



ORIGINAL RESEARCH PAPER

Pathology

CA-125 POSITIVITY IN MALIGNANT SURFACE EPITHELIAL TUMORS OF OVARY- A TERTIARY CARE EXPERIENCE

KEY WORDS: ovarian carcinoma, histopathology, ca-125

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ABSTRACT
Introduction: Ovarian carcinoma accounts for one of the commonest malignant tumours among women worldwide. Their early diagnosis and management plays an important role in determining the prognosis. Several biomarkers for tumour antigen are used as important diagnostic tool. CA-125 is one such marker which is elevated in serum as well as expressed by tissue malignant cells. Two year study of all ovarian tumours was carried out along with tissue expression of ca-125 in malignant surface epithelial ovarian tumors.
Results and observations: 32 cases of ovarian carcinoma were diagnosed histopathologically comprising of serous and mucinous type only. Ca-125 immunohistochemistry was done. 72.7% of serous carcinomas showed ca-125 positivity. None of the mucinous carcinomas were ca-125 positive.
Conclusion : Though histopathology is the mainstay of diagnosis; immunohistochemistry can aid in certain doubtful cases as well to confirm ovarian origin.

INTRODUCTION

Ovarian cancers accounts for approximately 6% of all cancers in the female and is the fifth most common malignant tumors among women in the US with an annual incidence of 22,000 new cases. In India the scenario is far more worse.^[1,2] The etiology of ovarian cancer is unknown. However, there is growing evidence of familial predisposition in a small group of patients and of a relationship with reproduction history.

Early diagnosis and management of ovarian tumours play a very important role in determining the prognosis. The biochemical markers for tumour antigen or tumour products in plasma are being used as important diagnostic tool. CA-125 is one such marker that is frequently elevated in epithelial tumours of ovary (particularly Serous and Endometrioid carcinoma).The malignant cells frequently express this marker on the surface and this can be identified by IHC technique. This is a marker which not only helps in early diagnosis but also in monitoring the disease progression and thus the prognosis of the patient. Cancer antigen 125 (CA-125) is a protein encoded by MUC16 gene, used as a tumor marker, because it is 79% sensitive for ovarian cancer; though it is not specific, because elevated in other tumors and in inflammatory conditions.

AIMS AND OBJECTIVE:

To study the Immunohistochemical marker CA-125 positivity in malignant ovarian tumours of epithelial origin.

MATERIALS AND METHODS

The present work is based on a study of 160 specimens of ovarian tumours received in the Department of Pathology, Silchar Medical College & Hospital from the Department of Obstetrics and Gynaecology of Silchar Medical College & Hospital during the period from 7th July 2013 to 6th July 2015.

Details of operative findings were collected to obtain information about the extent of the swelling and about involvement of the neighbouring structures if present. Peritoneal fluid in selected cases was sent for cytological examination for malignant cells.

The specimens were examined macroscopically and the results recorded according to standard protocol. Omentum, lymph nodes and other staging biopsy specimens when received were examined and reported in details.

Staining with H&E and immunohistochemistry (IHC) was

done as per standard protocol.

ANTIBODY STAINING ^[3]	CONTROL	PATTERN OF
CA-125	Normal ovary	Cytoplasmic/ membrane

RESULTS AND OBSERVATIONS

A total number of 160 ovarian tumour specimens obtained were diagnosed histopathologically and were classified on the basis of WHO classification (revised) 2014.

Out of 160 ovarian tumours, 110 (68.75%) were benign , 4(2.5%) were borderline and 46 (28.75%) were malignant. In this study, 94 cases (58.75%) were Epithelial tumours, 52 cases (32.5%) were Germ cell tumour, 10 cases (6.25%) were Sex cord stromal tumour and 4 cases (2.5%) were Metastatic tumour. In the benign tumour group, Serous cystadenoma accounted for 40 out of 110 cases (36.3%) and was the commonest. In the malignant group, serous adenocarcinoma was the commonest with 22 out of 46 cases (47.8%) .

Table 1 FREQUENCY OF DIFFERENT TYPES OF SURFACE EPITHELIAL TUMOURS

Histological type of Epithelial tumours	Number of cases	Percentage (%)
Serous cystadenoma	40	25
Mucinous cystadenoma	18	11.25
Papillary serous adenocarcinoma	14	8.75
Serous adenocarcinoma	8	5.0
Mucinous adenocarcinoma	10	6.25
Brenner (borderline) tumour type .	4	2.5
TOTAL	94 out of 160 cases	

Of the 94 epithelial tumours, 62 were of Serous type(65.9%), 28 of mucinous type(29.7%) and 4 of Brenner (borderline) tumour type(4.2%) Of all the malignant cases, surface epithelial carcinomas comprised 69.5%(32 of 46 cases).

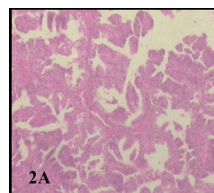


Fig1: Histological section of Papillary Serous carcinoma.(H & E).

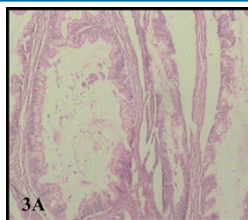


Fig2: Histological section of Mucinous cyst adenocarcinoma.(H & E).

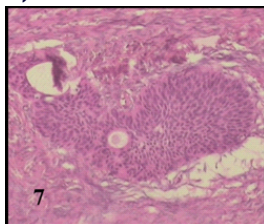


Fig3: Histological section of Brenner tumour (Bord erline).

