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Pathology

IMMUNOEXPRESSION OF VEGF IN ENDOMETRIAL CARCINOMA AND ITS HISTOPATHOLOGICAL CORRELATION

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ABSTRACT **AIM OF THE STUDY:** The aim of this study is to study the spectrum of Histopathology of Endometrial carcinoma with special reference to Immunohistochemical expression of VEGF in Endometrial carcinoma.

OBJECTIVES:

1. To analyse the spectrum of Histopathological features of Endometrial carcinoma.
2. To Correlate the expression of VEGF in Histopathological types of Endometrial carcinoma and its targeted therapy.

Methods : In this study histopathological types and immunohistochemical expression of VEGF in 32 cases of Endometrial carcinoma was observed for a period of one year. **Result :** Out of 32 cases 20 cases are of Type I endometrial carcinoma (12 cases of well differentiated and 8 cases of moderately differentiated histological type) and 12 cases of Type II endometrial carcinoma (8 cases of uterine papillary serous type , 3 of clear cell type and 1 case of carcinosarcoma). The period of study was one year. Based on intensity of staining the percentage of cells were analysed and scoring was given from 0 - 3+ **Conclusion:** VEGF staining is increased in subset of aggressive endometrial carcinoma and appears to play regulatory roles in endometrial carcinoma angiogenesis. The observation in my study open up new perspective including novel markers that, combined together may be useful in patient screening for endometrial carcinoma aggressiveness. The combination of antivascular therapy with Docetaxel is proved to be highly efficacious.[3]

KEYWORDS :

INTRODUCTION :

In world today both in developed and developing countries endometrial carcinoma is the third most common malignancy of female genital tract. The incidence of endometrial carcinoma is rising as life expectancy increases mostly in post menopausal women and associated with high estrogen exposure, DM and HT.[1] The common age group noted is between 55 – 65 years with occurrence in younger than 40 years being 2 – 12% . Neoadjuvant chemotherapy followed by interval debulking is a valuable treatment for endometrial cancer with transperitoneal spread as cytoreduction was achieved with low morbidity.[2]

MATERIALS AND METHODS

The present is a Prospective study conducted in Department of Pathology on IMMUNOEXPRESSION OF VEGF IN ENDOMETRIAL CARCINOMA AND ITS HISTOPATHOLOGICAL CORRELATION " for a period of one year. 32 cases of endometrial carcinoma were analysed during the period of 1 year.

Specimen :

All endometrial carcinoma specimen – Biopsy and hysterectomy specimen proven by histopathology.

Collection of data:

Methodology and techniques:

10 % Formalin fixed specimen are received and the gross (macroscopic) features are noted. Then the tissue is processed routinely. Paraffin sections are cut at 4- 5 micrometres thickness and stained with haematoxylin and eosin stain and examined under light microscope. The tumour sections are classified into Type I and Type II based on Histopathological features. For immunohistochemical study, the sections of 4mm thickness are cut and taken in coated slide.

The coated slides with sections are incubated overnight at 58 degrees. The incubated slides are ready for immunohistochemistry study which is carried by two step indirect technique.

Immunohistochemical markers used: VEGF(Vascular Endothelial Growth Factor)

Interpretation:

VEGF positivity will be indicated by cytoplasmic positivity of tumour cells.

A semi quantitative score based on two parameters to describe the intensity and immunostaining for VEGF is used. Based on percentage of positive cells and intensity of colouration the score summed up.

Base intensity of staining:

0 - Negative, 1 – Weak, 2 - Moderate, 3 - Strong

Percentage of positive cells :

0 - Negative (no or 0% immunopositive cells)
1 - positive in < 25% of tumour cells ,
2 - positive in 26 – 50% of tumour cells ,
3 - positive > 50% of tumour cells cytoplasm

Final score:

Following the immunohistochemical reaction final score obtained by summing up the two parameters

Negative - (0 – 2), Moderate Positive - (3 – 4), Strong Positive - (5 – 6)

Statistical analysis:

The data collected in my study is coded and entered in Microsoft excel spread sheet and is analyzed using percentage and ratios. Correlation between the histopathologicals results and immunohistochemical reaction were calculated using Chi – square test.

