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Clinical Spectrum of Adnexal Mass Lesions in a Tertiary Care Hospital

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Abstract: ***Introduction****: Adnexal masses can have a wide variety of etiology, and therefore can represent a diagnostic dilemma. Preoperative differential diagnosis of adnexal masses their source of origin, possibility of it being malignant or benign is important so as to determine the optimal mode of management.* ***Material and Methods****: The women who presented with complaints of pain abdomen, abdominal distension, decreased appetite, menstrual complaint and were diagnosed with adnexal mass on the basis of clinical examination and other imaging modality were included for this study. Asymptomatic women with a USG report of pelvic mass were also included.. All obstetric patients were excluded.* ***Result****: A Total of 59 patient were reviewed in this study who were operated in our institute for various adnexal masses. and were categorized on the basis of their malignant potential based on clinical and investigative protocol and to determine the optimal mode of management. Patients were assessed in different age groups .Adnexal masses were studied for cyst size, ascites adnexal masses which were unilocular, complex ,solid or heterogenous on ultrasound and Serum CA-125 level.Based on these variables surgery was contemplated and the findings confirmed peroperatively and final diagnosis was made by histopathology. On histopathology, 49 (83%) masses were benign, 1(1.7%) was borderline and 9(15.3%)were of malignant pathology.* ***Discussion****: Adnexal masses can have a wide variety of etiology, and therefore can represent a diagnostic dilemma. The study helps in estimating the risk of malignancy in a woman with adnexal mass. It was seen that the risk of malignancy in unilocular ovarian cyst is very low. In contrast, complex, solid or heterogeneous ovarian masses are associated with high risk of malignancy CA-125 is the most extensively studied and used tumor marker for predicting the risk of malignancy.*

1. Introduction

Adnexal masses can have a wide variety of etiology, and therefore can represent a diagnostic dilemma. Preoperative differential diagnosis of adnexal masses their source of origin, possibility of it being malignant or benign is important so as to determine the optimal mode of management. But often it is difficult to make an accurate diagnosis. The variables which need to be considered at outset is patient's age, menstrual , obstetric history and reproductive status in making the final diagnosis[1] .Diagnosing malignancy needs to be the focus of evaluation as ovarian masses, benign or malignant do present as adnexal masses. According to data reported by Surveillance Epidemiology and End Result Program 2009-13 the median age for the diagnosis of ovarian cancer was 63yr out of which 69.4% of patient were 55yr or older.[2]Although chances of malignant ovarian masses are more in postmenopausal women, yet most adnexal masses in postmenopausal women are benign[3].The most important risk factor associated with ovarian malignancy is age, with sharp increase in the incidence after menopause[2].Other risk factors related to ovarian malignancy are strong family history of breast and ovarian cancer,nulliparity, early menarche, late menopause, white race, infertility and endometriosis[5-7].

Diagnosis making requires a thorough History regarding risk factors, comprehensive examination and other diagnostic modalities. Transvaginal ultrasonography is the recommended imaging modality for a suspected pelvic mass. Even though there is no superiority of CT/MRI over TVS to recommend its routine use[4**], A CT scan helps in detection of metastasis and lymph node status for a malignant ovarian mass, and confirm primary cancer site and origin of adnexal mass weather ovarian pancreas or colon . .**Tumor markers especially CA-125 is extensively studied and is helpful in determining the risk of malignancy in an ovarian mass, although its use is far from accurate. Nongynaecological masses though rare need to be considered in the differential diagnosis. Metastatic cancers of stomach, colon and breast can also present as adnexal masses[4].

Purpose of the Study

This prospective study was carried out to co-relate the epidemiology, clinical presentation, differential diagnosis, with strategies for evaluation and management of the non obstetric adnexal masses according to various age groups that is pre-menarchal, reproductive,peri-menopausal and post-menopausal in Uttarakhand population.

2. Material and Methods

This is a cross-sectional prospective study which included women of various age group presenting to the gynecology OPD of AIIMS, Rishikesh which were found to have adnexal masses.

