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Pathology

HISTOPATHOLOGICAL SPECTRUM OF OVARIAN TUMORS: A DESCRIPTIVE STUDY

Dr Ronnak Kumari Jain	Assistant Professor, Department of PATHOLOGY, ZMCH, DAHOD, GUJARAT, PIN-389151.
Dr Shalibhadra V Shah*	Assistant Professor, Department of PATHOLOGY, ZMCH, DAHOD, GUJARAT, PIN-389151.*Corresponding Author
Dr Pinal Shah	Assistant Professor, Department of PATHOLOGY, ZMCH, DAHOD, GUJARAT, PIN-389151.

ABSTRACT Surface epithelial ovarian tumors was the most common category of ovarian tumors followed by germ cell tumors, sex cord stromal tumors and metastatic tumors in decreasing order of frequency. Incidence of benign tumors was much higher than malignant tumors with benign serous cystadenoma being the most common benign tumor and serous cystadenocarcinoma being the most common malignant tumor. Reproductive age group showed higher incidence of ovarian tumors whereas there was increasing incidence of malignancy with increasing age group. Exception to this was the higher incidence of malignant germ cell tumors in adolescent age group. Although nulliparity and low parity showed higher risk of malignancy, early menarche did not reveal any significant increase in malignancy. Pain in abdomen was the most common symptom whereas ascites was more commonly seen with malignant tumors. Menstrual complaints were observed more commonly with tumors with functional stroma with possible role of hormonal influence. Benign tumors showed cystic morphology and there was significant increase in incidence of malignancy in tumors with complex or solid morphology. Thus age more than 50 years, post menopausal age group, solid and complex tumor morphology, presence of ascites, nulliparity or low parity and bilaterality of tumors significant increased incidence of malignancy and thus these parameters can be used to predict the risk of malignancy in ovarian tumors. This was a descriptive study and analysis of data was done using chi square test and logistic regression analysis.

KEYWORDS : Ovarian cancer,Types,Incidence.

INTRODUCTION

Ovarian cancer is the fifth most common malignancy among women and second most common gynecologic malignancy. It is the most common cause of death due to malignancy of female genital tract. Ovarian malignancies constitute about 4% of the total cancers in females and 25% of malignant tumors of the female genital tract. In India, the ovary is next in importance to cervix as the seat of cancer of female genital tract. Surface epithelial ovarian tumors constitute two thirds of all ovarian tumors and malignant forms account for 90% of ovarian cancers. They exist in different histological patterns and exhibit varying degree of aggressiveness. Ovary is subjected to monthly endocrine and traumatic insults during normal ovulatory cycles and becomes susceptible to tumorogenesis. Repeated ovulatory rupture and repair theoretically creates opportunities for malignant gene mutations. This may explain the apparent protective effects of oral contraceptives, late menarche, early menopause, multiparity, and breast feeding. Each of these factors decrease the occurrence of ovulation. Although no age group is free 2 from the tumors, different tumors tend to involve different age groups preferentially. The complex anatomy of the ovary and its peculiar physiology with the constant cyclical changes from puberty to menopause give rise to number of cell types, each of which is capable of giving rise to tumors. Both primary and secondary tumors of the ovaries are relatively frequent showing a variety of histopathological patterns. Since germ cells are totipotential, it is not surprising that a very wide variety of neoplasms may develop from them. Germ cell tumors are the commonest ovarian neoplasms in young age group and constitute two thirds of ovarian tumors in this age group, out of which one third are malignant. These tumors account for 25-30% of all ovarian tumors, with great majority of them in the category of mature cystic teratoma, the most common variety of ovarian neoplasm in humans.3 Ovarian tumors in children and adolescent girls constitute an important part of gynecological oncology. Detection of these tumors at such a young age creates much anxiety to parents and throws up a great challenge to doctors in charge as the question of operative safety, chance of malignancy and prospects of future child bearing associated with treatment. Practice of fertility sparing surgery, replacement of 3 radiotherapy by chemotherapy and arrival of newer chemotherapeutic drugs has made the prognosis much better today. The main aim lies in distinguishing ovarian neoplasms from the wide spectrum of nonneoplastic lesions. Their characteristics with regard to age, size, laterality, gross features were evaluated. Incidence of benign versus malignant tumors was also studied.

MATERIALAND METHODS

It is a descriptive study.This study was conducted in the Department of Pathology for one year.This study included all the specimens of ovarian tumors sent for histopathological examination to the Department of Pathology.

