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Role of P53 in Serous Ovarian Carcinomas.

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Abstract: *Approximately 50% of human malignancies have p53 mutations , which is the most common tumor suppressor gene mutated in human malignancies. In particular, about 50-80% of ovarian carcinomas shows p53 gene mutation. The objective of this study is to analyse the role of p53 in serous ovarian carcinomas.*
Keywords: *Ovarian tumors ,P53,Serous Carcinomas, Two-tier grading.*

I. Introduction

Ovarian tumors account for 30% of tumors of female genital tract. important risk factors associated with increased prevalence of ovarian tumors are age, positive family history, inheritance of BRCA-1,BRCA-2 gene mutations.Histological subtyping of surface epithelial tumors into benign,borderline,malignant category and histological grading has therapeutic and prognostic significance.Serous ovarian carcinomas are classified into low grade and high grade based on recent two-tier grading system. P53 immunohistochemical staining is done for both low grade and high grade serous carcinomas.

II. Materials And Methods

This study was conducted in the department of pathology over a period of 18 months. About 120 cases of ovarian neoplasms were studied. All the specimens were fixed intoto in 10% Neutral buffered formalin and processed routinely. sections of 3-5 microns thickness were made and routine staining with haematoxylin and eosin was done. Out of 120 ovarain neoplasms,103 cases were of surface epithelial tumors . They are classified histologically into benign, borderline & malignant. In particular, serous carcinomas are histologically graded according to recent two tier grading system. Immunohistochemistry is done with P53 antibody for serous carcinomas.

III. Results

Table -1 shows the distribution of histological types of ovarian neoplasms in this study. Of a total of 120 cases , 103 cases were surface epithelial in origin. Of the 103 cases, 21 cases showed malignant histology. Table – 2 shows distribution of malignant surface epithelial neoplasms . Of a total of 21 malignant surface epithelial tumors, 18 cases were serous carcinomas. They are classified histologically into low grade and high grade based on recent two tier grading system and P53 immunohistochemical staining is applied. Table -3 shows the pattern of P53 expression in serous carcinomas. Results were interpreted as positive when the tumor cells shows diffuse and intense nuclear staining. Fig-1" shows the H& E Picture of Low grade serous carcinoma & Fig"-2 shows the P53 IHC staining pattern. Fig"-3 shows the H&E Picture of High grade serous carcinoma & Fig"-4 shows P53 IHC staining pattern.

Table- 1 Distribution Of Histological Types Of Ovarian Neoplasms

S.NO	Histological type	No.of cases	Total
1.	Surface epithelial tumor: Benign Borderline Malignant	 72 10 21	 103
2.	Germ cell tumor Benign Malignant	 12 -	 12
3.	Sex cord stromal tumor Benign Malignant	 5 -	 5
	Total	120	120

Table-2 Distribution Of Malignant Surface Epithelial Tumors Of Ovary

S.No	Histological type	No of cases
1.	Low grade serous carcinoma	4
2.	High grade serous carcinoma	14
3.	Mucinous carcinoma	4
4.	Clear cell carcinoma	1
	Total	21

Table-3 Pattern Of P53 Expression In Serous Carcinomas:

S.NO	Type of serous carcinoma	P53 expression
1.	Low grade(3/4)	Negative(75%)
2.	High grade(12/14)	Positive (85%)

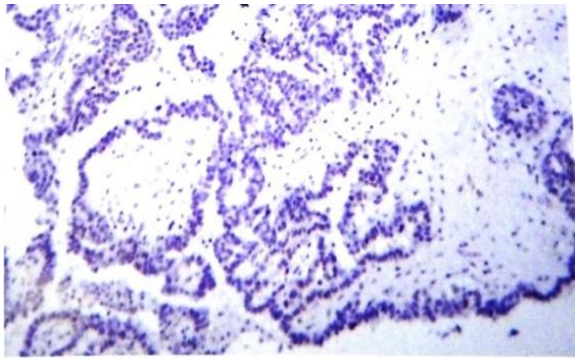

Figure-1 Low Grade Serous Carcinoma- (H&E)

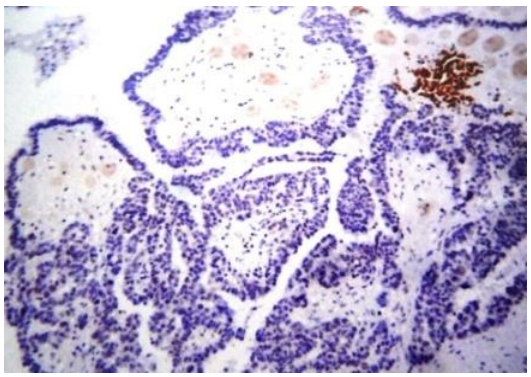

Figure -2 Low Grade Serous Carcinoma- (P53 IHC)