Results :

ASSOCIATION OF CLINICAL VARIABLES WITH HISTOPATHOLOGIC GRADES [N=32]

	HISTOPATHOLOGIC TYPES				
	TYPE I	(%)	TYPE II	(%)	sig
AGE					
31 - 40	2	6%	0	0%	>0.05
41 - 50	4	16%	7	19%	
51 - 60	7	13%	2	19%	
61 - 70	7	13%	1	13%	
> 70 Years	0	3%	1	0%	
SYMPTOMS	20	63%	12	37%	>0.05
DUB	8	25%	4	13%	
AMENNORHOEA	2	6%	1	3%	
PAIN ABDOMEN	7	22%	3	9%	
PAINBLEEDING	0	0%	1	3%	

PM BLEEDING	3	9%	3	9%	
Types	20	63%	12	37%	<0.01
MDE	8	25%	0	0%	
UPSC	0	0%	8	25%	
WDE	12	38%	0	0%	
CC	0	0%	3	9%	
CS	0	0%	1	3%	
Positivity of cells	20	63%	12	37%	<0.05
1+	8	25%	3	9%	
2+	12	38%	2	6%	
3+	0	0%	7	22%	

Endometrial carcinoma is usually occurred in women with age group above 55 years. In my present study most common age group presenting with Endometrial carcinoma is 41-50 years. According to above study, the mean age is 54.96 years.

ENDOMETRIAL CARCINOMA - HISTOLOGIC TYPES :

Among the Histologic types of Endometrial carcinoma, the histological variants, WDE and MDE of Type I constitute 38% & 25% respectively. The Histological variants of Type II, UPSC, CC and CS constitute 25%, 09% and 03% respectively.

Intensity of VEGF staining pattern in Endometrial Carcinoma was tabulated. Out of 32 cases studied, 47% of cases showed moderate intensity of staining followed by 31% weak intensity of staining and 22% strong intensity of Staining.

ASSOCIATION OF HISTOPATHOLOGICAL TYPES OF ENDOMETRIAL CARCINOMA WITH INTENSITY OF STAINING OF VEGF

	INTENSITY OF STAINING OF VEGF				
TYPES	Weak	Moderate	Strong	Total	Percentage
WDE	7	5	0	12	38%
MDE	0	8	0	8	25%
UPSC	0	2	6	8	25%
CC	0	0	3	3	9%
CS	0	0	1	1	3%
Total	10	15	7	32	100%

(WDE- well differentiated, MDE- moderately differentiated, UPSC-uterine papillary serous carcinoma, CC-clear cell carcinoma, CS-carcinosarcoma.)

In the present study the association of histopathological types with intensity of staining of VEGF shows that Type I Endometrial carcinoma presented with weak and moderate intensity and Type II Endometrial Carcinoma with strong intensity of staining and with Significant P value (P<0.01).

DISCUSSION

In any solid tumours the vascular stroma must be induced to grow beyond size. Neoangiogenesis in tumour has an important effect in prognosis of the patient as well as in therapy. In Endometrial carcinoma angiogenesis has an important role in tumour growth, invasion, and in metastasis.

In Endometrial carcinoma VEGF (vascular endothelial growth factor), angiopoietin are major angiogenetic factors essential for angiogenesis and tumour progression. In present study Total of 32 cases of Endometrial carcinoma were studied histopathologically and the Immunoexpression of VEGF in Endometrial carcinoma was correlated. Among the 32 cases Type I Endometrial carcinoma was 20 cases and Type II Endometrial carcinoma were 12 cases.

In the present study the common age group of women was in between 40 – 60 years with usual presentation above 50 years. The mean age of the present study was 54.96 years.

The commonly presented symptom was dysfunctional uterine bleeding constituting 38%, followed by abdomen pain of 31%, amenorrhoea of 9% and postmenopausal bleeding of 3%.

Among the 20 cases of Type I Endometrial carcinoma in the present study 12 cases were of Well differentiated grade constituting 38% and 8 cases were of moderately differentiated grade constituting about 25%.

Of the 12 cases of Type II Endometrial carcinoma 8 cases were of Uterine serous papillary type constituting 25%, 3 cases were of clear cell type constituting 9% and 1 was of carcinosarcoma constituting 3%.

The common Architectural pattern in the present study is glands in 42% of cases and glands and sheets in 38% of cases. Solid pattern of growth in 20 % of cases.

EXPRESSION OF VEGF (Vascular Endothelial Growth Factor)

Expression of VEGF in Endometrial carcinoma Assessed by Semi quantitative score using Immunohistochemistry (the positivity of cells stained by VEGF and staining pattern), it is observed that 11 cases showed weak positivity constituting 34 % , 14 moderate positivity constituting 44% and 7 strong positivity constituting 22% (which included uterine papillary serous cell carcinoma and clear cell carcinoma).

INTENSITY OF STAINING PATTERN OF VEGF:

In the present study among the 20 Cases of Type I Endometrial carcinoma (Endometrioid) 7 cases showed weak staining and 13 cases moderate staining.