INCLUSION CRITERIA: 1. All the ovarian tumors, irrespective of their clinical features, stage of the disease or type of surgical procedure implemented were included. 2. Hysterectomy specimens with incidental ovarian tumors were also included.

EXCLUSION CRITERIA: Non neoplastic ovarian lesions like simple ovarian cyst, tuboovarian mass and polycystic ovaries were excluded.

METHODOLOGY: Relevant data like parity, clinical presentation, age of the patient was collected in a proforma. For proper fixation, tumors were cut serially at 1cm thickness. The specimens were fixed in 10% formalin for 24-48 hours. After fixation, sections were given from representative areas. Sections were cut at 4-5 micrometer thickness & stained with H&E. All stained histopathology slides were studied in detail. Histopathology reports for each tumor were retrieved from department of pathology. Special stains of PAS, Reticulin were done whenever necessary. All details of the specimen consisting of gross features, microscopic features and final diagnosis were studied. World Health Organization classification was used for classifying the tumors. Analysis of the data was done to find out the incidence of various types of tumors, age of presentation of various tumor types, gross features and histopathological patterns of individual tumor types. Incidence of benign versus malignant tumors was studied. This was a descriptive study and analysis of data was done using chi square test and logistic regression analysis.

RESULTS

The incidence and clinical presentation of the different ovarian tumors is extremely variable. The preoperative diagnosis of the tumors is often difficult with only clinical examination and even on exploration, though some investigations like peritoneal fluid cytology or serum LDH may help in predicting the nature of pathology. Hence one has to depend on the microscopic appearance of the tumor for further management. Totally 301 cases were studied in this period.

DISCUSSION

Because of the anatomical location, ovarian tumors may remain

unnoticed for a long period of time. These tumors can cause abdominal pain and abdominal distension. Based on histological patterns, these tumors are divided into benign, borderline and malignant. The common variants are epithelial cell tumors, germ cell tumors, and sex cord stromal Tumors. The ovary is one of the common sites to get metastatic deposits from other abdominal malignancies.

DISTRIBUTION OF OVARIAN TUMORS ACCORDING TO AGE: Ovarian tumors are common in all age groups and no age is exempted. The age range in the present study was 14 to 76 years. The youngest patient in this study was a 14 year old girl with left sided dysgerminoma measuring 17x14x10 cms which is the most common germ cell tumor of adolescent age group. She presented with mass per abdomen. The oldest patient was a 76 year old lady with unilateral serous cystadenocarcinoma with omental deposits. She presented with ascites and the tumor was measuring 5x4x3 cms. The maximum number of cases in present study were between 21 and 60 years. This age group included 89.7% of tumors. The comparative analysis with above studies revealed similar results as present study. 2nd to 5th decade was the most common age group affected. Adolescent age group constituted 4.32 % in this study. This is also comparable to study done by Deshpande et al where the incidence of ovarian tumors in this age group was 4.2 %. PARITY STATUS: Increasing parity is associated with a reduction in the risk of ovarian cancer, but it is not clear whether this association applies to all the histopathological types and to borderline tumours. Nulliparity and low parity were associated with increased relative risk of ovarian tumors in the present study. In this study, tumors in nullipara and women with low parity (two children) contributed to 57.80 % of all tumors which was consistent with findings of study done by Kayastha et al. 65 In their study tumors in nullipara and women with low parity contributed to 58.93 %. Similar results were obtained in study by Adami et al.

AGE OF MENARCHE: Increased risk of ovarian tumors associated with early menarche is put forward by various studies like study by Adami et al and Hildreth et al. 68,69 In the present study only 18.60 % patients attained menarche before 12 years of age. This is in contrast to the above mentioned studies. As in present study, Kayastha et al recorded similar finding of 91.7 % tumors in patients with menarche after age of 12 years.65 This difference may be explained by the fact that both studies by Adami et al and Hildreth et al were conducted in western population where as the present study and study by Kayastha et al were conducted in Indian subcontinent. The onset of menarche is influenced by female biology, as well as genetic and environmental factors, especially nutritional factors. Females from western countries have been shown to have younger age at menarche with possible role played by nutritional status.

MENSTRUAL STATUS: Similar to other studies, present study revealed higher incidence of ovarian tumors in reproductive age group. Higher incidence of ovarian tumors was observed in 21-40 years and premenopausal age group. In postmenopausal patients, comparatively higher incidence of malignant tumors was observed. Similar findings were recorded in study by R Jha et al and also in study by Pilli et al and by Merino et al.