The inclusion and exclusion criteria of patient were

1) The symptomatic women who presented and were diagnosed with adnexal mass on the basis of clinical examination and other imaging modality were included for this study.
2) Asymptomatic women with a USG report of pelvic mass were also included.
3) All obstetric patients were excluded.

All cases of adnexal masses were enrolled into the study from 2013 to April 2017. The women were subjected to thorough history taking including the history of pain its onset and duration. General and pelvic examination was done. They were then subjected to Transvaginal/ Transabdominal Sonography for morphological features [Table 4]. High level of suspicion regarding malignancy was kept for patients with cyst size greater than 10 cm, morphologically papillary or solid components, irregularity, presence and thickness of septations, presence of ascites, and increased color Doppler blood flow, laterality. Adnexal masses which had suspicious origin or were suspected of

being malignant, MRI and CECT were done. Tumor marker like CA-125, CEA, CA-19-9, AFP, beta HCG and LDH were also done **pre-operatively.** The above findings were co-related with their Intra operative finding and extent of surgery was decided. Histopathology report was later seen and requirement of chemotherapy or radiotherapy was decided.

3. Result

A Total of 59 patient were reviewed in this study who were operated in our institute for various adnexal masses. Out of 59 women,47(79.7%)were of reproductive age group , 3(5%) were premenopausal, 5(8.5%) were perimenopausal and 4(6.8%)were postmenopausal. 27(45.8%)Women had cyst size of 10cm or more with largest cyst size being 25x20 cm weighing 4.5 kg. Ascites was found to be present in 5 (84.5%)%.

17(28.8%%) patients had unilocular cystic masses,8(13.6%)patients had adnexal masses which were complex on ultrasound and 10(17%) patients had solid or heterogeneous masses(Table 2).9(47.4%)out of 18 complex or solid heterogeneous 9 masses were found to be malignant on histopathology, whereas 10(52.6%) were benign masses.

Serum CA-125 level was more than 35 units/ml in19 (46.78%) patients and was more than 120 units/ml in 11(18.6%).Rest of the patients had normal serum CA 125 values.

Intra-operatively,15(25.4%)patients were found to have benign ovarian masses with 1 patient having leiomyoma and 1 patient with para-ovarian cyst. 1 mass which looked benign(endometrioma)intra operatively but was diagnosed as mixed seromucinous cystadenocarcinoma on histopathology. 6(10.2%) patients had ovarian masses which looked malignant and their removal was done along with pelvic lymphadenectomy,infracolic omentectomy and peritoneal biopsy was taken. 1 complex cystic mass with retroperitoneal and pelvic lymphadenopathy was operated as malignant ovarian mass but was found to be of tubercular origin(Benign).

On histopathology, 49 (83%) masses were benign, 1(1.7%) was borderline and 9(15.3%)were of malignant pathology. **The most common type of ovarian malignancy was epithelial ovarian carcinoma (n=6, 8.5%).Among epitheloid ovarian carcinoma 3(33.3%) had CA-125 more than 120 units/ml and only 1(cystadenocarcinoma) had C-125 <35 units/ml. Among malignant adnexal masses, 7(77.8%) had CA-125 more than 35units.** 2(3.3%) had more than 60 units/ml and rest two patients had CA-125 level between 35 to 60 units/ml.

Among benign adnexal masses,4 of the patient with tuberculosis had CA-125 of >120units/ml.

Out of 17 patients who had endometrioma on histopathology 6(35.3%) had CA-125 of more than 35units/ml. Highest CA-125(463units/ml) was although found in a benign ovarian tumor which was reported as Fibroma.

Although the risk of ovarian malignancy increases with age (69.4%) in our study all 9 ovarian malignancy was from the premenopausal age group. (Table 3).

