ORIGINAL RESEARCH PAPER

Pathology

KEY WORDS: Endometrial carcinoma, TTF 1

A STUDY OF EXPRESSION OF THYROID TRANSCRIPTION FACTOR (TTF-1) IN ENDOMETRIAL ADENOCARCINOMA OF UTERINE CORPUS

Dr .M. Brinda Assistant Professor, Department Of Pathology, Thanjavur Medical College Thanjavur ,Tamilnadu .

Dr. S. Maheswari* Assistant Professor, Department Of Pathology, Government Mohankumara mangalam Medical College, Salem, Tamilnadu *Corresponding Author

Dr. Sasikumar Sambasivam Consultant Radiation Oncologist, Meenakshi Mission Hospital ,Thanjavur, Tamilnadu.

ABSTRACT

Among females endometrial carcinoma is the most frequent malignancy worldwide. Thyroid transcription factor has been regarded as a specific and sensitive marker for tumors arising in thyroid and lung. But some studies state that TTF 1 marker is also expressed in endometrial adenocarcinoma. The aim of this study is to probe the incidence of Thyroid transcription factor expression in primary uterine endometrial adenocarcinoma and to correlate the percentage of expression of TTF-1 with the grade of endometrial adenocarcinoma. TTF 1 immunohistochemistry was done for 50 cases out of which two cases of moderately differentiated endometrioid adenocarcinomas and 1 case of poorly differentiated endometrioid adenocarcinoma showed focal and diffuse positivity respectively .

INTRODUCTION

Among females endometrial carcinoma is the most frequent malignancy worldwide[1]. Each year about one lakh fifty thousand cases are diagnosed world wide[2,3].It is the second most frequent malignancy of gynecological tract in developing nations having an incidence of approximately six cases per one lakh population.[4,5].The mean age for the occurrence of endometrial carcinoma is between the age range of fifty to sixty years.

Endometrial carcinoma is classified broadly in to two categories TYPE I and TYPE II. Estrogen stimulation is strongly associated with TYPE 1 carcinoma. In TYPE II carcinoma mostly postmenopausal women are affected whereas in TYPE I both premenopausal and postmenopausal women are involved. Mostly TYPE I tumors are low grade , TYPE II tumors are associated with high grade tumors.

The main features of prognosis of endometrial adenocarcinomas depends tumor on type, stage and grade[6]. Thyroid transcription factor (TTF-1) immunostain is typically associated with lung and thyroid malignancies. Some studies have stated its positivity in endometrial carcinomas ,also in ovarian and cervical carcinomas[6,7,8].

This study is undertaken to probe Thyroid transcription factor positivity in primary uterine endometrial adenocarcinoma and also in malignant mixed mullerian tumour .

AIMS AND OBJECTIVES

1) To study the incidence and distribution of Thyroid transcription factor in endometrial adenocarcinoma.
2) To correlate the percentage of expression of TTF-1 with the grade of endometrial adenocarcinoma and assess the prognosis based on the expression of TTF-1 for the patients who were on follow up.

MATERIALS AND METHODS

This study is a prospective and retrospective study of endometrial cancer in hysterectomy specimens conducted in the Institute of pathology at Institute of obstetrics and gynaecology ,Madras Medical College and Rajiv Gandhi Government General Hospital,Chennai during the period between January 2010 to December 2014.

Inclusion criteria:

Patients diagnosed as Endometrial adenocarcinoma - conventional type & its variants, Malignant mixed mullerian tumor of uterus.

Exclusion criteria:

Benign tumors and non epithelial tumors of uterus. A total of 93 endometrial carcinoma cases were reported at Institute of pathology, Institute of obstetrics and gynaecology Madras medical college during the period of January 2010 to December 2014 .

Detailed history of the cases regarding age, menstrual status, clinical history, parity, and staging laparatomy were obtained for all the 93 endometrial carcinoma cases reported during the period of study from surgical pathology records. Hematoxylin and Eosin stained 4 µ thick sections of the paraffin tissue blocks of specimens were reviewed and fifty cases were randomly selected and their representative formalin fixed and paraffin embedded tissue samples was subjected for TTF 1 immunohistochemistry. Sections from thyroid were used as positive control.

