Primary Carcinoma of the Fallopian Tube: A Clinicopathologic Analysis of 27 Patients

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Objectives: *To analyze the clinicopathologic features of women with primary fallopian tube carcinoma.*
Design: *Descriptive cross sectional study*
Material and Method: *Twenty-eight women diagnosed with primary fallopian tube carcinoma treated at Chiang Mai University Hospital between January 1997 and December 2004.*
Results: *During the study period, the primary fallopian tube carcinoma accounted for 0.48% of all gynecologic malignancies. Of the 28 patients, one was excluded for unavailable medical records. Mean age at diagnosis was 53 years (range, 38-76 years). Seventeen (63.0%) were menopausal women. The most common clinical presentation was pelvic mass (55%), followed by abnormal vaginal bleeding (18.5%). Hydrops tubae profluens was present in three (11.1%) women. The rare presenting symptoms included pelvic peritonitis and abnormal glandular cells on cervicovaginal smear were noted in one (3.7%) woman of each category. In all women, primary fallopian tube carcinoma could not be diagnosed preoperatively. During the operation, an abnormal tubal lesion was suspected in only eleven (40.7%) women. Histology were serous adenocarcinoma (70.4%), endometrioid adenocarcinoma (22.2%), undifferentiated adenocarcinoma (3.7%) and carcinosarcoma (3.7%). As opposed to epithelial ovarian cancer, the majority of women in the present study were in the early stages of the disease.*
Conclusion: *Primary fallopian tube carcinoma is a rare gynecologic malignancy that has various and nonspecific presentations. Definite diagnosis is usually made postoperatively. This malignancy should be considered in differential diagnosis of peri- and postmenopausal women who present with complex adnexal mass, unexplained uterine bleeding, abnormal glandular cells on cervicovaginal smear and complicated pelvic inflammatory disease.*

Keywords: *Fallopian tube carcinoma, Characteristics, Hydrops tubae profluens*

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Primary carcinoma of the fallopian tube is one of the rarest malignant tumors, accounting for 0.3-0.8% of all gynecologic malignancies[1]. This malignant tumor resembles epithelial ovarian cancer in its clinical behavior and response to treatment. Thus, management is generally similar to that of epithelial ovarian cancer, i.e. cytoreductive surgery followed by combination chemotherapy preferably platinum compound-based regimen[2]. Because of the rarity of this disease and the low level of suspicion by the attending physicians, diagnosis of this cancer is not made preoperatively. The syndrome of "hydrops tubae profluens" in which a patient presents with a pelvic mass, profuse watery vaginal discharge, and pelvic pain that is greatly relieved by the sudden disappearance of the mass is rarely encountered but is almost pathognomonic. The aim of the present study was to analyze the clinicopathologic features of women diagnosed with primary fallopian tube carcinoma in a single institute. The atypical presenting symptoms of patients with this tumor were also described.

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Material and Method

Between January 1, 1997 and December 31, 2004, twenty-eight women with primary fallopian tube carcinoma were identified from the statistical report of the Gynecologic Oncology Division, Chiang Mai University Hospital. The age at diagnosis, presenting signs and symptoms, menopausal status, preoperative diagnosis, stage, postoperative histopathologic features and tumor grade were analyzed. Surgical staging and cytologic grading were assessed using the modification of the International Federation of Gynecology and Obstetrics (FIGO) nomenclature of epithelial ovarian cancer[3]. Optimal (≤ 1 cm) and suboptimal (> 1 cm) residual disease was defined according to the criteria of the Gynecologic Oncology Group (GOG)[4].

Results

During the study peroid, 5872 malignancies of the female genital tract were diagnosed including 28 women with primary fallopian tube carcinoma which accounted for 0.48%. One was excluded as the medical record was unavailable. Accordingly, 27 women were available for study. The mean age at diagnosis was 53 years (range, 38-76 years). Of the 27 women with primary fallopian tube carcinoma, 17 (63.0%) and 10 (37.0%) were postmenopausal and premenopausal women, respectively. Seventeen (63.0%) were parous, 10 (37.0%) were nulliparous and 7 of these had a history of primary infertility.

