STUDY OF Ki-67 EXPRESSION IN ENDOMETRIAL CARCINOMA.

Pathology

Dr. Prateek. D. Deshmukh*	Post graduate trainee, Department of pathology, KMCRI, HUBLI. *Corresponding Author
Dr. Sateesh Chavan S	Professor, Department of pathology, KMCRI, HUBLI.
Dr. Sunita S Vernekar	Professor and Head, Department of pathology, KMCRI HUBLI.

ABSTRACT

Endometrial carcinoma is the fourth most common malignancy in women and incidence is increasing both in developed and developing countries. Ki-67 is a well known marker of cell proliferation and its expression is upregulated in many cancers. The aim is to study the immunoexpression of ki-67 in endometrial carcinoma. The study was conducted from July 2022 to January 2024. Immunohistochemistry for Ki-67 was done for 10 cases of endometrial carcinoma. 6 cases of endometrial carcinoma showed high ki-67 index, followed by 3 cases showing low Ki-67 index and 1 case showed intermediate Ki-67 index. Ki-67 expression increased as the lesion progressed from well differentiated to poorly differentiated tumour.

KEYWORDS

Ki-67 (Kiel), MIB-1 LI (Mindbomb homolog-1)

INTRODUCTION

The expression of Ki-67 is strongly associated with tumor cell proliferation and growth, and is widely used in pathological investigations as a proliferation marker. The nuclear protein Ki-67 (pKi-67) is an established prognostic and predictive indicator for the assessment of biopsies from patients with cancer. Clinically pKi-67 has been shown to correlate with metastasis and the clinical stage of the tumours. In addition it has been shown that Ki-67 expression is significantly higher in malignant tissues with poorly differentiated tumour cells, as compared with normal tissue. The expression of Ki-67 reflects the tumour proliferation rate and correlates with initiation, progression, metastasis and prognosis of a number of types of tumours. Studies thus far have shown a positive correlation between Ki-67/MIB-1 LI and tumour grade in human malignancy.

There is a need for the pathologist to widen the thought process to find the right diagnosis, because diagnosis is the need for exact treatment. The incidence and mortality rate of endometrial cancer has been registering an increasing trend in the world.

Endometrial carcinoma is one of the most important malignancies affecting women all over the world accounting for 37.7 % of all other disorders affecting the female reproductive system. The expression of the Ki-67 protein is related to the proliferative behaviour of malignant tumour cell populations of their own, allowing it to be used as a marker of tumour aggressiveness. Apart from the genital area, the frequency of appearance of endometrial cancer follows the breast, colon and lung cancers. The maximum incidence is registered in post menopause between 60 and 64 years old, but an increase in the premenopausal endometrial carcinoma has also been registered.

Despite its relative frequency, the molecular events that contribute to the development and progression of endometrial carcinoma remains poorly understood.

The normal human endometrium is characterised by hormone dependent variation during menstrual cycle.

MATERIALS AND METHODS :

The study was carried out in the department of pathology KIMS HUBLI from July 2022 to January 2024. Patients who underwent dilatation and curettage and hysterectomy were included in the study. Clinical data regarding age, menstrual history, presenting complaints were obtained. Tissues were formalin fixed and paraffin embedded and were sectioned and stained with haematoxylin and eosin.

Ki-67 IMMUNOSTAINING :

The conventional 3-4 micron sections are cut from paraffin blocks and the immunohistochemical staining procedure is performed using the heat induced antigen retrieval method with specific murine monoclonal antibody M1B1 and the labelling index is done. Labelling index is measured as percentage of M1B1 positive cells in a 1000 randomly selected tumour cells. Only nuclear staining is regarded as positive, weak nuclear or cytoplasmic staining is regarded as negative. The percentage of positively stained nuclei within 3 high power fields (x 40 magnification) randomly selected across the tumour was calculated, ensuring at least 1000 nuclei were counted.

Ki-67 LABELLING INDEX :

The conventional 3-4 micron sections are cut from paraffin blocks and the immunohistochemical staining procedure is performed using the heat induced antigen retrieval method with specific murine monoclonal antibody M1B1 and the labelling index is done. Labelling index is measured as percentage of M1B1 positive cells in a 1000 randomly selected tumour cells. Only nuclear staining is regarded as positive, weak nuclear or cytoplasmic staining is regarded as negative. The percentage of positively stained nuclei within 3 high power fields (x 40 magnification) randomly selected across the tumour was calculated, ensuring at least 1000 nuclei were counted.

SAMPLE SIZE ESTIMATION

Since it is a time bound study, all the specimen received during study period (July 2022 to January 2024) will be considered for the study satisfying inclusion and exclusion criteria.

Inclusion Criteria: all dilatation and curettage and uterus specimens received in the department of pathology KMCRI HUBLI.

Exclusion Criteria: autolysed uterus specimens.

RESULTS

A total of 21 cases of endometrial carcinoma were studied. A total of 10 cases of endometrial carcinoma were IHC stained. 6 cases (60 %) of endometrial carcinoma showed high Ki-67 index, followed by 3 cases (30 %) showing low Ki-67 index and 1 case (10 %) showed intermediate Ki-67 index.