In 12 cases of Type II Endometrial carcinoma, weak staining was observed in 2 cases, moderate staining in 3 cases and strong staining in 7 cases.

On Chi-square analysis, the weak staining pattern more commonly associated with Type I Endometrial carcinoma constitute 70 % and strong staining pattern more associated with Type II Endometrial carcinoma constituting > 90 % with significant P value of < 0.5 (P < 0.5).

In the present study analysis of the association of staining intensity of VEGF with Histopathological types, showed 7 cases with weak staining intensity which were of well differentiated endometrioid, 8 cases are of with moderate intensity of staining which were Moderately differentiated Endometrioid and 7 cases of strong intensity which were uterine papillary serous carcinoma and clear cell carcinoma. Based on staining pattern it was evident that Type I endometrial carcinoma were associated with weak and moderate staining and Type II carcinoma with strong intensity of staining.

Strong expression of VEGF in tumour cells provided an evidence of VEGF as an important angiogenetic regulator which provided base for antiangiogenetic therapy[4,5].

CONCLUSION:

1. VEGF staining is increased in a subset of aggressive endometrial carcinoma and appears to play regulatory roles in endometrial carcinoma angiogenesis .

2. Recently studies are done for anti – angiogeneic targeted therapy based on immunoexpression of VEGF which help in reduction of the tumor size and prevent metastasis. Recent drugs like Bevacizumab and Docetaxel are used in targeted therapy.

3. The observation in my study open up new perspective including novel markers that, combined together, useful in patient screening for endometrial carcinoma aggressiveness[4].

4. The combination of targeted therapy drugs like Bevacizumab and Docetaxel are used in targeted therapy along with surgery may be more useful and has an increased survival rate[3]

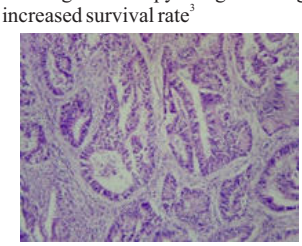

Figure 1: H&E shows well differentiated endometrioid carcinoma (40X)

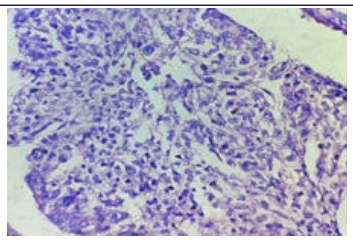

Figure 2: H&E shows clear cell carcinoma (40X)

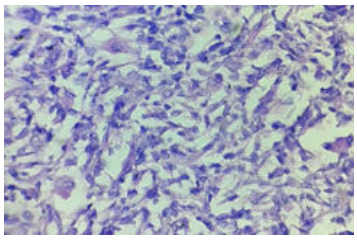

Figure 3: H&E shows carcinosarcoma – Sarcomatous component (40X)

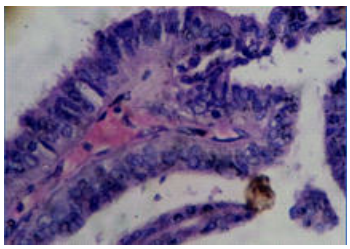

Figure 4: H&E shows uterine papillary serous carcinoma (40X)

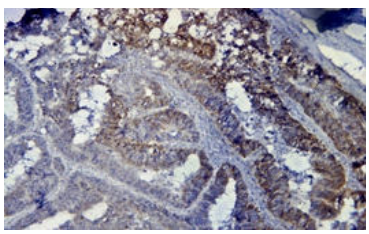

Figure 5: Immunoexpression of VEGF showing focal and weak positivity in WDE (10X)

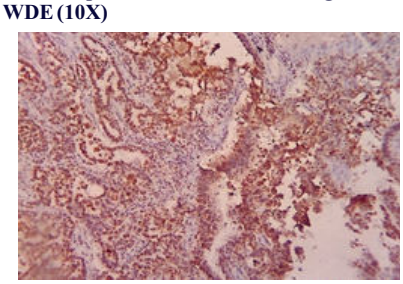

Figure 6: Immunoexpression of VEGF showing moderate intensity and positivity (10X)

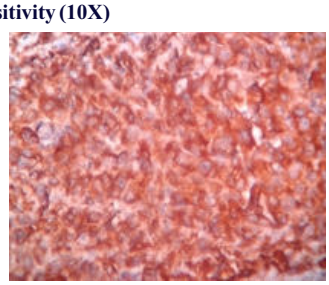

Figure 7: Immunoexpression of VEGF showing strong and diffuse positivity in carcinosarcoma (40X)

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