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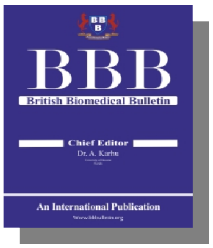

Original

An Observational Study of Cytopathological Analysis of Peritoneal Washing or Ascitic Fluid in Ovarian Tumor and its Correlation with Histopathological Type and Staging

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A B S T R A C T

Ovarian cancer is one of the leading causes of mortality in women. Early detection and prompt management is the key to improve survival rate among the affected. 5 year survival rate for epithelial ovarian cancer is reported to be directly related to surgical stage. The majority of epithelial cancers has an exophytic growth on ovarian surface that provide them a direct contact with peritoneal cavity. Methods of detection of microscopic disease in ovarian cancer are therefore of significant interest and may reduce the mortality rate for this disease by enabling an earlier diagnosis of primary recurrent ovarian cancer. Our study aimed at finding the rate of positivism of malignant cells in ascitic or peritoneal washing fluid, to observe correlation between cytologically positive pelvic peritoneal washing and histological types of ovarian tumor, and to correlate the cytological findings with the FIGO staging of the tumor.

Introduction

Ovarian cancer is one of the leading causes of mortality in women, although mortality rates have been declining over the past decade. It is the sixth most common cancer with 26000 new cases reported in 2004[1]. Cancer of ovary represents about 30% of all cancers in the female reproductive tract. It is as common as cancers of the uteri (35%) and invasive carcinoma of cervix (27%) in developed country[2]. It is the fourth most common cause of cancer related deaths in American women of all ages & the most frequent cause of death from gynecologic malignancies in the US. In India, it ranks after cervical cancer.

Although ovarian cancer is a disease of postmenopausal women, only 15% are discovered in premenopausal patients. Median age of diagnosis of epithelial ovarian cancer, the most common histological type is between 60-65 years. 90% of ovarian cancers are sporadic, only 10 % of it has a strong hereditary component. The high mortality rate is partially attributable to the vague, nonspecific symptoms. Greater than 70% of patients with epithelial ovarian carcinomas (EOC) are at an advanced stage at the time of diagnosis[3]. 5 year survival rate for the EOC is reported to be directly related to the surgical stage (94.6% for the stage I vs. 28.2% for stage III). The majority of epithelial cancers has an exophytic growth on ovarian surface that provide them a direct contact with peritoneal cavity. They typically disseminate by trans-coelomic spread & peritoneal seedling by tumor cells produce ascites.

Early detection of microscopic disease in ovarian cancer may reduce the mortality rate of this disease by enabling an earlier diagnosis of primary recurrent ovarian cancer. Staging of ovarian cancer is mainly surgical. The pelvic peritoneal wash was introduced as a formal procedure by Keetel & Elkins in 1950 with the stated objective of detecting early spread in patients undergoing surgery for suspected malignancy[4]. In 1976; FIGO incorporated it into staging protocols. Significant survival benefits were demonstrated by the FIGO staging.

Aims and objectives

This study was conducted to find out the rate of positivism of malignant cells in ascitic fluid or peritoneal washing, to observe correlation between cytologically positive pelvic peritoneal washing and histological types of ovarian tumor, and to correlate the cytological findings with the FIGO staging of the tumor.

Methodology

This hospital based prospective study was conducted among those with negative cytology compared with those with positive cytology. Those patients of ovarian tumors who were posted for staging laparotomy were included in our study. 100 cases were taken for this study after considering the inclusion and exclusion criteria.

Inclusion criteria

1. Patients of ovarian tumor willing to participate in this study.
2. Clinically diagnosed ovarian tumor confirmed by imaging (USG/CT/ MRI) posted for laparotomy.

Exclusion criteria

1. Only clinical diagnosis of ovarian tumor without radiological documentation.
2. Patient refusal of participation.
3. Patients who had previous FNAC for diagnosis.
4. Patients who had previous laparotomy for ovarian tumor.
5. Those patients who had lumps of another origin other than ovarian tissue.

6. Emergency laparotomy for ovarian tumor: e.g. twisted tumor, acute rupture or intracystic hemorrhage.

Materials and methods

100 cases of ovarian tumors, diagnosed clinically and by imaging (USG/CT/MRI) posted for laparotomy were included in this study. During laparotomy, after opening the abdomen, ascitic fluid was taken for analysis. If ascites was absent, then pelvic peritoneal washing was taken for analysis. 50-100 ml of normal saline wash was aspirated and collected in a heparinised container for analysis. The samples were then centrifuged, and deposits were used to smear, stained with MGG stain, Papanicolaou's stain, and H&E stain. In case of delay of more than 30 minutes in preparation, the specimens were preserved at 4^0C after adding 50% ethanol. The specimen of ovarian tumor was collected and examined microscopically after proper tissue processing and staining with H&E stain. Results were interpreted as whether cytological specimens were positive or negative for malignant cells. Further grading and typing of the tumor was done on histopathological examination. Only unequivocal positive diagnosis was considered positive for staging purpose in this study. Anything less, atypical or suspicious was treated as negative.