MODE OF PRESENTATION : Some of the ovarian tumors may be incidentally diagnosed on ultrasound whereas others may be symptomatic. Present study reveals that the presentation of the ovarian tumors is variable. If patient presented with more than one complaint then the predominant symptom was considered as the presenting symptom. In the present study the commonest presenting symptom was pain in the abdomen 209 (69.43%) followed by mass abdomen 43 (14.28 %). Ascites was present in 23 (7.64 %) patients whereas menstrual irregularities including post menopausal bleeding in 19 (6.31 %). Asymptomatic patients were only 7 (2.32 %) with these tumors being incidentally diagnosed on ultrasound done for other cause or as a routine work up. The results comply well with a study carried out by Rashid et al, in which abdominal pain was the commonest presenting complaint (59%) followed by abdominal mass/distension (37%).71 Study done by Sumaria Yasmin et al showed similar findings.7 In contrast to this, in another retrospective analysis by Jamal et al the commonest mode of presentation was bleeding per vaginum, followed by pain abdomen, pelvic mass and gastric intestinal symptoms.

UNILATERAL / BILATERAL PRESENTATION: In the present study most of the tumors were unilateral. Only 33 out 301 tumors (constituting almost 11%) had bilateral presentation. Among bilateral tumors 21 (64%) were malignant. Thus among bilateral tumors, malignant tumors are more common . 21 out of 76 (27.63 %) malignant tumors presented bilaterally as against 12 out of 225 (5.33 %) benign tumors. This finding was similar to study done by R Jha et al who encountered only 6.7 % benign tumors and 42.3 % malignant tumors presenting bilaterally.64 Compared to the present study, higher incidence of bilaterality was present in the study by Kar et al which showed 26.8% bilaterality.66 Out of 12 cases of endometrioid carcinoma present in this study 6 (50%) had bilateral presentation. Serous carcinoma showed 42.85 % and mucinous carcinoma 33.33 % bilaterality. The most common benign tumor to present bilaterally was mature cystic teratoma, which showed 23.8 % bilaterality. Tumours in the sex cord stromal category are almost always confined to a single ovary, similar observation is made in this study.7 From 32 sex-cord stromal tumors, none had bilateral presentation. As seen in study by Zhao et al most of the meatastatic tumors occur in premenopausal patients and have bilateral presentation.60 In the present study all the metastatic tumors had bilateral presentation. Ovarian dermoids can be bilateral in 15% cases.

SIZE OF THE TUMOR: Largest dimension of the tumor was utilized to categorize the tumors according to the size. In present study tumors ranged in size from 3cms to 32 cms. Almost all the tumors i.e. 276 (91.69%) were less than 20 cms in the largest dimension. Only 24 tumors had their largest dimension between 21 to 30 cms. The largest tumor was measuring 32x25x12 cms which was unilateral benign serous cystadenoma affecting a 27 year old lady. Bilateral endometrioid adenocarcinoma was the smallest tumor in this study measuring 3x2x1.5 cms present in a 55 year lady.This finding correlated with study by Pilli et al, In their study the largest tumor measured 33x23x22 cms and smallest one measured 3x2x1 cms.

GROSS FEATURES : In the present study, 215 out of 301 (71.43 %) tumors had purely cystic architecture. Solid tumors were 57 out of 301 and thus comprised 18.94 %. Combined solid and cystic presentation was present in 29 tumors (9.63 %). Study done by Kar et al had 58.21 % cystic tumors, 13.43 % solid and 28.36 % combined solid and cystic tumors.66 The relatively high proportion of tumors with complex architecture and less percentage of cystic tumors in study by Kar et al can be explained by the fact that this study had more number of malignant tumors. Patients with solid or complex ovarian tumors are at high risk of ovarian malignancy was shown in study done by McDonald JM et al.

HISTOPATHOLOGICAL PATTERNS: In this study WHO classification was implemented to classify the tumors. Surface epithelial tumors constituted the most common category in the present study contributing to 80.73 % of all tumors followed by germ cell tumors, sex cord stromal tumors and metastatic tumors in decreasing order of frequency as seen in other studies from India and neighboring countries like Pakistan and Nepal.

