of ovarian cancer. If a malignant change can occur in uterine endometrium, it is possible that the same might occur in ectopic endometrium or endometriosis of the ovary or elsewhere in the pelvis (Van Gorp et al.,2004). However, the relation of ovarian cancer and endometriosis in our region is still limited. This retrospective study was undertaken to evaluate the clinicopathologic features and prognosis of ovarian cancer patients who had evidence of pelvic endometriosis.

Materials and Methods

Following Research Ethics Committee approval, the medical records of ovarian cancer patients who had histological evidence of endometriosis treated at Chiang Mai University Hospital between January 1996 and December 2005 were reviewed. We also included the patients whose previous surgery showed endometriosis. All available slides of these patients were reviewed by our co-author (S.K).

Patients were followed regularly after completion of treatment, with a minimal follow – up time of 3 months (3-105, median 18 months). During follow-up, progression of

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disease was defined either by physical examination and imaging study showing re-growth of tumor.

The following data were extracted by chart reviewed, i.e. demographic data, presenting symptom, use of contraception, previous gynecologic surgery, histology, stage, details of adjuvant postoperative therapy, recurrent status and disease free survival that was defined as the interval from date of primary surgery until the date of recurrence or tumor progression.

Statistical analysis of the data was carried out by the SPSS for Window program (version 10.0). Disease- free survival was estimated by the Kaplan-Meier method.

Results

During the study period, there were 1,076 ovarian cancer patients. Of these patients, 37 (3.4%) had tumors associated with endometriosis. The demographic data of these patients are showed in Table I. The mean age was 44 years with a range of 25-62 years. The most common presenting symptom was abdominal mass followed by abdominal pain. Twenty-one (56%) patients were nulliparous and 24 (65%) no contraceptive used. Fourteen patients (37.8%) were single. The majority of these patients were in stage I. Three patients had two primary carcinomas comprising synchronous ovarian and endometrial cancers. Synchronous stage IA endometrioid carcinoma of the ovary and stage IB endometrial cancer was noted in 1 patient, the remaining 2 were stage IB endometrioid ovarian cancer with stage IB endometrial cancer and stage IA endometrioid ovarian cancer with stage IIB endometrial cancer each.

Concerning the histology, the pathology slides were available for reviewing in only 15 patients (40.5%). Clear cell adenocarcinoma appeared to be the most common histology (45.9%) followed by endometrioid carcinoma (29.7%). Tumors arising from endometriosis were identified in 24 patients (64.9%). The endometriosis was found in the pelvic region in 10 (27%). Only 2 had endometriosis in the contralateral ovary and 1 patient did not have endometric lesions when subsequently developing ovarian cancer. This patient underwent right salpingo-ophorectomy 8 years previously for ovarian endometrioma before developing IC of clear cell carcinoma in the left ovary.

Two patients revealed uncommon pathologic lesion associated with endometriosis, one case was diagnosed as stage IC squamous cell carcinoma (grade 2) of the ovary arising from endometriosis. She was 52 year-old and presented with abdominal pain. The operative findings showed rupture of the left ovarian tumor. After radical surgery, she was treated with cisplatin and 5- fluorouracil chemotherapy. The other one was diagnosed as stage II immature teratoma (grade 2), the endometriotic lesion was also detected in her pelvis. She received combination chemotherapy consisting bleomycin, etoposide and cisplatin. Both of them were lost to follow up after 1 cycle of chemotherapy.

The majority of patients received chemotherapy after definite surgery. The most common regimen was carboplatin and paclitaxel (PT) (51.3%) followed by cisplatin and cyclophosphamide regimen (21%). Three patients received second line chemotherapy after resistant to PT regimen.

Table1. Clinicopathological Features

Presenting symptoms	Abdominal mass	12 (32.4%)
	Abdominal pain	10 (27.0%)
	Abdominal distension	7 (18.9%)
	Abnormal uterine bleeding	3 (8.1%)
	Others	5 (13.5%)
Stage	I	24 (64.9%)
	II	4 (10.8%)
	III#	5 (13.6%)
	IV	1 (2.7%)
	2 primaries	3 (8.1%)
Histology	Clear cell	17 (45.9%)
	Endometrioid CA	11 (29.7%)
	Serous cystadenocarc	1 (2.7%)
	Immature teratoma	1 (2.7%)
	Mucinous cystadenocarc	1 (2.7%)
	Borderline endometrioid CA	1 (2.7%)
	Squamous cell CA	1 (2.7%)
	Mixed type	4 (10.8%)
Adjuvant treatment	None	3 (8.1%)
	PT	19 (51.3%)
	PC	8 (21.6%)
	Single carboplatin	3 (8.1%)
	Cisplatin & 5FU	1 (2.7%)
	BEP	1 (2.7%)
	Radiation	2 (5.4%)
Mean course of chemotherapy (range)		5(1-8 courses)

1 case was primary peritoneal carcinoma PT = carboplatin and paclitaxel, PC = cisplatin and cyclophosphamide, BEP = bleomycin, etoposide, cisplatin

The estimated 5-year disease-free survival of the ovarian cancer patients who had associated endometriosis was 55.4%, with a mean follow up time of 73 months (3-117 months) as shown in Figure 1.