Results

Among 100 cases of ovarian tumors, 64% were benign, 6%borderline, and 30% were malignant. Amongst benign tumors, 70.3% were of epithelial origin, 28.1% germ cell origin, and 1.6% was of sex-cord stromal tumors.

64.4% of benign epithelial tumors were found between 4th to 5th decade, 11% between 11-20 years, 15% between 21-30 years, & 6.6% were between 51-60 years. Occurrences of benign germ cell tumors were maximum among 2nd to 3rd decade (55.5%). All malignant germ cell tumors were among 2nd to 3rd decade. It was seen that 89% of malignant epithelial tumors were in the age group between 5th to 6th decades.

Only 4.5% of borderline epithelial tumors were bilateral. 22.2% of benign germ cell tumors & 25% of borderline mucinous tumors were bilateral whereas 50% of borderline serous tumors were bilateral. Malignant serous tumors were bilateral in 50% cases. Metastatic tumors were noted bilateral in 66% cases, whereas sex-cord stromal tumors were all found unilateral.

In 45% cases of high stage malignancy, malignant cells were seen in ascitic fluid, while they were seen in 25 % cases in low stage malignancy. The detection rate was 33% in peritoneal washing in high stage malignancy while all cases in low stage malignancy were cytologically negative in peritoneal washing. To 62.5% of serous carcinomas, malignant cells were seen in ascitic fluid, and 25% in peritoneal washing. For serous carcinomas of higher stage, the detection rate was 80% in ascitic fluid and 50% in peritoneal washing.

Among the borderline serous tumors, 50% cases showed invasive peritoneal implants, malignant cells in ascitic fluid and higher stage at presentation. All borderline mucinous tumors were associated with low surgical stage, negative malignant cells in ascitic fluid, and invasive peritoneal implants. Serous epithelial ovarian carcinomas (EOC) were associated with invasive peritoneal implants and positive malignant cells with ascitic fluid in 50% cases. 58% of serous carcinomas presented at a higher stage, 42% in lower stage. For mucinous EOC, the malignant cell detection rate of ascitic fluid was 16.7%. Germ cell tumors presented at a higher stage in 50% of cases.33% of germ cell tumors were associated with invasive

peritoneal implants, but all were cytologically negative for malignant cells. All sex-cord stromal tumors were presented in lower stage. Malignant cells were detected cytologically in 33% cases of metastatic ovarian tumors.

50% of serous borderline tumors, which had papillary component were associated with invasive peritoneal implants. 86% of malignant serous carcinoma with papillary component was associated with invasive peritoneal implants and 71% of them had malignant cells in ascites or peritoneal washing. Malignant serous carcinoma without papillary component were associated with positive malignant cell cytology in 20% cases only, none had invasive peritoneal implants.

Discussion

In this study, 64 cases were benign (64%), 6 cases were borderline, (6%), and 30 cases were in the malignant tumor group. In this study, it was seen that 89% of malignant epithelial tumors were in the age group between 5th to 6th decades. Katsube in 1982 reported that, benign epithelial ovarian tumors may occur at any age, but most commonly during 5th decade, and malignant ones are mostly seen between ages of 40-70 years[6]. In our study, serous epithelial ovarian carcinomas (EOC) were associated with invasive peritoneal implants and positive malignant cells with ascitic fluid in 50% cases. 58% of serous carcinomas presented at a higher stage, 42% on the lower stage. In 2004, Fadare *et al*[5]. Reported pelvic peritoneal wash were found to be significantly more likely to yield malignant cells in the higher stage group. In this study, 16.7% of pelvic wash were positive & this positivity were all from serous borderline ovarian tumors, result corroborating with our study. In this study, germ cell tumors presented at a higher stage in 50% of cases.33% of germ cell tumors were associated with invasive peritoneal implants, but all were cytologically negative for malignant cells. Valente PT[7] in 1992 reported that rarely in germ cell malignancy & dysgerminoma, malignant cells were detected cytologically. Segal GH[8] in 1992, reported that due to exophytic surface growth had a 94% diagnostic sensitivity rate in the presence of synchronous implants in patients with borderline tumors, peritoneal washing should have a comparatively higher positive rate with stage IC (or greater) with this micro-papillary pattern. In the present study, 50% of serous borderline tumors, which had papillary component were associated with invasive peritoneal implants. 86% of malignant serous carcinoma with papillary component was associated with invasive peritoneal implants and 71% of them had malignant cells in ascites or peritoneal washing.

