

Clinicopathological and Prognostic Features of Ovarian Tumors – An Institutional Look

Aisha Akbar, Ahmareen Khalid and Ashok Kumar

Abstract: Ovarian cancer is one of the most common malignancies in Pakistan. Due to high incidence and mortality rate, it is important to determine changing trends in ovarian tumors in different settings.

Knowing histological subtypes, grading and staging of tumor also has prognostic significance. The present study was carried out to determine histopathology and clinico-pathologic features of malignant ovarian tumors.

Methods: It is retrospective study of 80 cases of malignant ovarian masses in 3 years, received in Histopathology Department of Pakistan Institute of Medical Sciences, Islamabad. Histological typing and grading of the tumor was done according to WHO criteria. Undifferentiated tumors were identified using immunohistochemistry panel. Different clinico-pathological parameters were assessed including age of the patient, peritoneal fluid involvement ovarian surface involvement, omental metastasis, nodal involvement, and invasion of other adjacent organs.

Results: 80 cases of malignant ovarian neoplasms were included. 51(63.7%) patients presented in age group 20-40 years. Majority of the patients 45 (52%) presented with high tumor grade (poorly differentiated and undifferentiated tumors). Most frequent tumors were surface epithelial tumors comprising 53 (66.2%) of all cases. Serous cystadenocarcinoma was most common among epithelial tumors. Dysgerminoma was most common in germ cell tumors comprising 21(26.2%) cases. Positive peritoneal fluid cytology for malignant cells was seen in total 37(46.25) cases, most commonly in dysgerminoma. 17 (53.1%) cases of serous adenocarcinoma and 3 (50%) cases of endometrioid carcinoma showed capsular invasion.

Conclusion: Higher frequency of ovarian tumors was seen in reproductive age group. Epithelial tumors were most common in our setup, most frequent being serous cystadenocarcinoma. Peritoneal fluid cytology was positive in majority of the patients being an important independent prognostic marker. Serous and endometrioid carcinoma showed association with poor prognostic factors like capsular invasion and omental metastasis.

Key Words: Ovarian tumors, Ovarian Malignancy, Serous Cystadenocarcinoma, Mucinous Cystadenocarcinoma, Dysgerminoma.

Introduction

Ovarian Cancer affects almost 2% of women in the developed world.¹ It is the 4th commonest gynecological malignancy in Pakistan.² The reasons for the relatively high rates of ovarian carcinomas in Pakistan are not known. Ovarian cancer is usually diagnosed at a late stage and has no efficient screening approach. ³ Tumors of ovary may be asymptomatic, incidentally seen, or the patient might present in emergency like torsion. Almost 75% of ovarian tumors have metastasized at the time of diagnosis.¹

There is marked variation in the histological types of ovarian tumors showing different behavior therefore it is important to subtype the tumor.⁴ Knowing morphological subtypes of ovarian tumors has not only diagnostic but also prognostic significance.⁵ Prognosis is also predicted by the degree of differentiation of the tumors. The stage and laterality of the tumor indicates the behavior of the tumor.

Present study analyzes various subtypes of ovarian tumors along with clinic-pathological and prognostic parameters in our Institution to determine prevalence of these tumors in our population.

AUTHOR'S CORRESPONDENCE:

Material & Methods

80 cases of primary ovarian tumors were analyzed, received in Pathology Department of PIMS from July 2011 to June 2014. All samples showing suspicion of

malignancy by clinical correlates and biopsies were included. All cases went total abdominal hysterectomy with bilateral salpingo-oophorectomy. Omental and pelvic node sampling was considered. Peritoneal fluid cytology was included. All clinically benign lesions and metastatic tumors were excluded. After gross examination, representative sections were stained with H&E stain. Histological subtypes and grading was established using WHO guidelines. Different parameters including age of the patient, capsular invasion, omental and lymph node involvement along with involvement of adjacent organs were analyzed keeping in view the important staging factors by International Federation of Gynecology and obstetrics (FIGO).(6).

