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Original Article

Distribution of gynecologic malignancies in an epidemiologic study from southeast of Turkey

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Abstract. Retrospective evaluation of 105 patients with gynecologic malignancy. One hundred and five patients with gynecologic malignancies diagnosed at Obstetrics and Gynecology Clinics of Medical School, Dicle University, Diyarbakir, between 2001 and 2005 were analyzed retrospectively. Gynecologic malignancies were classified. Distribution of 105 patients with gynecologic malignancies were; cervical cancer 19.04 % , endometrial cancer 21.90 %, uterine sarcoma 10.47%, primary ovarian cancer 40.95%, metastatic ovarian cancer 5.71%, carcinoma of the fallopian tubes 0.95%, choriocarcinoma 0.95%. 17 of 20 (85 %) patients with invasive cervical cancer were in stage≤IIa. Endometrioid cancer was the predominant (86.95%) histologic type in 23 patients with endometrial cancer. Leiomyosarcoma was the most frequent (72.72%) histologic type in 11 patients with uterine sarcoma. 33 of 43 patients (76.74%) with ovarian cancer had epithelial type carcinoma. Six patients had metastatic ovarian cancer and 4 patients (66.66%) in this group had Krukenberg tumors (signet-ring cells), 1 patient had primary tubal adenocarcinoma and 1 patient had choriocarcinoma. Ovarian cancer was the most frequent gynecologic malignancy in our study.

Key words: Gynecologic malignancy, epidemiology

1. Introduction

Epidemiology is science of searching causes of disorders by using frequencies and distributions (1). Epidemiologic studies are carried out to determine frequencies and distributions of diseases, to reveal out causes and try to establish appropriate therapy. Gynecologic cancers are malignancies of female genital tract. Uterus (cervix, corpus) and ovarian cancers are the leading types of gynecologic cancers. Vulvo-vagina, fallopian tubes cancers and chorion epithelioma are less frequent sites for female genital malignancies (2). Worldwide incidence and mortality rates (per 100.000) of gynecological cancers are respectively as follows: cervical cancer 16.1 and 7.99, endometrial cancer 6.4 and 1.5, ovary and other gynecological cancers 6.5 and 3.8 (3). Gynecological cancers accounts for 1/3 of entire female malignancies (3). Prompt diagnosis and appropriate therapy plays a crucial role in the course of gynecological cancers. Annually, more than 370.000 cases of cervical cancer are diagnosed worldwide and approximately 190.000 cases die (4). Abnormal vaginal bleeding is the most frequent symptom of cervical cancer. Cervical cancer is considered to be a preventable cancer as a result of widespread use of cervical screening programs and effective treatment of preinvasive lesions. Generally endometrial cancer is supposed to be a treatable disease due to earlier diagnosis prior to extrauterine metastases in majority of cases. Ovarian cancer has the highest mortality rate; frequency of disorder increases in the postmenopausal period. Risk factors for ovarian cancer are advanced age, nulliparity and family history. Most frequent symptoms of early stage ovarian cancer are abdominal distention, pain, dyspepsia, polyuria and constipation. Majority of symptoms are nonspesific. Abdominal distention, weakness and weight loss are dominantly observed in advanced stage ovarian cancer. Uterine sarcomas are malign tumors originated

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from mesodermal cells and they are extremely infrequent malignancies. Early detection and advances in treatment of gynecologic malignancies have improved survival rates of patients (5).

Our aim is to present a detailed retrospective evaluation of 105 patients with gynecologic cancers that were diagnosed in our clinics.