Conclusion

The rate of positivity of malignant cells in ascitic fluid, pelvic peritoneal wash & for combined ascitic fluid, pelvic peritoneal wash were 30.7%, 10% and 25% respectively. Epithelial ovarian carcinomas were more cytologically detected than germ cell malignancy & malignant sex cord stromal tumor. Among the epithelial ovarian carcinomas, serous type was more likely detected than mucinous type. Among all ovarian tumors, 64% were benign, 6% were borderline, and 30% were malignant. Of all malignant tumors, there was increased incidence of germ cell malignancy (22.1%) & mucinous carcinoma (63.1%). The benign and borderline epithelial tumors were mostly in between 4th and 5th decade, whereas malignant epithelial tumors were mostly seen in between 5th and 6th decade. Most of the benign germ cell tumors & all malignant germ cell tumors were between 2nd and 3rd decade. Serous borderline tumors & serous carcinomas with papillary component had higher chances of having bilateralism and invasive peritoneal implants. In higher stages of malignancy, cytologically malignant cell

detection rate was more (45% in ascitic fluid & 33% in peritoneal washing) than in lower stage malignancy (22% in ascitic fluid & none in peritoneal washing).

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Table 1. Distribution of different ovarian tumours

Type	Total no. of cases	Sub-types	No.
Benign	64	Serous	32
		Mucinous	12
		Brenner	1
		Germ cell	18
		Sex cord	1
Borderline	6	Serous	2
		Mucinous	4
Malignant	30	Serous	12
		Mucinous	6
		Endometrioid Ca	1
		Dysgerminoma	3
		Immature teratoma	2
		Yolk sac tumour	1
		Metastatic	3

Table 2. Age distribution of different types of ovarian tumors

Type of Ov. tumor	Sub types	11-20yrs	21-30yrs	31-40yrs	41-50yrs	51-60yrs	>60yrs
Benign	Epithelial	5	7	13	16	3	1
	Germ cell	6	5	4	2	1	
	Sex cord stromal				1		
Borderline	Serous			2			
	Mucinous				4		
Malignant	Serous Ca			1	7	4	
	Mucinous Ca			1	4	1	
	Endometrioid Ca					1	
Germ cell (malignant)	Dysgerminoma	1	2				
	Immature teratoma	1	1				
	Yolk sac tumor	1					
Sex cord stromal (malignant)	Sertoli-leydig		1				
	Adult granulosa		1				
Metastatic					1	2	

Table 3. Distribution of laterality of ovarian tumor

Type of ovarian tumors	Sub-type of ovarian tumors	Unilateral	Bilateral	Total
Benign	Epithelial	43(95.5%)	2(4.5%)	45
	Germ cell	14(78%)	4(22%)	18
	Sex-cord stromal	1(100%)	0	1
Borderline	Serous	1(50%)	1(50%)	2
	Mucinous	3(75%)	1(25%)	4
Malignant	Serous Ca	6(50%)	6(50%)	12
	Mucinous Ca	4(67%)	2(33%)	6
	Endometrioid Ca	1(100%)	0	1
	Germ cell (malignant)	4(67%)	2(33%)	6
	Sex-cord stromal	2(100%)	0	2
	Metastatic	1(33%)	2(67%)	3

Table 4. Co-relation between number of ovarian tumors, cytological positivity of malignant cells and surgical staging, Total cases: 30

Types	Ascitic fluid						Pelvic peritoneal wash					
	High stage			Low stage			High stage			Low stage		
	+ve	-ve	Total	+ve	-ve	Total	+ve	-ve	Total	+ve	-ve	Total
EOC (s)	4	1	5	1	2	3	1	1	2	0	2	2
EOC (m)	1	3	4	0	2	2	0	0	0	0	0	0
EOC (e)	0	0	0	0	0	0	0	0	0	0	1	1
Germ cell	0	2	2	0	1	1	0	1	1	0	2	2
Sex cord	0	0	0	0	0	0	0	0	0	0	2	2
Metastatic	0	0	0	1	2	3	0	0	0	0	0	0

(EOC-epithelial ovarian carcinoma, S- serous, M-mucinous, E- endometrioid)

Table 5. Co-relation between peritoneal implants, cytological positivity of malignant cells and surgical staging (borderline & malignant) of ovarian tumors: total cases-36

Type of ovarian tumors	Sun-type of ovarian tumors	Total cases	Peritoneal implants	Cytological positivity of malignant cells		Surgical staging	
				+ve	-ve	High	Low
Borderline	Serous	2	1	1	1	1	1
	Mucinous	4	0	0	4	0	4
Malignant	EOC(S)	12	6	6	6	7	5
	EOC (M)	6	2	1	5	3	3
	EOC (E)	1	0	0	1	0	1
	Germ cell	6	2	0	6	3	3
	Sex-cord	2	0	0	2	0	2
	Metastatic	3	0	1	2	0	3
Total		36	11	9	27	14	22

Table 6. Correlation between papillary component, peritoneal implants, cytological positivity of malignant cells and surgical staging, (Total no. of cases = 14)

Type of ovarian tumour	Component	No of cases	Peritoneal implants	Cytological positivity of malignant cells	Surgical staging
Borderline	Papillary	1	1	1	III
	Non papillary	1	0	0	IA
Malignant	Papillary	7	6	5	IIIC, IA_1
	Non papillary	5	0	1	IA_3, IB_1, IC_1