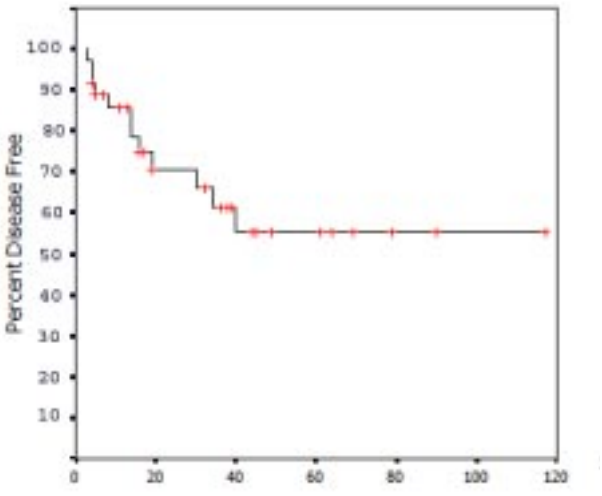

Figure 1. Disease- free Survival of the 37 Patients with Endometriosis-associated Ovarian Carcinomas

Discussion

The incidence of associated endometriosis in patients with ovarian cancer in the present study was 3.4%, which was lower than those reported in the literature which were in the range of 4-29% (Aure et al.,1971, Vercellini et al., 1993, Ogawa et al., 2000). The differences in the incidence of endometriosis concomitantly present with ovarian cancer depend on the number of pathology slides per case and the thoroughness of pathologic examination. The highest incidence was from the study of Ogawa et al (2000). The mean number of slides per case examined in their study was as high as 15.6. Whereas in our retrospective study, only 40% of the patients were operated at our institute and the pathologic specimens could be reviewed or re-cut. This limitation underestimated the incidence of such association.

The most common histology in our study was clear cell carcinoma followed by endometrioid carcinoma, as in previous reports (Aure et al.,1971, Vercellini et al., 1993, Ogawa et al., 2000). The majority of patients had early stage of disease, again in line with ovarian cancer patients with associated endometriosis tending to be diagnosed at earlier stage (Erzen et al., 2001).

Two rare tumors were found in our study. One was squamous cell carcinoma of ovary arising from endometriosis. This event is extremely uncommon. Pins et al (1996) reported a large series of 37 patients with primary ovarian squamous cell carcinoma. Only 7 were associated with endometriosis. The mean age of these 7 patients was 49 years old with a range of 29-70 years old. The distribution by stage was 1 in stage I, 3 in stage II, 1 in stage III and 2 in stage IV. All tumor were grade 3. When compared the prognosis with the patient who had squamous cell carcinoma of ovary without endometriosis, those who had associated endometriosis had worse overall survival. In our study, such patient was in stage IC and the prognosis could not be evaluated because she was lost to follow up. One patient had immature teratoma with endometriosis in her pelvis. There is no report on this association in the literature.

Several epidemiological studies reported the increased risk of ovarian cancer in patients who had endometriosis with odds ratio of 0.78-1.73 (Brinton et al., 1997, Ness et al., 2002,Olson et al., 2002). In our study, six patients had previously diagnosed endometriosis. These patients developed ovarian cancer later with a range of 5 months to 11 years after the diagnosis of endometriosis. The final pathology revealed tumor arising from endometriotic lesions in only one case. This minimal occurrence might be underestimated because the tumor may obliterate the tissue of origin and eliminate the histological evidence of endometriosis.

The prognosis of patients who had ovarian cancer with endometriosis in our study was better than that in the previous report (Komiyama et al., 1999). This was due to the younger age and the earlier diagnosis of the patients.

In conclusion, ovarian cancer associated with endometriosis is uncommon. Most patients present with abdominal mass and abdominal pain. The most common pathology was clear cell carcinoma followed by endometrioid carcinoma. Three fourths of the patients are in stage I. Patients with such tumors appear to have a favorable survival outcome.

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