IHC

Ca-125 ihc was done on cases which were diagnosed histopathologically as malignant surface epithelial tumours on HPE.

Table 2:-CA-125 POSITIVITY IN MALIGNANT EPITHELIAL OVARIAN TUMOUR

Serial No.	Type of tumour	CA-125(+)	CA-125(-)	HPE
1	Serous adenocarcinoma	16	6	22
2	Mucinous adenocarcinoma	0	10	10
Total		16	16	32

In this study, 16 out of 22 cases (72.7%) of serous carcinoma showed ca-125 positivity.

Out of 10 cases of mucinous carcinoma, none of cases showed ca-125 positivity.

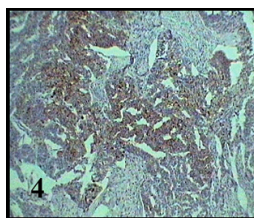


Fig4: Photomicrograph showing tissue expression of CA-125 in a case of papillary serous cystadenocarcinoma.

Table3- FREQUENCY OF SENSITIVITY AND SPECIFICITY OF CA-125 IN EPITHELIAL OVARIAN TUMOUR

Sl No.	Type of tumour	True positive	False negative	True negative	False positive	HPE	Sensitivity (%)	Specificity (%)
1	Serous adenocarcinoma	16	6	-	-	22	72.7	-
2	Mucinous adenocarcinoma	-	-	10	-	10	-	100
	Total	16	6	10	0	32	72.7	100

Following statistical analysis, it was found that demonstration of ca-125 in serous adenocarcinoma holds a sensitivity of 72.7%. On the other hand, mucinous adenocarcinoma did not stain positive for ca-125 in any of the cases therefore holding a specificity of 100%

Overall sensitivity of ca-125 in malignant surface epithelial ovarian tumours is 72.7%.

DISCUSSION

Useful humoral markers^[4,5] for epithelial ovarian carcinomas have been found to assist in diagnosis and treatment. Fetal proteins are expressed during embryonic development but are generally not found in normal adult tissue. These markers are however re-expressed in malignant tissue.

Out of total 160 ovarian tumours in the present study, 110 (68.75%) were benign, 4(2.5%) were borderline and 46 (28.75%) were malignant. In a study by Lubna et al^[6] comprising of the 80 cases of ovarian tumours, benign lesions were more common (75%) than malignant lesions (25%).

In our study, 94 cases (58.75%) were Epithelial tumours, 52 cases (32.5%) were Germ cell tumour, 10 cases (6.25%) were Sex cord stromal tumour 4 cases (2.5%) were Metastatic tumour.

In the benign group, serous cystadenoma was the commonest accounting for 36.3% (40 out of 110 cases). In the malignant group, serous adenocarcinoma was the commonest with 22 out of 46 cases (47.8%); majority being papillary serous adenocarcinoma with 14 cases. Of all the malignant cases, surface epithelial carcinomas comprised 69.5% (32 of 46 cases).

Lubna khan et al^[6] reported serous cystadenoma as the commonest benign tumor (45%). Overall surface epithelial carcinomas made up 70% of all malignant lesions among which serous cyst adenocarcinoma was most common (45%).

Of the 94 epithelial tumours in our study, 65.9% were of Serous type, 29.7% of mucinous type and 4.2% of Brenner (borderline) tumour type. Thus serous tumors were commonest followed by mucinous type.

IHC

In our study, 72.7% of serous carcinomas showed ca-125 positivity. None of the mucinous carcinomas were ca-125 positive. Out of 32 cases of malignant epithelial ovarian tumor, 16 cases (50%) showed ca-125 positivity and were serous adenocarcinomas. Study by Lubna et al^[6] showed 60% serous carcinomas with CA125 positivity and 100% mucinous carcinomas were negative for CA125. Neunteufel et al^[7] reported ca125 positivity in 85% serous carcinomas with all the mucinous tumors being CA 125 negative. According to study by Kriplani et al^[3] 77.27% serous tumors expressed CA125 showing membranous pattern of staining. Goldstein et al^[8] and Loy et al.^[9] have reported a luminal and cytoplasmic staining of tumor cells with CA125 in 83% and 92% of the serous tumors respectively. 86.04% serous ovarian carcinomas showed ca-125 expression in a study by Karaferic et al.^[10] Thus various studies across literature showed variation in ca-125 expression in serous carcinoma.

Though studies by Kriplani et al^[3] and Karaferic et al^[10] demonstrated 20% and 33.3% ca-125 expression in mucinous tumors respectively concluding CA-125 may be expressed, though in relatively low percentage, none of the cases in our study were positive.

Kriplani et al^[3] and Tornos et al^[11] stated that tissue expression of ca-125 is often useful to differentiate between primary ovarian adenocarcinoma and metastatic adenocarcinomas specially those of colorectal origin.

CONCLUSION

Ovarian tumours comprised one of the major neoplasms in female detected in this institution with benign tumours being more common than malignant tumours. The incidence of common epithelial tumours is more than other groups of

ovarian tumours in our institution. The immunohistochemical positivity for CA125 is seen in 72.7% cases of serous adenocarcinoma and all the mucinous carcinomas were negative. Hence ca-125 can be used as an adjunct for diagnosing in cases of conflicting histopathology as well as to confirm ovarian origin of tumour.

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