2. Materials and methods

One hundred and five patients with newly diagnosed gynecologic cancers in Obstetrics and Gynecology Clinics of Medical School, Dicle University, Diyarbakir, Southeast Region of Turkey, between 2001 and 2005 were analyzed retrospectively. Gynecologic malignancies were classified. Physical examinaton (inspection-palpation), biopsy; when necessary, cystoscopy-rectoscopy, and radiologic evaluation were used for examination of patients with cervical cancer. Peritoneal washing fluid was obtained by saline solution during laparotomy. Radical hysterectomy and pelvic-paraaortic lymphadenectomy were performed for patients with cervical cancer in stage I and IIa. Radiotherapy was given to patients with vascular invasion beside pelvic lymph node metastasis and deep cervical invasion and to patients in clinical stage ≥IIb. Diagnosis of endometrial cancer was confirmed by fractional curettage, endometrial sampling by pipelle in patients with abnormal or postmenopausal bleeding. Peritoneal washing fluid was obtained by saline solution during laparotomy. Total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO) and pelvic-paraaortic lymph node dissection were carried out. Radical hysterectomy was performed for patients with cervical stromal invasion. Frozen section was obtained for patients in stage I and occult stage II. Surgical staging was practised by complete pelvic and paraaortic lymphadenectomy for patients with myometrial invasion more than 50% and cervical involvement. Selective pelvic and paraaortic lymphadenectomy were performed for patients with superficial endometrial invasion or grade I myometrial penetration less than 50% and grade II tumors smaller than 2 cm. Postoperative radiotherapy was given to patients in stage I, grade II or III and myometrial invasion more than 50% or extrauterine involvement with evident lymph node invasion. Surgical staging and therapeutic approaches of uterine sarcomas were similar to that of endometrial cancers. Premenopausal patients with a cystic mass larger than 8 cm detected in pelvic examination and ultrasound (US) or persisting solid and semisolid masses, and postmenopausal patients with adnexal masses were prepared for laparotomy. Median incision was applied for intraabdominal accessing, intraabdominal fluid was used for cytologic examination and in the absence of free intraabdominal fluid, peritoneal washing was performed. Cytoreductive surgery was preferred for the removal of tumor and metastasis in advanced stage ovarian cancers. It was aimed to achieve macroscopic residue of 1 cm or less. Unilateral oophorectomy and contralateral ovarian biopsy were performed for younger patients. When indicated, single or combined agent chemotherapy was instituted subsequent to surgical staging procedure. Patients were followed up by physical examination, measurement of CA–125, abdominal US, posteroanterior chest graphy and computerized tomography. Metastatic ovarian cancers originated from extragenital sites. Surgical procedure was applied. Therapeutic approach for the fallopian tubes cancer was similar to that of ovarian cancers. The patient with choriocarcinoma was 53 years old and she had children. That is why she underwent TAH, BSO and consequent methotrexate therapy.

3. Results

Distribution of 20 patients with invasive cervical cancer aged between 32–77 years according to staging were; 17 patients ≤ stage 2a. Histopathological distribution of 20 patients with cervical cancer were as follows: 17 patients (85%) had squamous cell carcinoma, 2 patients (10%) had adenocarcinoma and 1 patient (5%) had adenosarcoma. Table 1 points out the histopathologic types of invasive cervical cancer.

Table 1. Histopathologic types of invasive cervical cancer.

	Case (n)	Grade I	Grade II	Grade III
Squamous cell	3	1	1	1
Large cell keratinizing	11	3	7	1
Large cell nonkeratinizing	3	-	-	3
Small cell				
Adenocarcinoma	2	-	1	1
Adenosarcoma	1	-	-	1
Total	20	4	9	7

Surgical procedure was performed for 17 patients in stage I –IIa. Radiotherapy was given to 2 patients with vascular invasion beside pelvic lymph node metastasis and deep cervical invasion and to 3 patients in clinical stages IIb and IIIb.

23 patients with endometrial cancer were between 34–72 years old and 8 patients (34.78%) were in premenopausal and 15 patients (65.21%) were in postmenopausal period. A 34-year-old patient had a long-term history of polycystic ovary syndrome and anovulation. Histopathologic distribution of 23 patients were; endometrioid cancer 86.95%, indifferentiated cancer 8.69 % and adenosquamous cancer 4.34%. According to the surgical staging of 23 patients; 19 patients (82.60 %) were in stage I, 3 patients (13.04 %) were in stage II and 1 patient (4.34 %) was in stage IV. Table 2 shows the distribution of endometrial cancers according to surgical staging.

Table 2. Distribution of patients with endometrial cancers according to surgery staging.