HISTOPATHOLOGICAL PATTERNS: In this study WHO classification was implemented to classify the tumors. Surface epithelial tumors constituted the most common category in the present study contributing to 80.73 % of all tumors followed by germ cell tumors, sex cord stromal tumors and metastatic tumors in decreasing order of frequency as seen in other studies from India and neighboring countries like Pakistan and Nepal. Benign serous cystadenoma was the commonest tumor type with 35.54% of tumors. This was followed by benign mucinous cystadenoma having incidence of 21.26%. Cases of Serous, mucinous and endometrioid cystadenofibromas were also reported. Among malignant tumors, serous cystadenocarcinoma was the most common category followed by mucinous cystadenocarcinomas. Cases of endometrioid and clear cell carcinomas were also present. In borderline surface epithelial tumor category borderline mucinous tumor dominated the category along with only 2 cases of serous borderline tumors. No transitional cell tumors were seen in this study. Benign mature cystic teratoma was the most common germ cell tumor whereas fibroma and granulosa cell tumor were the most common sex cord stromal tumors. Metastatic Krukenberg tumors were also present. Single case of sex cord tumor with annular tubules was seen. Some differences in incidence of certain ovarian tumors in the study population were noticed when

compared to other studies. The most marked one was the higher incidence of endometrioid adenocarcinoma in the present study, with 12 cases being reported. Another important feature regarding this tumor category was high incidence of bilateral presentation which was observed in 50% cases. Another important difference was in the incidence of the borderline surface epithelial tumors with higher incidence recorded in present study. Both differences in tumor morphology, the higher incidence of endometrioid carcinoma type and borderline grade are among better prognostic criteria.

BENIGN / BORDERLINE / MALIGNANT: Out of 301 cases studied, majority were benign tumors [225 (74.75%)], followed by malignancy [63(20.93 %)] and [13(4.32 %)] cases of borderline malignancy were found. These findings were similar to studies done by Pilli et al and Nasser et al other studies recorded higher incidence of benign tumors.

AGE WISE DISTRIBUTION OF BENIGN / BORDERLINE / MALIGNANT TUMORS: Under age of 20 years, benign tumors were common than malignant tumors. All the malignant tumors in this age group belonged to germ cell tumors, dysgerminoma or malignant mixed germ cell tumor. Under age of 40 years majority of the tumors were benign with malignant tumors contributing to only 14.10%. Above the age of 40 years much higher incidence of malignancy was noted with 37.88% malignant tumors.

VARIABLES RELATED TO RISK OF MALIGNANCY: Chi square test and logistic regression analysis were applied to evaluate the risk of malignancy associated with various parameters analyzed in the present study. To find out the risk factors to predict malignancy in tumors, seven independent variables were selected. These were age, parity, age at menarche, menstrual status, laterality, size and tumor morphology. Out of these risk factors studied, increasing age nulliparity or low parity, postmenopausal status, bilaterality and complex or solid tumor morphology conferred higher risk of malignancy. Early menarche and size of the tumor did not correlate with the increased risk of malignancy. Among all the risk factors evaluated, bilaterality conferred 4 times increased risk of malignancy over unilateral tumors. Tumor morphology was the most important risk factor, predicting 23 times increased risk of malignancy in complex and solid tumors compared to cystic tumors. Using these seven risk factors together as a model to predict the risk of malignancy in a given tumor, 92.44 % of the cases could be correctly predicted as being malignant and 73.68 % of the cases as benign. Overall, the model predicted 87.71% of the cases correctly into their respective groups.

CONCLUSION

Surface epithelial ovarian tumors was the most common category of ovarian tumors followed by germ cell tumors, sex cord stromal tumors and metastatic tumors in decreasing order of frequency. Incidence of benign tumors was much higher than malignant tumors with benign serous cystadenoma being the most common benign tumor and serous cystadenocarcinoma being the most common malignant tumor. Reproductive age group showed higher incidence of ovarian tumors whereas there was increasing incidence of malignancy with increasing age group. Exception to this was the higher incidence of malignant germ cell tumors in adolescent age group. Although nulliparity and low parity showed higher risk of malignancy, early menarche did not reveal any significant increase in malignancy. Pain in abdomen was the most common symptom whereas ascites was more commonly seen with malignant tumors. Menstrual complaints were observed more commonly with tumors with functional stroma with possible role of hormonal influence. Benign tumors showed cystic morphology and there was significant increase in incidence of malignancy in tumors with complex or solid morphology. Thus age more than 50 years, post menopausal age group, solid and complex tumor morphology, presence of ascites, nulliparity or low parity and bilaterality of tumors significant increased incidence of malignancy and thus these parameters can be used to predict the risk of malignancy in ovarian tumors.

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