Clinicopathologic features of the 27 patients are shown in Table 1. Most of the patients presented with a pelvic mass followed by abnormal vaginal bleeding, excessive vaginal discharge, and nonspecific pelvic pain. Three women presenting with excessive vaginal discharge also had occasional pelvic pain and adnexal mass on pelvic examination which are generally called "hydrops tubae profluens". Twenty one (77.8%) patients were given the diagnosis of ovarian cancer preoperatively. One patient, endometrioid carcinoma of the fallopian tube was incidentally found during radical hysterectomy for cervical cancer. No patient was diagnosed with primary fallopian tube carcinoma preoperatively. Cytologic grading were well differentiation in 2 (7.4%) patients, moderate differentiation in 6 (22.2%), poor or undifferentiation in 18 (66.7%) patients, and unknown grading in 1 (3.7%) patient. At the time of initial operation, abnormal gross appearance of the fallopian tube including, hydrosalpinx, hematosalpinx, pyosalpinx and tubal mass were observed in only 11 (40.7%) patients and 10 of these were in the early stage of disease.

Table 1. Clinicopathologic features of the 27 women with primary fallopian tube carcinoma

Characteristics	Number (%)
Presenting signs and symptoms	
Pelvic mass	15 (55.5)
Abnormal vaginal bleeding	5 (18.5)
Excessive vaginal discharge	3 (11.1)
Nonspecific pelvic pain	2 (7.4)
Abnormal Pap smear	1 (3.7)
Pelvic inflammatory disease	1 (3.7)
Preoperative diagnosis	
Ovarian cancer	21 (77.8)
Endometrial cancer	2 (7.4)
Uterine leiomyoma	2 (7.4)
Cervical cancer	1 (3.7)
Tubo-ovarian abscess	1 (3.7)
FIGO stages	
I	7 (25.9)
II	12 (44.4)
III	7 (25.9)
IV	1 (3.7)
Histologic subtypes	
Serous adenocarcinoma	19 (70.4)
Endometrioid adenocarcinoma	6 (22.2)
Undifferentiated adenocarcinoma	1 (3.7)
Carcinosarcoma	1 (3.7)

Approximately 70% of the patients were in stage I and II of tubal cancer. Among 19 women with Stage I and II diseases, only 7(38.9%) underwent complete surgical staging procedure. Of the 12 remaining patients, 6 underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy, 4 underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy with infracolic omentectomy, and 2 underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy with peritoneal washing cytology. Cytoreductive surgery was preformed in 8 women with advanced stage of the disease. Only 3 (37.5%) of these patients had optimal residual tumor.

Discussion

Primary carcinoma of the fallopian tube is an uncommon gynecologic malignancy accounting for only 0.3-0.8% of all female genital cancer[1]. Carcinoma of the fallopian tube is generally recognized as a disease of menopausal women[3]. In the present study, 63% of the patients were in menopausal status. The

etiology of fallopian tube cancer is still unclear. Some factors have been postulated to increase the risk of this cancer, i.e. infertility, chronic tubal inflammation, endometriosis, nulliparity, smoking and genetic predisposition[5,6]. Ten (37%) of 27 patients in the present study were nulliparous and 7 of these had primary infertile problems. One woman had a history of treatment for complicated pelvic inflammatory disease. Because of the relative small number of patients in the present study,the authors could not solidly confirm the etiologic role of these factors in the development of primary fallopian tube cancer.

The most frequent presenting signs and symptoms of patients in the current study were pelvic mass followed by abnormal vaginal bleeding, excessive vaginal discharge, and nonspecific pelvic pain which were in accordance with previous studies[1,7,8]. Whereas, the most characteristic presentation of fallopian tube cancer including profuse watery vaginal discharge, colicky lower abdominal pain, and pelvic mass, the so called "hydrops tubae profluens" were encountered in only 3 (11%) patients in the present study. These findings were consistent with previous studies which reported that the full range of this symptom complex was infrequently encountered in women with this malignancy[5,7-10].

Although pelvic pain is frequently observed in women with fallopian tube carcinoma, this tumor is rarely recognized in the differential diagnosis of pelvic peritonitis. Recently, there has been a report of successful diagnosis of fallopian tube carcinoma by ultrasonography in 4 women who presented with clinical symptoms of acute adnexitis[7]. Romagosa et al also described 2 menopausal women whose examination revealed pelvic peritonitis and were unresponsive to medical treatment. Hysterectomy with bilateral adnexectomy in both patients showed poorly differentiated adenocarcinoma of the fallopian tube and were in FIGO stage IIC[11]. In the present study, one woman aged 42 years underwent total abdominal hysterectomy and bilateral adnexectomy for tubo-ovarian abscess. The right fallopian tube was markly dilated with serosanguinous content. All pelvic organs were inflamed with purulent reactions. The histology showed moderately differentiated serous adenocarcinoma of the fallopian tube consistent with FIGO stage IIC. Thus, carcinoma of the fallopian tube should be suspected in women with pelvic peritonitis with tubal pathology and were unresponsive to medical treatment.

