P53 over Expression in Ovarian Neoplasms - An Immuno Histochemical Study

Dr. C. Aparna. M. D.

Associate professor, Department of pathology, Guntur medical college. Guntur. Andhra Pradesh.

Abstract:
Aim: *to study the frequency of P53 over expression in ovarian neoplasms, to evaluate the usefulness of P53 in differentiating benign from malignant tumors and also to correlate over expression with size, grade and stage of the tumor.*
Methods: *the study was done over a period of two years. Total of 96 cases were registered. For all the tumors routine H&E and Immuno Histo Chemistry (IHC) for p53 marker were done.*
Results: *out of 96 cases 61 cases were benign. 30 cases were malignant, 5 cases were borderline. All the benign tumors were negative for P53 except two cases. All the 30 malignant cases were positive for P53.*
Conclusion: *though p53 is strongly positive in malignant tumors it cannot differentiate borderline tumors from malignant tumors.*
Keywords: *P53, Immunohistochemistry, ovarian tumors.*

I. Introduction

P53 gene located on the short arm of chromosome 17 is a tumor suppressor gene. In response to DNA damage P53 is phosphorylated by genes that sense the damage and are involved in DNA repair. P53 assists in DNA repair by causing G1 arrest and inducing DNA repair genes. A cell with a damaged DNA that cannot be repaired is directed by P53 to undergo apoptosis.The ability of P53 to control apoptosis in response to DNA damage has important therapeutic , practical implications. [1]

II. Material And Methods

Ninety six cases were collected from 1-1-2012 to 31-12-2013. This is a retrospective study. Routine H&E stain was done and special stains like PAS were done whenever necessary. I HC was done on microwave fixed paraffin embedded sections for P53 marker. Representative sections were taken on poly l lysine coated slides using DAKO monoclonal antibody.

III. Statistical Analysis

Histopathology of the tumors was used as the gold standard for diagnosis. Statistical evaluation was done using chi-square test. A P value of < or equal to 0.05 was considered as significant and P value of < or equal to 0.01 as highly significant.

IV. Results :

Table1: showing the incidence of malignant tumors.

Serous cystadeno carcinoma	10
Mucinous cystadenocarcinoma	5
Endometriod adenocarcinoma	3
Granulosa cell tumor	5
Dysgerminoma	4
Embryonal carcinoma	1
Yolk sac tumor	1
Krukenberg tumor	1
Total	30

Table2 ; showing the result of P53 staining in benign and malignant cases.

	Benign	Malignant
positive	2	30
negative	59	0

V. Discussion

P53 is a tumor suppressor gene. P53 links cell damage with DNA repair, cell cycle arrest, and apoptosis. In response to DNA damage,p53 is phosphorylated by genes that sense the damage and are involved in DNA repair. P53 assists in DNA repair by causing G1 arrest and inducing DNA repair genes. A cell with

damaged DNA that cannot be repaired is directed by p53 to undergo apoptosis. In view of these activities p53 has been rightfully called as guardian of the genome. With loss of function of p53, DNA damage goes unrepaired, mutations accumulate in dividing cells, and the cell marches along a one way street leading to malignant transformation.

The ability of p53 to control apoptosis in response to DNA damage has important practical therapeutic implications. Irradiation and chemotherapy, the two common modalities of cancer treatment, mediate their effects by inducing DNA damage and subsequent apoptosis. Tumors that retain normal p53 are more likely to respond to such therapy than tumors that carry mutated alleles of the gene. [1]

However the clinical significance of p53 overexpression in patients with ovarian carcinoma is uncertain. Previous studies have yielded conflicting results. The biggest diagnostic dilemma in ovarian surface epithelial tumors is differentiating between borderline and invasive carcinomas. In the present study, out of 61 benign tumors, 59 tumors were negative(photo4,9) and two cases were positive. All the 30 malignant tumors were positive(photo1,2,3,5,6,7,8). All the five Borderline tumors were also positive, this is in contrast with" Monisha chowdary's" study.[1] out of 18 surface epithelial tumors all were positive. All six germ cell tumors were positive in contrast with" Monisha chowdary's" study. The intensity of staining is same in both borderline and invasive carcinomas. In the present study there was significant difference between benign and malignant tumors. This is in correlation with other studies.[2,3,4,5]