Stage	Case(n)	Percent(%)
I	19	82.60
II	3	13.04
III	-	-
IV	1	4.34

Except 2 patients with febrile morbidity due to wound infection, no other complication was observed. Radiotherapy was given to patients with grade III tumor and 1/3 external myometrial invasion or cervical involvement and pelvic or parametric lymph node metastasis. Eleven patients with uterine sarcoma aged between 22–78 years. Distribution according to histopathologic types of cancers were as follows: leiomyosarcoma (72.72%), malign mixed Mullerian tumor (18.18%) and endometrial stromal sarcoma (ESS) (9.09%). Entire abdominal radiotherapy was given to a patient with peritoneal washing fluid positivity and peritoneal metastasis and to another patient with bladder and bowel serosal infiltration. 27 of 43 patients (62.79 %) with ovarian cancer aged between 12 and 73 years were in postmenopausal or perimenopausal period and the remaining of 16 patients (37.20 %) were in premenopausal period. The majority of patients (60%) were asymptomatic however 40% of patients had abdominal pain or distention. 26 patients (60.46 %) had CA–125 levels higher than 35 U/ml and 12 patients (27.90 %) had CA 19,9 levels higher than 33 U/ml. Histopathologic types of ovarian cancers were epithelial ovary cancer (76.74 %), malignant germ cell tumor (13.95%), and malignant sex cord stromal tumor (9.30%). Distribution according to stages were; stage I 51.16 %, stage II 18.60 %, stage III 25.58 % and stage IV 4.65 %. Distribution according to subtypes of epithelial ovarian cancer were; papillary serous cystadenocarcinoma 72.72 %, mucinous adenocancer 12.12 %, clear cell cancer 9.09 %, endometrioid cancer 3.03 % and undifferantiated cancer 3.03 %. Five patients had disgerminoma (83.33 %) and 1 patient had endodermal sinus tumor in germ cell malignant tumors group. 3 of 4 patients (75%) with sex cord stromal tumor had malignant granulosa cell tumor and 1 patient (25%) had Sertoli-Leydig cell tumor. Table 3 points out the distribution of patients with ovarian cancers according to histopathological subtypes and stages.

Table 3. Distribution of patients with ovarian cancers according to histopathologic subtypes and stages.

Histopathologic type	stage I	stage II	stage III	stage IV
Serous cystadenocarcinoma	11	4	7	2
Mucinous cystadenocarcinoma	-	1	3	-
Clear cell carcinoma	2	1	-	-
Endometrioid carcinoma	1	-	-	-
Undifferantiated carcinoma	1	-	-	-
Malignant disgerminom	5	-	-	-
Endodermal sinus tumor	-	-	1	-
Malignant granulosa cell tumor	2	1	-	-
Sertoli- Leydig cell tumor	-	1	-	-

One patient underwent segmental colon resection, 1 patient underwent liver left lobe resection and cholecystectomy and 1 patient underwent segmental intestinal resection in the cytoreductive surgery group. None of 6 patients in stage Ia, grade I underwent postoperative adjuvant therapy. Adjuvant chemotherapy was given to the remaining patients. Six patients had metastatic ovarian tumor, 4 patients had Krukenberg tumor, 1 patient had invasive

lobulary carcinoma of the breast and 1 patient had non-Hodgkin lymphoma, 1 patient had primary tubal adenocarcinoma and 1 patient had choriocarcinoma. In the followup period of a patient who was operated for endometrial cancer in stage II a relapse in the vaginal cuff. The patient in stage IV that underwent postoperative radiotherapy survived for 2 years and 4 months. The mortality rate of patients with ovarian cancer that were resistant to chemotherapy or relapsed, was 46,5% in the follow-up period of 3 to 49 months.

4. Discussion

Cervical cancer is a preventable disease due to valid and widespread screening programs, long-lasting preinvasive period and effective treatment (6). Cervical cancer is an uneliminated disease, however incidence rates diminish and surveillance prolongs if diagnosed earlier. In our study, the majority of cases were observed in stage IIa or less. It is related to regular use of screening programs and effective treatment of preinvasive neoplasms. Risk factors for cervical cancer are young age at first intercourse, multiple male sexual partners, early age at first pregnancy, race, cigarette smoking, immunosuppression from any cause, sexually transmitted diseases and low socioeconomic status. The mean age for cervical cancer is 52.2 years, and the distribution of cases is bimodal, with peaks at 35 to 39 years and 60 to 64 years of age (7). In developing countries, cervical cancer accounts for 15% of female malignancies (4). Mean age of our patients with cervical cancer was 57.42 years and cervical cancer accounts 19.04 % of female malignancies.