Abnormal cervicovaginal cytology had been reported as an atypical presentation of primary fallopian tube carcinoma[10,12,13]. One patient aged 60 years in the present study presented with adenocarcinoma on Pap smear. She was referred to our hospital after cervical conization and endometrial curettage which revealed chronic cervicitis and no endometrial tissue. The review of all cytopathology slides showed serous subtype of the abnormal cell on Pap smear. A repeat endometrial curettage demonstrated endocervical polyps and scant endometrial tissue. A computed tomography of the whole abdomen showed only small calcified subserous uterine leiomyoma. After careful counselling, she agreed to undergo total abdominal hysterectomy and bilateral salpingo-oophorectomy because endometrial cancer could not be ruled out. A 1.5 cm - polypoid mass at the junction of uterine cornu and right fallopian tube was detected.A small calcified subserous uterine leiomyoma was also noted. Histologic examination revealed moderately differentiated serous adenocarcinoma of the right fallopian tube consistent with FIGO stage IIA. Likewise, primary fallopian tube carcinoma should be considered in differential diagnosis of women having abnormal glandular cells on cervicovaginal smear especially in the case of no significant cervical and endometrial pathology.

Of the 5 patients with abnormal vaginal bleeding, one presented with perimenopausal bleeding on and off for 1 year. Fractional curettage revealed scant secretory endometrium. She still experienced multiple episodes of recurrent uterine bleeding which did not respond to hormonal therapy. Total abdominal hysterectomy and bilateral salpingo-oophorectomy was carried out with a preoperative diagnosis of recurrent dysfunctional uterine bleeding. Hematosalpinx with cauliflower mass at the distal part of the left fallopian tube was detected. Histology showed poorly differentiated papillary serous adenocarcinoma consistent with FIGO stage IA. Thus, women with perimenopausal uterine bleeding who do not respond to hormonal therapy should be intensively investigated for possible fallopian tube carcinoma.

Some atypical presentations of women with primary fallopian tube carcinoma included supraclavicular lymph node involvement of tumor metastasis, secondary infertility and coexisting with tuberculous salpingitis[8,12-15]. Coxistence of breast cancer has been reported as high as 35% of women with fallopian tube carcinoma in a study of Slanetz et al[16]. This uncommon feature might reflect the genetic predisposition of this malignancy.

Preoperative diagnosis of primary fallopian tube carcinoma is difficult due to the rarity of the dis-

ease, the lack of specific findings and silent natural course. The majority of women in the present study were operated on with the preoperative diagnosis of malignant ovarian tumor. These findings were similar to the reports of Piura et al[8] and Inal et al[17] which also failed to achieve a correct preoperative diagnosis of primary fallopian tube carcinoma in all cases. However, there are several studies on the successful preoperative diagnosis of primary fallopian tube carcinoma using various imaging methods[7,13,18,19]. The largest series by Kurjak et al reported the successful preoperative diagnosis of fallopian tube carcinoma using trans - vaginal color and pulsed Doppler ultrasonography. They suggested that a low vascular resistance index obtained within the tubal wall was a predictor of fallopian tube carcinoma[7]. In another study by Kurjak et al, a three - dimensional transvaginal ultrasonography was superior to the two - dimensional one which revealed more distinct delineation of tubal wall irregularity due to small papillary projection[19].

An additional interesting finding in the present series was that ten (52.6%) of 19 women with early stage primary fallopian tube carcinoma had obviously abnormal fallopian tube during the surgery while only one (12.5%) of 8 women with advanced stage of disease had. These findings have demonstrated that the accurate diagnosis of primary fallopian tube carcinoma is still difficult even at the time of operation especially in advanced disease.

Available studies have shown that primary fallopian tube and ovarian carcinoma behave clinically in a similar pattern, management scheme of ovarian carcinoma has accordingly been applied in primary fallopian tube carcinoma[2]. However, there is a distinct difference between these two gynecologic malignancies. While approximately 2/3 of ovarian carcinoma are generally in the advanced stage of disease (stage III and IV), 2/3 of primary fallopian tube carcinoma are in the early stage (stage I and II)[3,2,20]. This finding was also noted in the present study in which 19 (70.4%) women were in the early stage of the disease. A comparable lower incidence of advanced stage is seen in women with primary fallopian tube carcinoma than those with ovarian carcinoma,which may be theoretically explained by two possible reasons. First, women with primary fallopian tube carcinoma, symptoms such as abnormal vaginal bleeding and/or vaginal discharge occur fairly early, enabling these women to be earlier diagnosed and treated. Second, advanced disease of primary fallopian tube carcinoma may be misdiagnosed as advanced ovarian carcinoma because of an identical histological picture and spreading pattern.