A p value of< 0.01 was calculated, which is highly significant. stage of the tumors ranged from stage 1c to stage 2b. . Some authors have demonstrated higher rate of P53 positivity in advanced cases.[6] No correlation between the stage of the tumor and P53 staining was found in the present study. No correlation between P53 expression between serous and non serous type was found in the present study which is in correlation with other studies. [7]Mean diameter of benign tumours was12.07cms, and that of malignant tumors was 12.8 cms. No significant association between size of the tumors and malignancy was found. Some authors like Inoue etal have found correlation of nuclear staining with missense mutations but not with nonsense mutation. No correlation between overall survival and p53 over expression was found in the present study which is in correlation with other studies.. [5]

VI. Conclusion

P53 protein immunostaining is associated with several other prognostic factors in epithelial cancers, it may not have independent prognostic value. It cannot differentiate borderline tumors from malignant tumors.

References

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[6]. Eltabbakh GH[1], Belinson JL, Kennedy AW, Biscotti CV, Casey G, Tubbs RR, Blumenson LE.p53 overexpression is not an independent prognostic factor for patients with primary ovarian epithelial cancer. Cancer. 1997 Sep 1;80(5):892-8.

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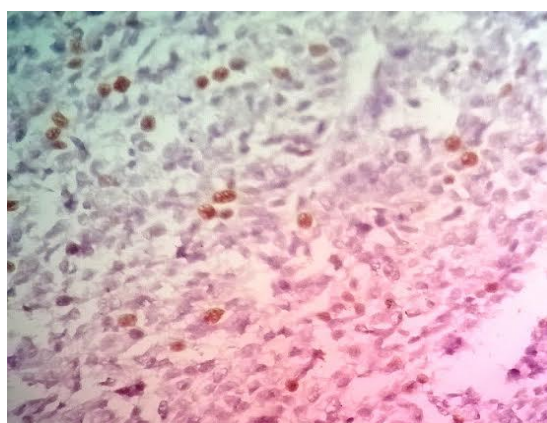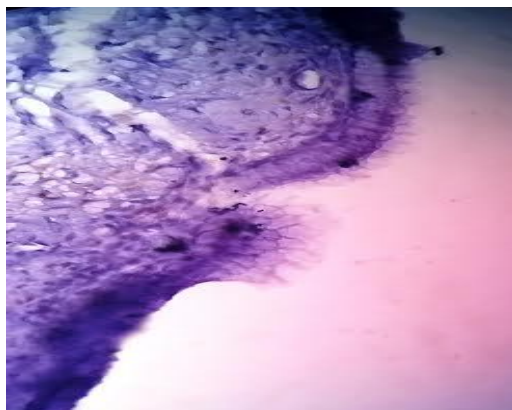
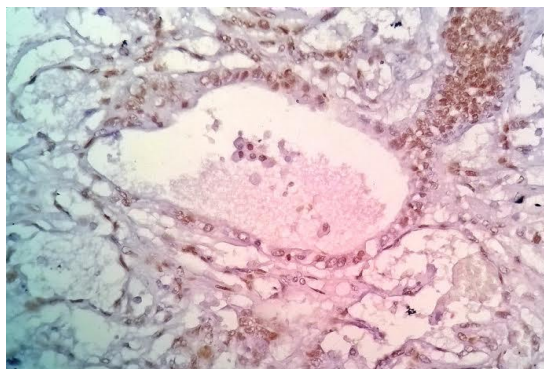**Fig1** showing nuclear positivity in endometriod ovarian cancer(IHC for p53)
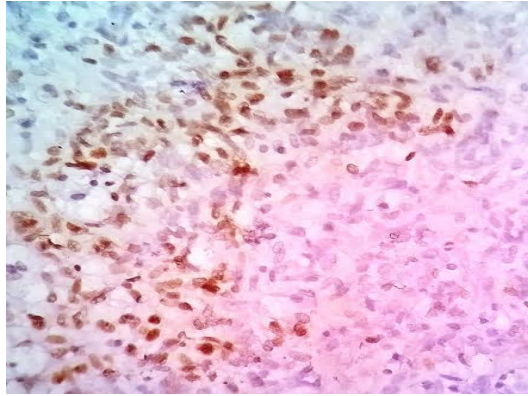
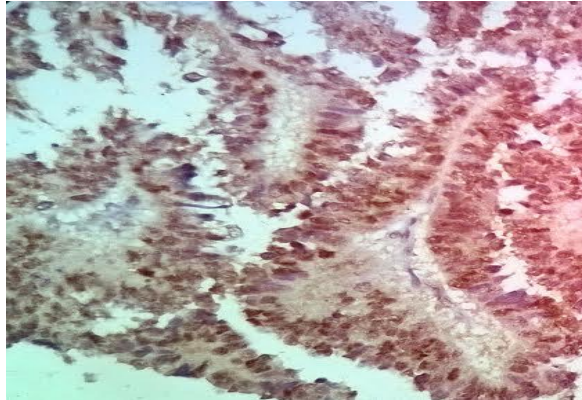**Fig2** showing nuclear positivity in granulosa cell tumor(IHC for p53)
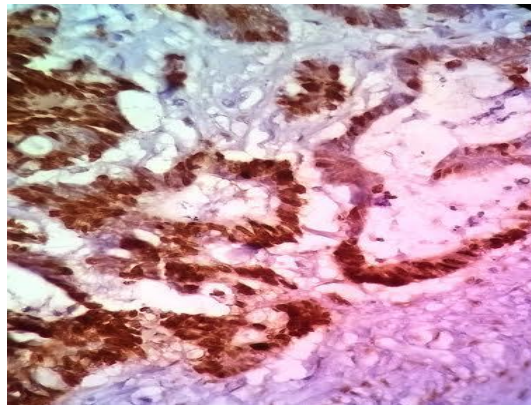
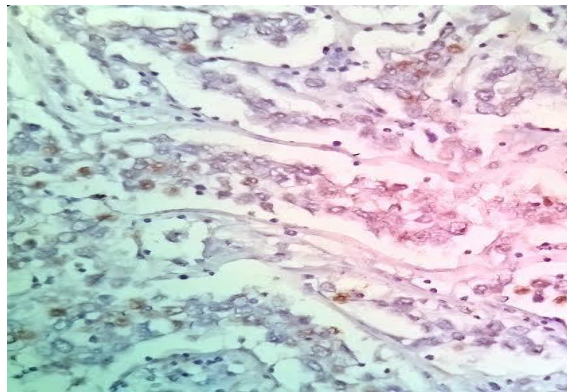**Fig3** showing strong nuclear positivity in mucinous cystaenocarcinoma.(IHC for p53)

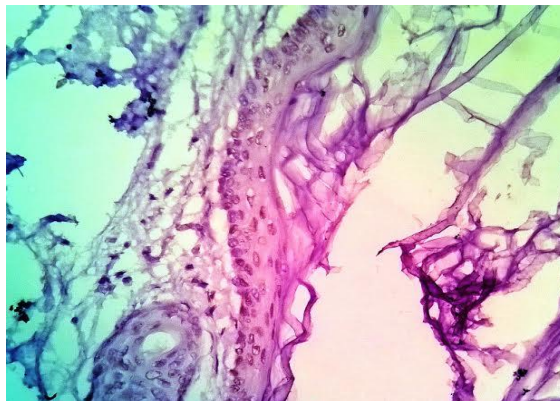**Fig4** showing negative nuclear staining in mucinous cystadenoma.(IHC for p53)

Fig5 showing nuclear positivity in mixed germ cell tumor.(IHC for p53)

Fig6 showing strong nuclear positivity in papillary serous cystadenocarcinoma.(IHC for p53)

Fig 7 showing occasional nuclear staining in dysgerminoma (IHC for p53)

Fig 8 showing negative nuclear staining in mature teratoma(IHC for p53)