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Original Research Paper

Pathology

APOPTOTIC INDEX- A PROGNOSTIC PARAMETER IN ENDOMETRIAL LESIONS - HYPERPLASIA AND CARCINOMAS

Dr Natasha Makkar MD Patholgy Assistant Professor, Department Of Pathology, Government Doon Medical College, Dehradun

ABSTRACT

BACKGROUND: Endometrial cancer is the most common gynaecological malignancy affecting women in developed countries and the second most common gynaecological malignancy world-wide. The apoptotic index, defined as the percentage of morphologically identified apoptotic cells per 100 non apoptotic cells. Apoptosis is observed at increasing levels in the hyperplasia, atypia, adenocarcinoma sequence.

METHODS: In all hysterectomy cases, histological findings and apoptotic index was noted. The cases were divided into five categories. Mean apoptotic index was calculated in each category and comparison was done.

RESULTS: Edometrial carcinoma had significantly higher apoptotic index than other categories (p-value =0.000). An increasing mean apoptotic index was noted in complex hyperplasia categories than in simple hyperplasia ones.

CONCLUSION: Apoptotic index gradually increases with increasing complexicity in endometrium.

KEYWORDS : Endometrial carcinoma, Endometrial hyperplasia, Apoptotic Index

INTRODUCTION

Endometrial cancer is the most common gynaecological malignancy affecting women in developed countries and the second most common gynaecological malignancy world-wide, due to the higher rates of cervical cancer in the developing world[1].Most women are diagnosed at an early stage and have relatively good survival rates; however, women who are diagnosed with advanced-stage or recurrent disease have a poor prognosis[2]. The incidence of endometrial carcinoma is steadily increasing, largely owing to an ageing population and escalating rates of obesity[3].

Endometrial hyperplasia is a uterine pathology representing a spectrum of morphological endometrial alterations. It is predominantly characterized by an increase in the endometrial gland-to-stroma ratio when compared to normal proliferative endometrium. The clinical significance of endometrial hyperplasia lies in the associated risk of progression to endometrioid endometrial cancer and 'atypical' forms of endometrial hyperplasia are regarded as premalignant lesions[4]. The incidence of endometrial hyperplasia is roughly three times higher than endometrial carcinoma and certain atypical forms of endometrial hyperplasia are considered to represent direct precursor lesions to endometrioid endometrial carcinoma[5].

Apoptosis is a complex and finely regulated process linked to cellular proliferative activity. Apoptotic index is defined as a measure of the rate of death of cancer cells within a tumour. This is estimated by determining the proportion of dying or apoptotic cells per 100 cancerous cells[6]. It is an important prognostic marker which can be easily predicted for patients with malignant tumours, and this possibility has been tested in patients with several tumour types[7].

The apoptotic index, defined as the percentage of morphologically identified apoptotic cells per 100 non apoptotic cells. Apoptotic index can be readily estimated in routine hysterectomy specimens showing endometrial lesions. A high apoptotic index shows an association with features normally correlated with a poor clinical outcome although its value as an independent prognostic index has yet to be established[8].

AIM

The aim of this study was to determine if any association exists between apoptotic index and endometrial lesions (hyperplasia and carcinoma) in hysterectomy specimens.

MATERIALS AND METHODS

A retrospective study was conducted in the Department of pathology, Combined Medical Institute, on the hysterectomy specimens obtained from June 2013 to May 2016. In each case, a detailed clinical history and histological findings were noted along with assessment of apoptotic index.

On basis of histological findings, endometrial lesions were divided into two broad categories- hyperplasia and carcinoma. Hyperplastic lesions were further categorised into four categories based on The World Health Organisation 1994 classification of EH [09].

Apoptosis was assessed in light microscopy by using high magnification (oil immersion X 100 lens)[10]. For calculation of apoptotic index, 10 high power fields were analyzed. Number of apoptotic bodies per 100 non apoptotic cells was the apoptotic index for that tumour[11]. Areas of artefactual change, necrosis and inflammatory exudates along with luminal apoptotic bodies were excluded[12].