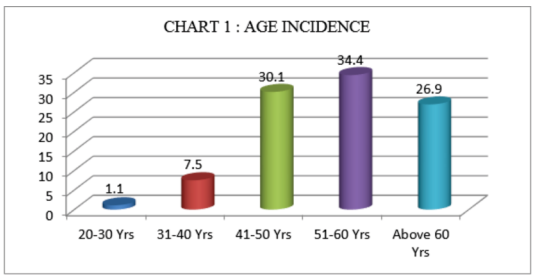
TTF 1 nuclear staining was scored based on scoring done by W Glen McCluggage[6].

1) Negative (absent)
2) Focal (< 50 % nuclear staining)
3) Diffuse (>50% nuclear staining)

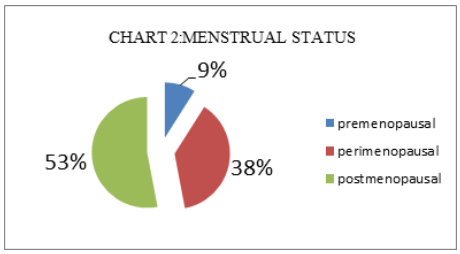
OBSERVATION AND RESULTS

Majority about 53 cases were well differentiated endometrioid adenocarcinoma including one villoglandular variant,15 cases were endometrioid adenocarcinoma moderately differentiated , 16 cases were endometrioid adenocarcinoma poorly differentiated , 1 serous carcinoma, 3 clear cell carcinoma , 4 cases of malignant mixed mullerian tumour and 1 case of undifferentiated carcinoma were reported.

In our study about 32 cases were reported in age group fifty one to sixty years years. The youngest age and oldest age at which endometrial carcinoma was diagnosed in this study is 27 years and 78 years.



In our study, most women with endometrial carcinoma were postmenopausal .

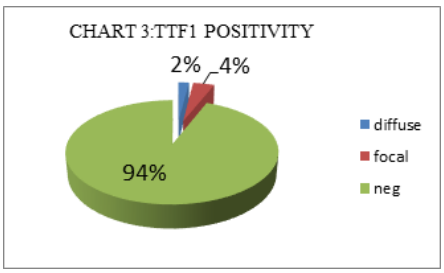


The parity status was 82.8 % multiparous and 17.2 % women were nulliparous .

The incidence of Type 1 carcinoma was 73% and Type 2 carcinoma 27%. Majority of cases of endometrial carcinoma in this 5 year study presented in stage IA with a percentage of 46.2%, 25 cases presented in stage IB ,12 cases in stage II,6 cases in stage IIIA, 1 case in stage IIIB,2 cases each in stage IIIC1 and IIIC2,1 case in stage in stage IVB.

For 50 cases paraffin blocks were retrieved and TTF 1 immunohistochemistry was done, out of which 30 cases were well differentiated endometrioid carcinoma (Grade 1),8 cases were Grade 2,7 cases were Grade 3 endometrioid carcinoma, 2 cases were clear cell carcinoma and 3 cases MMMT.

Only 3 cases showed positivity for TTF 1. On correlating TTF1 expression with grade of endometrioid carcinoma diffuse positivity was present for one case of poorly differentiated endometrioid carcinoma, focal positivity was present for 2 cases of moderately differentiated endometrioid carcinoma.



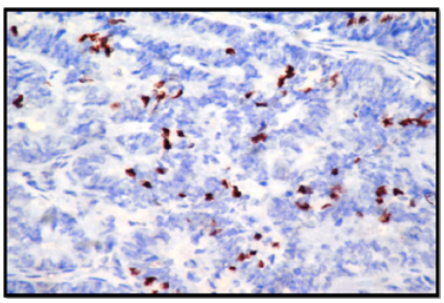


Figure 1 : Focal nuclear positivity for TTF 1 in moderately differentiated endomatrioid adenocarcinoma

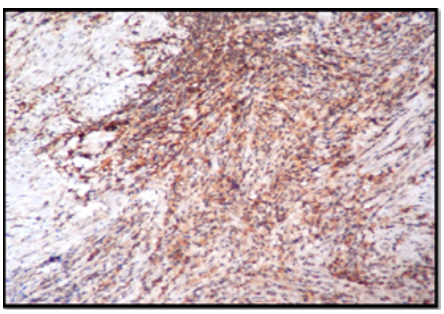


Figure 2: Diffuse nuclear positivity for TTF 1 in poorly differentiated endometrioid adenocarcinoma