Table 1 Showing Endometrial Carcinoma Types

| Types of Endometrial Carcinoma	Number of Cases	Percentage
Well differentiated endometrial carcinoma	9	42.85
Moderately differentiated endometrial carcinoma	10	47.61
Endometrial carcinoma with squamous differentiation	1	4.76
Clear cell variant of endometrial carcinoma	1	4.76

Majority of endometrial carcinoma were moderately differentiated (10 cases, 47.61 %) followed by well differentiated (9 cases, 42.85 %)

and least were endometrial carcinoma with squamous differentiation and clear cell variant (1 case each, 4.76 %)

Table 2 Showing Myometrial Invasion Of Endometrial Carcinoma

Myometrial invasion	Number of Cases	Percentage
Less than half of thickness of myometrial invasion	8	38.09
More than half of thickness of myometrial invasion	13	61.90

More than half of endometrial carcinoma (61.9 % , 13 cases) showed myometrial invasion of more than half of thickness of myometrium and rest (8 cases, 38.09 %) were within half of thickness of myometrium.
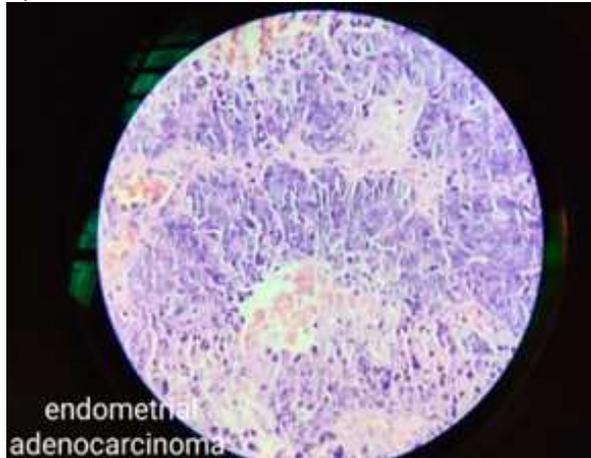
Figure 1 : Microscopic image of endometrial adenocarcinoma 40 x
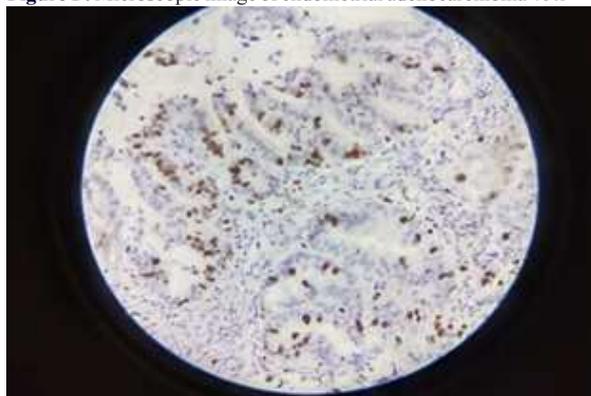
Figure 2 : IHC image showing ki-67 positive endometrial carcinoma

Figure 3 : Cut surface of utero cervix specimen

DISCUSSION

Ki – 67 : the positive expression of ki-67 was defined as the presence of brown yellow granules in cell nuclei or in both cell nuclei and cell membrane. Ki-67 protein is a marker of cell proliferation. Ki-67 is an antigen present in the nuclei of all the phases of cell cycle as well as in mitosis, but quiescent cells in the G0 phase do not express it. Ki-67 is an excellent marker to determine the growth fraction of a cell population. The fraction of ki-67 positive tumour cells is often correlated with the clinical course of the cancer.

Table 3 Comparative Analysis Of Endometrial Carcinoma Observed

Endometrial lesion	Present study	Sarika et al
Endometrial carcinoma	16.27 %	1.98 %

Table 4 Distribution Of Endometrial Carcinoma Types

Types of endometrial carcinoma	Present study (n = 21)	Gouthaman S et al (n = 35)
Endometrial carcinoma	20	30
Clear cell variant of endometrial carcinoma	1	-
Papillary serous carcinoma	-	4
Mixed carcinoma	-	1

Table 5 Showing Myometrial Invasion Of Endometrial Carcinoma

Myometrial invasion	present study (n = 21)	Goutham S et al (n = 35)
Less than half of thickness of myometrium	8	27
More than half of thickness of myometrium	13	8

Table 6 Showing Endometrial Carcinoma And Ki-67 Index

	Low ki-67 index	Intermediate ki-67 index	High ki-67 index
Present study	30 %	10 %	60 %
Alunmaiyi et al	50 %	50 %	-
Sarah Kitson et al	-	37 %	68 %

CONCLUSION

The expression of the Ki-67 protein is related to the proliferative behaviour of the proliferating cell populations, allowing it to be used as a marker of tumour aggressiveness. Ki-67 protein expression is believed to be a valuable marker of cell growth and proliferation. Endometrial carcinoma showed rise in ki-67 score from low to high as it invades myometrium beyond half of its thickness.

Majority of endometrial carcinoma were moderately differentiated (10 cases, 47.61 %) followed by well differentiated (9 cases , 42.85 %) and least were endometrial carcinoma with squamous differentiation and clear cell variant (1 case each, 4.76 %). Over half of them (61.9 %, 13 cases) showed myometrial invasion of more than half of thickness of myometrium and rest (8 cases, 38.09 %) were within half of thickness of myometrium.

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