Results

A total of 80 cases of ovarian neoplasm were studied in three years. 51(63.7%) patients presented in the reproductive age group.(Table1)

Table-1: Age Distribution of Ovarian Tumors

| Histologic type of tumor | Age up to 20 years n (%) | 21-40 years n (%) | 41-60 years n (%) | >61 years n (%) |
|--------------------------------------|--------------------------|-------------------|-------------------|-----------------|
| Epithelial tumors (n=53) | | | | |
| Serous tumors (n=32) | 3(9.3%) | 27(84.3%) | 3(9.3%) | 2(6.25%) |
| Mucinous tumors (n=12) | 0 | 8(66.6%) | 4(33.3%) | 0 |
| Endometrioid tumors (n=6) | 0 | 2 (33.3%) | 3(50%) | 1(16.6%) |
| Clear cell adenocarcinoma (n=3) | 0 | 0 | 1(33.3%) | 2(66.6%) |
| Germ cell tumors (n=24) | | | | |
| Dysgerminoma (n=12) | 0 | 8(66.6%) | 3(25%) | 0 |
| Immature teratoma (n=8) | 2(25%) | 4(50%) | 0 | 0 |
| Yolk sac tumor (n=4) | 4 (100%) | 0 | 0 | 0 |
| Mixed Germ cell tumor (n=2) | 0 | 1 (50%) | 2 (50%) | 0 |
| Sex cord-stromal tumors (n=3) | | | | |
| Granulosa cell tumor(n=3) | 0 | 1 (33.3%) | 2 | 0 (66.6%) |

Majority of the patients 42 (78.7%) presented with high tumor grade (poorly and undifferentiated tumors) (Table 2).

Table-2: WHO grading system of Ovarian Tumors

| Grade of the tumor | Total no of patients (n=80) |
|-------------------------------|-----------------------------|
| G-X Grade cannot be assessed | 0 |
| G-1 Well differentiated | 17 (21.2%) |
| G-2 Moderately differentiated | 21 (26.2%) |
| G-3 Poorly differentiated | 40 (50%) |
| G-4 Undifferentiated | 2 (2.5%) |

The commonest histological pattern observed was surface epithelial tumors, accounting for 53 (66.2%) of all cases. Serous tumors were the commonest followed by mucinous tumors. Ovarian surface involvement, capsular invasion, omental metastasis, positive lymph nodes and involvement of adjacent organs were frequently seen in surface epithelial tumors. (Table 3)

Table-3: Clinico-pathologic features of Ovarian Tumors

| Histologic Type of Tumor | Positive peritoneal washings/ cytology n (%) | Ovarian surface involvement/ capsular invasion n (%) | Omental metastasis n (%) | Involvement of pelvic structures Uterus/fallopian tubes | Lymph node involvement n (%) | Distant metastasis n (%) |
|------------------------------|--|--|--------------------------|---|------------------------------|--------------------------|
| Serous tumors (n=32) | 5 (15.6%) | 17 (53.1%) | 4 (12.5%) | 4 (12.5%) | 2 (6.25) | 2 (6.25) |
| Mucinous tumors(n=12) | 1 (8.3%) | 3 (25%) | 1 (8.3%) | 3 (25%) | 2 (16.6%) | 1 (8.3%) |
| Endometrioid carcinoma (n=6) | 0 | 3 (50%) | 0 | 0 | 0 | 1 (16.6) |
| Clear cell (n=3) | 0 | 1 (33.3%) | 0 | 2 (66.6%) | 0 | 0 |
| Dysgerminoma (n=12) | 8 (66.6%) | 1 (8.3%) | 1 (8.3%) | 0 | 0 | 0 |
| Immature teratoma (n=8) | 0 | 1 (12.5%) | 1 (12.5%) | 0 | 0 | 0 |
| Yolksac (n=4) | 0 | 0 | 0 | 0 | 0 | 0 |
| Mixed germ cell tumor (n=2) | 0 | 0 | 0 | 0 | 0 | 1(50%) |
| Granulosa cell tumor (n=3) | 0 | 0 | 0 | 0 | 0 | 0 |

Germ cell comprises of 24 cases out of which 12 (50%) were dysgerminoma. (Fig 2) Positive peritoneal fluid cytology for malignant cells was seen in total 37(46.25).6 cases of epithelial tumors showed positive cytology for malignant cells. (Table 3) (Fig 1) 8 (66.6%) cases of dysgerminoma showed positive peritoneal fluid cytology showing dis-cohesive atypical cells with prominent cellular outlines

and conspicuous nucleoli with lymphocytes in the background. (Fig 1)

Table-4: Stage of the disease at diagnosis

| Stage | No. of patients (%) |
|-------|---------------------|
| I | 57 |
| II | 14 |
| III | 4 |
| IV | 5 |

Maximum frequency of capsular invasion and ovarian surface involvement was seen in the case of epithelial tumors. 17 (53.1%) cases of Serous adenocarcinoma and 3 (50%) cases of endometrioid carcinoma showed capsular invasion. (Fig 3)

Involvement of adjacent viscera was observed in mixed germ cell tumor and epithelial tumors.