DISCUSSION

Endometrioid carcinoma represents about 90% of the total cases in this study. This is in accordance with the study done by **Nirmala et al** [9] , in which endometrioid type constitutes 75–80 %

In our study out of 38 cases, only 2 cases of low grade endometrioid adenocarcinoma showed focal positivity for TTF 1 accounting for 5%. This is in concurrence with the study by **Aaron ervine et al** [6] where for 100 cases of low grade endometrioid carcinoma only 2 cases showed positivity for TTF 1.

Out of 7 cases of poorly differentiated endometrioid carcinoma only one case showed diffuse positivity accounting for 14%.This is in concurrence with the study done by **Aaron et al** [6], where out of total 101 cases of poorly differentiated endometrioid carcinoma , 89% cases are negative, 7% cases are diffusely positive, 4% are focally positive.

TTF 1 was negative in two cases of clear cell carcinoma in our study. This is in concurrence with the study by **Jaudah Al-Maghrabi et al** [7]. But in another study **Aaron et al** , TTF 1 positivity was found in 2 cases out of 29 cases.For 3 cases of MMMT ,all were negative for TTF 1.But according to **Zhang et al** [124],TTF 1 expression present in 82% cases of MMMT.

The three cases which showed positivity for TTF 1 ,in one case staging was not done as the specimen was received in fragments and the other two low grade endometrioid carcinoma ,one was in stage IA and other was in stage IB.

According to the study done by **Aaron et al** [6],TTF 1expression in low grade endometrioid carcinoma is associated with poor prognosis but in our study out of the 2 positive cases of low grade endometrioid carcinoma ,follow up could not be traced for one and in the other case which was followed up for 18 months no difference in survival was noted , so comment on the prognosis can be made only on long term follow up.

CONCLUSION

In this study, only 3 cases of endometrial carcinoma showed positivity for TTF 1 and the relationship between TTF 1 positivity with grade of endometrial carcinoma was significant though majority of cases of endometrial carcinoma were negative for TTF 1 .

REFERENCES

1) N.colombo et al .Endometrial cancer:ESMO clinical practice guidelines for diagnosis,treatment and follow up. Annals of oncology 24(supplement 6) vi 33–vi38,2013.
2) Parazzini F et al (1997). The epidemiology of female genital tract cancers. Int J Gynecol Cancer 7:169–181.
3) Parazzini F et al (1991). The epidemiology of endometrial cancer. Gynecol Oncol 41:1–16.
4) Jemal A,Bray F et al.Global cancer statistics.CA Cancer J Clin2011;61:69-90.
5) Siegel R,Ward E et al.Cancer statistics 2011:The impact of eliminating socioeconomic and racial disparities on premature cancer deaths.CA Cancer J Clin 2011;61:212-36.
6) Aaron ervine &WGienn McCluggage et al. Thyroid transcription factor-1 immunoreactivity is an adverse prognostic factor in endometrioid adenocarcinoma of the uterine corpus..Histopathology 2014,64,840-846.
7) Jaudah Al-Maghrabi(MD, FRCPC)et al .Expression of Thyroid Transcription Factor-1 (TTF-1) in Endometrial Carcinoma..Life science journal 2014:11(4).
8) Kubba LA,McCliggage et al.Thyroid transcription factor 1 expression in ovarian epithelial neoplasms.Mod.Pathol.2008;21;485-490.
9) Nirmala Srikantia et al.Endometrioid endometrial adenocarcinoma in a premenopausal woman with multiple organ metastases.Indian J Med Paediatr Oncol.2009 Apr-Jun;30(2):80-83.
10) Zhang PJ, Gao HG, Pasha TL, Litzky L, LivolsiVA. TTF-1 expression in ovarian and uterineepithelial neoplasia and its potentialsignificance, an immunohistochemicalassessment with multiple monoclonal antibodiesand different secondary detection systems. Int JGynecol Pathol 2009;28(1):10-18.