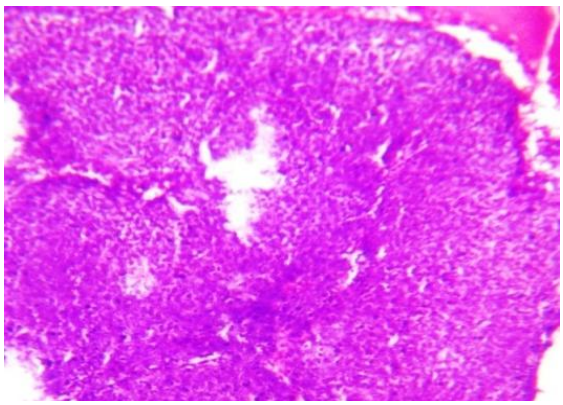

Figure-3 High Grade Serous Carcinoma- (H&E)

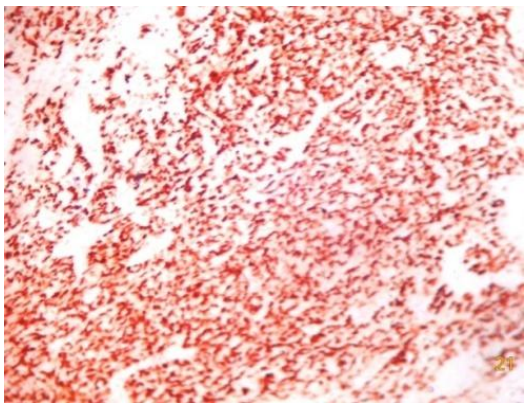

Figure-4 High Grade Serous Carcinoma- (P53 IHC)

IV. Discussion

In this study, a total of 120 ovarian neoplasms were studied, of which 103 cases were Surface epithelial tumors. Among them, 21 cases showed malignant histology. 18 cases were malignant serous tumors. They are classified into low grade and high grade serous carcinomas , based on Recent Two-tier grading system. According to Anais malpica et al[1] , this grading system includes two defined criteria, primarily on the degree of nuclear atypia with mitotic activity as a secondary feature. Low grade:1.Mild-moderate nuclear atypia and as secondary feature 2. <12 mitoses/10hpf.High grade:1.Marked nuclear atypia and as secondary feature 2. >12 mitoses/10hpf. Since this system is based on defined criteria that are easy to follow and because it involves only two diagnostic categories, it provides better reproducibility in the grading of serous carcinomas The two tier grading system is based on the evidence that low grade and high grade serous carcinomas have different pathogenesis .According to Glen Mc Cugage et al[2] low grade serous tumors are much less common and arises from a serous borderline tumor. In this study there are about 18 cases of serous carcinomas, of which 14 cases were high grade(77%), 4 cases(22%) were low grade. Of the 4 cases of low grade serous tumors, 3 cases showed areas of borderline histology. According to Jeffray et al[3] surface epithelial tumors are classified into type I and type II tumors which corresponds to two main pathway of tumorigenesis.

According to Russel vang etal [4] type I tumors are indolent neoplasms that develop in stepwise process from borderline tumors. They typically present as stage I tumors and remain as low grade tumors but can progress to high grade tumors. They include serous carcinomas,mucinous carcinomas,endometroid

carcinomas,malignant Brenner and clear cell carcinoma. In contrast type II tumors are high grade, arise as denovo, rapidly evolving,aggressive neoplasms and they typically present as advanced stage disease. They include high grade serous carcinomas,malignant mixed mullerian tumor and undifferentiated carcinoma.

In addition to clinical and pathological differences , low grade and high grade serous carcinomas have different genetic pattern. According to Ramzy et al[5], High grade serous carcinomas shows higher expression of P53, whereas KRAS &BRAF mutations are common in low grade serous carcinomas. In this study, P53 IHC was applied to both low grade and high grade serous carcinomas. Of the 14 high grade serous tumors, 12 cases(85%) stained positively for P53 , of the 4 cases of low grade tumors ,3 cases(75%) stained negatively for P53 .This finding in this study is well correlated with the studies conducted by Gad singer et al[6] and Buchynska etal[7] . Detecting P53 mutations in low grade and high grade serous tumors, helps to understand the pathogenesis and also to justify the use of recent two tier grading system in ovarian serous carcinomas in routine practice**.**

V. Conclusion

In this study a total of 120 ovarian neoplasms were evaluated histologically, of which 21 cases were malignant serous carcinomas, They are graded according to Recent Two tier grading system. P53 immunohistochemical staining was done for low grade and high grade serous carcinomas .This grading system reflects difference in pathogenesis and detecting P53 mutations helps to understand the pathogenesis of serous ovarian carcinomas which justifies the use of 2tier grading system in routine practice. Understanding the pathogenesis of these tumors provides clues for new approaches to early detection and treatment. Although discrepancies exist, epithelial ovarian malignancies showing P53 aberrations are significantly less sensitive to platinum based chemotheraphy and more aggressive than those with functional P53 and hence overexpression of P53 is a poor prognostic factor[8],[9].

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