No ideal screening program for endometrial cancer has been developed yet. Endometrial sampling methods should be applied in patients with higher risk. Risk factors of endometrial cancer are nulliparity, early menarche, late menopause, obesity, long-term exposure of estrogen (polycystic ovary sendrome, functional ovarian tumor), diabetes mellitus, estrogen therapy without progesteron addition. Endometrial cancer is frequently observed in women in 6th and 7th decade and mean age is 60 years. Vaginal bleeding and discharge are frequently (90%) single symptom of women with endometrial cancer (8). Although frequency of endometrial cancer differs from one country to another, it is most frequently observed in developed countries. In a multicenter study carried out in 6 reference centers of our country, it was pointed out that ovarian and endometrial cancers were the first and second most frequent cancers, respectively (unpublished data) (9). In our study, endometrium cancer was the second most frequent gynecological cancer after ovarian cancer with a frequency of 21.90%. Mean age of our patients with endometrial cancer was 54.13 years.

Uterine sarcomas occupy 3% of uterine cancers. However uterine sarcomas gain importance due to histological variability, rapid doubling time and frequency in elderly ages (10). According to a study from our country, the rate of uterine sarcoma among uterine cancers is 7–8% (11). Uterine sarcoma occupied 20.37% of uterine cancers in our study. Postmenopausal portion of the patients with uterine sarcoma was 65.93% and the oldest patient was 78 years old. Mean age of our patients with uterine sarcoma was 56.36 years.

Ovarian cancer also remains the most frequently reported gynecologic tumor in the literature (12). Ovarian cancer was the most frequent (40.95%) gynecologic malignancy in our study.

Stage and histopathologic grade; especially for the patients in earlier stage, are crucial prognostic factors for ovarian cancers. No adjuvant therapy was administered to our patients in stage Ia, grade I tumor. Mortality rates of patients in chemotherapy groups are especially related to complications of chemotherapy rather than the disease. We aimed to minimize the rational size of tumor to 1 cm or less to maximize the benefits of chemotherapy for patients in advanced stage and who underwent cytoreductive surgery. It was pointed out that optimal tumor reduction would prolong surveillance in advanced stage. Mean age of our patients with ovarian cancer was 46.7 years.

Succession rates of adjuvant therapy are related to appropriate interpretation of surgical pathologic findings. Entire metastatic ovarian cancers originated from extragenital sites. Surgical procedure was performed to maximize results of adjuvant therapy. Therapy of patients with primary fallopian tubes carcinoma was adjusted like ovarian cancer and it was aimed to improve surveillance by large resection as much as possible. Primary fallopian tubes cancer occupy 0.18–1.6% of gynecologic cancers and mean age is 58.5 years (13,14). Our patient was 55 years old and carcinoma of the fallopian tubes account for 0.95% of female malignancies. Chemotherapy is the first choice of therapy for patients with choriocarcinoma. Hysterectomy is another therapeutic approach additional to chemotherapy. Hysterectomy provides 100%

remission rates for patients with children and no willing to have additional birth. Our patient with choriocarcinoma was 53 years old and she underwent TAH, BSO and methotrexate therapy.

Every patient with cancer requires private attention and approach. In addition to clinical evaluation, surgical staging is the primary step of adjusting an optimal therapeutic approach.

Epidemiologic studies are carried out to determine frequencies and distributions of diseases, to reveal out causes and try to establish appropriate therapy. Epidemiologic studies plays an important role in performing public health services and determining effectiveness of health care. We aimed to present distribution of gynecological malignancies in southeast region of Turkey by comparing data of Turkey and other countries. More epidemiologic studies with large number of cases are required to establish properties of effective and appropriate public health services.

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