Table 1: Patient Demographic variables, Tumor description and tumor Biomarker Profiles in women under study (n=59)

Age (mean)	34yr	
	Reproductive (15-39yr)	47(80%)
	Premenopausal (>50yr)	3(5%)
	Perimenopausal (40-50yr)	5(8.2%)
	Postmenopausal	4(6.8%)
Tumor size	<10cm	27
	>10cm	32
Ascites	Present	05
	Absent	54
CA 125 (units/mL)	Less than 35	40
	35–59	05
	60–120	03
	More than 120	11

Table 2: Ultrasound finding of patients

USG Feature	N=59
Unilocular clear cyst	17
Complex cyst	8
Endometrioma	11
Dermoid cyst	4
Multiloculated cyst with thin septa	5
Multilocular cyst with thick septa	1
Hemorrhagic cyst	2
Solid/cystic mass with heterogeneous echoes	10
Other pathologies	1(fibroid)

Table 3: Histopathological spectrum of adnexal mass according to age

Age group/HPR	Premenarchal	Reproductive (15-39yr)	Perimenopausal (40-50yr)	Premenopausal (>50yr)	Postmenopausal	Total (n=59)
BENIGN						
Endometrioma		16	1			17
Follicular cyst		5	1			6
Para ovarian cyst		1				1
Hemorrhagic cyst		1				1
Mature teratoma		4	1		2	7
Tuberculoma		3			1	4
Serous cystadenoma		3	1	1	1	6
Mucinous cystadenoma		5				5
Fibroma		1				1
Mucinous cystadenofibroma				1		1
Leiomyoma		1				1
MALIGNANT						

Endometriosis tumor		1				1
Micro papillary serous carcinoma		1				1
Papillary serous cystadenocarcinoma				1		1
Clear cell carcinoma		1				1
Dysgerminoma		1				1
Sertoli-leydig cell tumor		1				1
Granulosa cell tumor			1			1
Cystadenocarcinoma		1				1
Mixed sero mucinous cystadenocarcinoma		1				1

Table 4: CA 125 Related to Histology in Ultrasonographically Complex or Solid Adnexal Tumors (N=59)

CA-125 U/mlN	Total	<35	35-59	60-119	>120
HISTOLOGY					
BENIGN					
Endometrioma	17	11	3	1	2
Follicular cyst	6	6			
Para ovarian cyst	1	1			
Hemorrhagic cyst	1	1			
Mature teratoma	7	6	1		
Tuberculoma	4				4
Serous cyst adenoma	6	6			
Mucinous cystadenoma	5	4			1
Fibroma	1				1
Mucinous					
Cystadenofibroma (Borderline)	1	1			
Leiomyoma	1	1			
MALIGNANT					
Endometrioid tumor	1				1
Micropapillary	1				1
Serous carcinoma					
Papillary serous	1				1
Cystadenocarcinoma					
Clear cell carcinoma	1		1		
Dysgerminoma	1	1			
Sertoli-leydig cell tumor	1	1			
Granulosa cell tumor	1			1	
Mixed sero mucinous	1			1	
Cystadenocarcinoma					
Cystadenocarcinoma	1	1			
TOTAL	59	40	5	3	11

4. Discussion

Adnexal masses can have a wide variety of etiology, and therefore can represent a diagnostic dilemma. The aim of the study was to identify women who presented with adnexal masses to the opd and were diagnosed either clinically or on Ultrasound imaging, or presented with other symptoms but later were identified to have adnexal masses, and to categorize them on the basis of their malignant potential based on clinical and investigative protocol and to determine the optimal mode of management for the women having benign or malignant adnexal masses. The basis of categorization was by combination of clinical impression, ultrasonographic tumor morphology and serum CA-125 value. Doppler USG, CT scan and MRI were used selectively only in those cases with high suspicion for malignancy as the patients belonged to lower socioeconomic strata of the society and could not afford high cost investigations. The analysis of data related to patient demographics, findings ultrasonography findings and serum CA-125 values was done.