The mean apoptotic index was calculated for all the categories. ANOVA test was applied to find out whether or not the means of all the grades were equal by calculating p- value. Post-Hoc test was applied to find out which of the grades show significant difference in mean apoptotic index[13].

RESULTS

The present study was conducted over a period of 3 years comprised a total of 68 hysterectomy specimens. H&E sections were studied to determine the histological findings and apoptotic index. On basis of morphology, the cases were divided into five histological types (Table/Fig 1).

HISTOLOGICAL TYPE OF ENDOMETRIAL LESIONS. (Table/Fig 1)

DIAGNOSIS	CASES	PERCENTAGE (%)
Simple hyperplasia without atypia	22	32.4
Simple atypical hyperplasia	7	10.3
Complex hyperplasia without atypia	18	26.4
Complex hyperplasia with atypia	12	17.6
Endometrial Adenocarcinoma	09	13.3
TOTAL	68	100

Apoptotic index was calculated for all the cases in percentage. Mean apoptotic index was calculated for all the five categories along with the standard deviation. The mean apoptotic index was maximum for endometrial carcinoma i.e. 3.8±0.4 while it was minimum for simple hyperplasia without atypia i.e. 0.6± 0.05. (Table/Fig 2)

APOPTOTIC INDEX (Table/Fig 2)

DIAGNOSIS	MEAN APOPTOTIC INDEX	STANDARD DEVIATION (SD)
Simple hyperplasia without atypia	0.665	.05512
Simple atypical hyperplasia	1.334	.07309
Complex hyperplasia without atypia	1.991	.29178
Complex hyperplasia with atypia	2.913	.37793
Endometrial Adenocarcinoma	3.812	.41211

ANOVA test was applied to determine whether or not the means of the five groups are equal or not. The p- value was 0.000 (<0.05), suggesting mean apoptotic index for at least one of the grades is significantly different from others. In order to determine "which of the grades have significantly different mean?", Post Hoc tests were applied and it was found out that endometrial carcinoma had a significantly higher apoptotic index (p-value =0.000) while simple hyperplasia had a significantly low apoptotic index. The intermediate categories had an increasing trend of apoptotic index.

DISCUSSION

Endometrial cancer is the most common gynecologic malignancy and represents a major health concern because overall five-year survival rates have not improved in the last three decades[14]. Although the majority of cases of endometrial cancer are diagnosed at an early stage, differences in patient characteristics and histopathological features of the disease impact both on patient prognosis and the recommended treatment approach[15].

Apoptosis is encountered in various biological and pathophysiological processes, as well as in embryological development, where it truly represents "programmed cell death"[16]. Apoptosis is a process of controlled cell deletion by which the numbers of cells in a variety of tissues are regulated in physiological and pathological conditions. It operates in normal embryological development and is detected in both treated and untreated neoplasms[8].

Apoptosis maintains tissue homeostasis through its ability to control cell population and has been extensively studied in human cancers. Spontaneous apoptosis is a common finding in biopsy specimens of many cancers[17].The percentage of apoptotic cells and bodies in the total number of tumor cells counted is designated the apoptotic index and can be readily estimated using light microscopic examination of routine H and E stained histological sections, avoiding the need for specialist equipment and techniques[18].

Endometrial hyperplasia and endometrial carcinomas are often viewed as points on a continuum, which includes disordered proliferation, simple and complex hyperplasia, atypical hyperplasia and adenocarcinoma. Endometrial hyperplasia is also associated with abnormally high and prolonged estrogenic stimulation of the endometrial epithelium, unopposed by progesterone; this is considered to generate the above- mentioned spectrum. Thus there is an important etiological and functional overlap between the neoplastic sequence and DUB, although the duration and pattern of unopposed estrogenic stimulation differs. Apoptosis is observed at increasing levels in the hyperplasia, atypia, adenocarcinoma sequence[19].

CONCLUSION

Thus, apoptotic index increases with the increasing complexicity of enometrium. It is a useful parameter to assess the prognosis in endometrial lesions.

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