In accordance with previous publications[1,3,5,7,8,16,21], the authors observed that the most prevailing histology subtype was serous adenocarcinoma (70.4%), followed by endometrioid adenocarcinoma (22.2%). Undifferentiated carcinoma and carcinosarcoma were noted in 3.7% of each subtypes.

In conclusion, primary fallopian tube carcinoma is a challenge to the gynecologist. The diagnosis is very difficult in both pre- and intraoperative periods because of absence of a specific finding and silent natural course. Although a rare entity of disease was observed, the authors emphasize that primary fallopian tube carcinoma should be considered in the differential diagnosis in perimenopausal women with an adnexal mass, unexplained uterine bleeding, abnormal glandular lesions on cervicovaginal smears, complicated pelvic inflammatory disease and persistent profuse vaginal discharge especially when searching for the common primary etiology proves unrevealing.

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มะเร็งท่อนำไข่ชนิดปฐมภูมิ: ลักษณะทางคลินิกและพยาธิวิทยาในผู้ป่วย 27 ราย

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วัตถุประสงค์: *ศึกษาถึงลักษณะทางคลินิกและพยาธิวิทยาของผู้ป่วยมะเร็งท่อนำไข่ชนิดปฐมภูมิ*

รูปแบบการศึกษา: *การศึกษาเชิงพรรณนาแบบตัดขวาง*

วัสดุและวิธีการ: *ผู้ป่วยมะเร็งท่อนำไข่ชนิดปฐมภูมิที่มารับการรักษาที่โรงพยาบาลมหาราชนครเชียงใหม่ ระหว่างเดือนมกราคม พ.ศ. 2540 ถึง เดือนธันวาคม พ.ศ. 2547 จำนวน 27 ราย*

ผลการศึกษา: *ในช่วงที่ทำการศึกษา พบผู้ป่วยมะเร็งท่อนำไข่ชนิดปฐมภูมิทั้งสิ้น 28 ราย คิดเป็นร้อยละ 0.48 ของผู้ป่วยมะเร็งนรีเวชทั้งหมด ผู้ป่วย 1 รายถูกคัดออกจากการศึกษาเนื่องจากเวชระเบียนสูญหาย อายุเฉลี่ยขณะที่ได้รับการวินิจฉัยเท่ากับ 53 ปี ร้อยละ 63 เป็นสตรีที่หมดประจำเดือนแล้ว อาการแสดงที่พบมากที่สุดได้แก่ ก้อนในอุ้งเชิงกรานโดยพบร้อยละ 55 ของผู้ป่วย รองลงมาได้แก่ เลือดออกผิดปกติทางช่องคลอดพบร้อยละ 18.5 ของผู้ป่วย ส่วน hydrop tubae profluens พบเพียงร้อยละ 11.1 ของผู้ป่วยเท่านั้น ผู้ป่วยทั้งหมดได้รับการวินิจฉัยมะเร็งท่อนำไข่ชนิดปฐมภูมิภายหลังการผ่าตัดโดยมีเพียงร้อยละ 40.7ที่พบความผิดปกติของท่อนำไข่ในระหว่างการผ่าตัด ชนิดของมะเร็งท่อนำไข่ชนิดปฐมภูมิที่พบมากที่สุดได้แก่ serous adenocarcinoma พบร้อยละ 70.4 endometrioid adenocarcinoma พบร้อยละ 22.2 undifferentiated adenocarcinma และ carcinosarcoma พบร้อยละ 3.7 ของผู้ป่วยตามลำดับ ผู้ป่วยร้อยละ 70.3 อยู่ในระยะที่ 1 และ 2 ตามเกณฑ์ที่กำหนดโดยสหพันธ์สูติศาสตร์และนรีเวชวิทยานานาชาติ*

สรุป: *มะเร็งท่อนำไข่ชนิดปฐมภูมิเป็นมะเร็งทางนรีเวชที่พบได้น้อยมากและมีอาการแสดงที่หลากหลาย ไม่จำเพาะ ส่วนมากจะวินิจฉัยได้ภายหลังการผ่าตัด มะเร็งท่อนำไข่ชนิดปฐมภูมิควรอยู่ในการวินิจฉัยแยกโรคในสตรีวัยกำลังหมดประจำเดือนหรือหมดประจำเดือนแล้วที่มาด้วย ก้อนในอุ้งเชิงกราน เลือดออกผิดปกติจากโพรงมดลูกที่ไม่ทราบสาเหตุ การพบความผิดปกติของเซลล์เยื่อบุต่อมจากการทดสอบแพปและการอักเสบในอุ้งเชิงกรานที่ไม่ตอบสนองต่อการรักษามาตรฐาน*