Discussion

Ovarian cancer accounts for 5th most frequent cancer diagnosis in women in higher-resource regions. (7)

Approximately 90% of all ovarian tumors are malignant.(8) In order to minimize the adverse effects of aggressive surgical procedures and to preserve fertility in young women, it is essential to correctly evaluate prognostic features.(6)

Also due to marked variation in the histological types of ovarian tumors it is important to different histologic patterns of ovarian tumors.(9)

According to morphology, ovarian tumors are categorized as Surface epithelial tumors, germ cell tumors-cord stromal tumors and metastatic tumors. The mean age of presentation varies in different subtypes.

In our study patients, the patients presented in young age groups. Almost 70% of malignant epithelial tumors presented in reproductive age group. Asif et al also in their study experienced a higher age range with 51 years as the median age at presentation for epithelial tumors.(10)

According to Jason et al the malignant epithelial tumors is the most common cause of cancer associated deaths worldwide. (11) Most common tumors in our study were surface epithelial tumors. A similar finding was observed by Inbal et al et al. showing maximum cases of serous tumor in their study. (12)

Next in frequency were mucinous tumors. These tumors also showed adverse prognostic factors like capsular invasion and invasion of adjacent organs. Positive peritoneal fluid cytology seen in case of high

grade serous and mucinous markers is an independent prognostic marker. It also acts as a predictor ovarian surface involvement and peritoneal metastasis. (13)

In our study most of the epithelial tumors were high grade (poorly differentiated) with majority showing ovarian surface involvement. (8) The risk factors differ by histologic subtypes of tumors.(14) Gates et al observed close association of factors like age, duration of breast feeding, smoking and estrogen exposure in epithelial tumors. (15)

Two undifferentiated tumors showed positivity for WT1 hence were included in serous adenocarcinoma. Most of the tumors were unilateral. Family history is considered the single most important risk factor for the development of ovarian carcinoma.(15) Consanguineous marriages play an important role in the transmission of genetic disorders in Pakistan. (16)

Germ cells tumors comprises of 24(30%) of all tumors. The most common among germ cell tumors were dysgerminoma comprising 50% of the cases. Nogales et al and Shabaan et al also reported high incidence of dysgerminoma among germ cell tumors. (17)(18) Cytology showed presence of tumor cells in 8(66.6%) cases exhibiting prognostic importance of peritoneal washings.(19)(20) In this analysis in our settings, clinico-pathological features and biological behavior are similar to their Caucasian counterpart.(21)(22) In patients presenting with early stage germ cell tumors, the prognosis is more than 90%.(23)

All cases of Granulosa cell tumor were limited to the ovary. Capsule was intact, no tumor was found on the external surface and peritoneal washings were negative. (24) Zhang et al had similar findings with sex cord stromal tumor presenting in early stages. Women with stage I and II disease are reported to have survival rate of 95%. (24)

The restrictions of the study are that it is limited to an institutional experience and more research is needed.

Conclusion

Most of the clinico-pathological features of these tumors correspond to the similar studies in East.However, we noted a higher frequency of ovarian cancers in young age group. Patients presented with high grade tumors,mostly surface epithelial tumors. These tumors were associated with adverse prognostic features like capsular invasion, omental metastasis and lymph node involvement. Peritoneal washings/cytology signifies peritoneal spread of the tumor and is discrete prognostic indicator.

However due to lack of tumor registry, networking and awareness in Pakistan, proper data collection and interpretation is difficult. Further research is required to assess varying trends in different regions of the world

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| CONTRIBUTION OF AUTHORS | |
|-------------------------|---------------|
| Author | CONTRIBUTION |
| Dr. Mohsin Shakil | A - B - C - D |
| Dr. Mumtaz Ahmad Khan | E - F |

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