The study helps in estimating the risk of malignancy in a woman with adnexal mass. It was seen that the risk of malignancy in unilocular ovarian cyst is very low. In our study out of 17 patient who on USG were showing unilocular clear cyst, none were found to be malignant (Table 2). This conformed to the observation made by John M. McDonald et al in their study who too reported no case of borderline or malignant ovarian cancer in 139 patients who had unilocular ovarian cyst out of a total of 395 patients[8].It was also in accordance with results of L.Valentin and colleague[9]who in their study of 1148 patients with unilocular cyst,found a malignancy rate of 0.96%, out of which 0.54% was in premenopausal women and 2.76% in post-menopausal women. M Sarkar and colleagues followed 378 cases of unilocular ovarian cyst ultrasonologically,and they found One hundred and seventy-five cases (46.30%) of the 378 had spontaneous resolution ,30(7.94%) turned into complex cysts and 4 cases had(1.06%) significant increase in size. Only one patient developed papillary serous carcinoma (high grade) of the ovary (Table 5)[10]. In our review there were 11 patients with unilocular cyst with more than 10cm in dimension and none were found to be malignant on histopathology. Out of these 5 were reported as mucinous cyst adenoma, 4 were serous cystadenoma,1was paraovraian cyst and 1 was simple follicular cyst.

In contrast, complex, solid or heterogeneous ovarian masses are associated with high risk of malignancy. In our review, there were 19 patients had masses with either solid or complex heterogeneous appearance on USG out of which 9(39%) were found to be malignant histopathologically. This was consistent with results published by John M. McDonald et al who in their study found 131(48%) out of 272 patients with complex or solid pattern on USG [8] having ovarian malignancy.

CA-125 is the most extensively studied and used tumor marker for predicting the risk of malignancy.**CA-125 is more useful in follow up after chemotherapy and also to detect the recurrence**. The CA-125 level is raised in 80% of case of epithelial ovarian cancer but in stage1 disease it is found raised in only 50% cases [11].CA-125 has a sensitivity of 61-90% in distinguishing benign from malignant masses whereas specificity ranges from 71-93%. Positive

Predictive Value ranges from 35-91% and Negative Predictive Value ranges from 67-90% [12] Although the ability of CA-125 to predict cancer risk in premenopausal women is less as compared to in postmenopausal women, its extreme value should raise the suspicion for malignancy. According to American college of obstetricians and gynecologist 2016 practice bulletin there is no higher

threshold for CA-125 for referral to a gynecological oncologist which earlier was kept at 200U/ml. In our review 9(82%) out 11 women with values of CA-125 more than 35U/ml who had complex or heterogeneous morphology on USG had malignant ovarian cancer on histopathology(Table 4). This is supported by observation made by John M.Mcdonald, where more than three fourth of women with a complex or solid adnexal mass and a CA-125 more than 35U/ml had either borderline or frank malignant ovarian cancer. In our study the exception was a patient which had a solid morphology on USG with size more than 10cm and CA-125 value of 463U/ml (Table 5)but turned out to be a benign ovarian tumour that is Fibroma on histopathology. **Additional tumor marker testing like AFP, LDH, BHCG can also be done depending upon the age and ultrasound features of ovarian mass** even though **their efficacy is not proved.**

Although the risk of malignancy is less in premenopausal women, in our review, all the 9 patient with ovarian malignancy were of premenopausal age group, out of whom 7 were of reproductive age group (15-39yr). Therefore there should be high suspicion of malignancy in any woman who has a complex or heterogeneous mass on USG and or a high CA-125 value(Table 3) irrespective of their age. The survival rate for patient is significantly increased if a complete surgical staging is performed rather than a surgery done in haste and later found to have a diagnosis of ovarian cancer on histopathology.

5. Conclusion

As the number of women presenting with adnexal mass is increasing, it is useful to incorporate the clinical, ultrasonography findings and tumor markers in evaluating the individual risk of ovarian cancer. These findings help in making a correct diagnosis and decide the management protocols and the type and extent of surgery for ovarian mass so as to provide better survival benefit to the patient.

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