

Original article

Mast cell profile in myometrial lesions: a study of 577 cases

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Abstract

Introduction: The human uterus is considered to be relatively rich in mast cells compared to the other tissues of the body. However, there are only a limited number of studies correlating mast cell profile in various benign and malignant myometrial lesions.

Methodology: The present study comprised of 577 uterine hysterectomy specimens received from Department of Obstetrics and Gynaecology, Muzaffarnagar Medical College, Muzaffarnagar for histopathological examination which was conducted in the Department of Pathology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar.

Results: On analysing the myometrium of all the 577 cases, majority of the cases (230 cases) lacked any significant pathology which was found to be about 39.86% (Table 1). Leiomyoma (figure 1) was found to be the most common pathology in 139 cases (24.09%) followed closely by adenomyosis (figure 3) in 130 cases (22.53%). Cases with dual pathology comprising of both leiomyoma and adenomyosis accounted for 74 cases (12.82%) while 3 cases (0.52%) turned out to be endometrial adenocarcinoma invading the myometrium and one case (0.17%) was of myometritis.

Conclusion: Based upon the observations of this study, progressively decreasing mast cell count from benign to malignant lesions in myometrium was observed. It is suggested that mast cell count appears inversely proportional to the degree of dysplasia and may act as a good prognostic indicator of the benign nature of the lesions.

Key words: adenomyosis, mast cell, leiomyoma, toluidine blue

Introduction

Mast cells play a pivotal role in a variety of biological responses including inflammation, angiogenesis¹, physiologic wound healing, fibrosis² and tissue remodeling. They are an integral part of the body's defense system as well as a key effector cell in both innate and acquired immunity, capable of inducing and amplifying both these responses. Their functions can also contribute to the pathogenesis of allergy and allergic diseases like asthma as well as many other benign and malignant diseases affecting various organ systems of the body. The human uterus is considered to be relatively rich in mast cells compared to the other tissues of the body. Although there is limited information about the distribution and heterogeneity of mast cells in human uterine tissues, it is believed that myometrium is rich in mast cells³ with myometrial mast cells distributed in close association with smooth muscle cells as well as connective tissue^{4,5}. However, there are a limited number of studies correlating mast cell profile in various benign and malignant myometrial lesions. The present study was conducted as an attempt to solve the existing controversies regarding the distribution of mast cells in the various myometrial lesions.

Aims and objectives

To study the histopathological spectrum, distribution and concentration of mast cells in various myometrial lesions and an attempt to find a correlation with the clinical profile.

Material and methods

The present study comprised of 577 uterine hysterectomy specimens received from Department of Obstetrics and Gynaecology, Muzaffarnagar Medical College, Muzaffarnagar for histopathological examination which was conducted in the Department of Pathology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar. The study period was of 2 years; 1 year retrospective from January 2013 to May 2014 and 1 year prospective study from June 2014 to May 2015. Inadequate specimens consisting mainly of autolysed or necrosed tissue and non appreciable myometrial tissues were excluded.

Following gross examination, the myometrium in each hysterectomy specimen was histopathologically examined for uterine lesions. The uterine myometrium adjacent to the myometrial lesions acted as its control. All the cases received were stained with Harris Haematoxylin and Eosin (H&E) stain^{6,7} for routine histological examination and Toluidine Blue stain^{8,9} for examining the mast cells. Biopsy tissue of skin acted as positive control for the uterine specimen. They were stained with Toluidine blue and analyzed for the mast cells prior to analysis of the uterine tissue for the same. Categorization of the lesions was done on histological grounds. Number of mast cells in 10 consecutive high power fields (HPF) were counted in all sections of myometrium and tabulated.

Cases were categorized into reproductive (<40 years), perimenopausal (40-50 years) and postmenopausal (>50 years) age groups. In the retrospective study detailed clinical history was retrieved from the patient records of pathology department while in the prospective cases by interviewing the patient. The data was entered in Microsoft Excel 2013 and statistical analysis was carried out using SPSS17 package¹⁰. Percentages and mean values were calculated and compared using Pearson's Chi-square test and ANOVA. "P" value of less than 0.05 was accepted as indicating statistical significance at 95% confidence interval.

Observations and results

On analysing the myometrium of all the 577 cases, majority of the cases (230 cases) lacked any significant pathology which was found to be about 39.86% (Table 1). Leiomyoma (figure 1) was found to be the most common pathology in 139 cases (24.09%) followed closely by adenomyosis (figure 3) in 130 cases (22.53%). Cases with dual pathology comprising of both leiomyoma and adenomyosis accounted for 74 cases (12.82%) while 3 cases (0.52%) turned out to be endometrial adenocarcinoma invading the myometrium and one case (0.17%) was of myometritis.

Hence a total of 204 cases of adenomyosis were observed with a mean age of 42.86 years and mean mast cell count of 7.10 ± 4.70 (figure 4). The mean age in cases of 213 leiomyomas was 41.70 years with the mean mast cell count of 40.02 ± 25.34 (figure 2). A statistically significant difference (p value <0.001) between the mean age as well as mean mast cell count among various myometrial lesions was observed (Table 2).

A significant inverse correlation (p value <0.001) between the mean numbers of mast cells with the increasing age was observed in adenomyosis and leiomyoma as well as the normal adjacent myometrium. The mean number of mast cells in adenomyosis in reproductive, perimenopausal and post menopausal age groups was 11.15, 6.34 and 3.39 respectively. The mean number of mast cells in leiomyoma in reproductive, perimenopausal

and post menopausal age groups was 59.04, 35.86 and 12.47 respectively. Cases diagnosed as myometritis and invasive endometrial adenocarcinoma belonged to the post menopausal age group (Table 3).

Discussion

The literature is scarce regarding the distribution and potential relationship between mast cell and various conditions of the myometrium. Human uterus is considered to be relatively rich in mast cells compared to the other tissues of the body^{5,11}. Most of the studies have shown that endometrium contains lesser number of mast cells as compared to the myometrium. In the present study, a higher concentration of mast cells in the inner half of the myometrium than the outer half was also observed which is also concomitant with other reports^{3,12}.

Myometrial mast cells are also distributed in close association with smooth muscle cells as well as with connective tissue^{4,6}. Similar findings were observed in the present study which suggest that uterine mast cells may have a special function in the female reproductive tract, and that myometrial smooth muscle cells and the vascular network supplying these cells may be principal targets of the bioactive agents in mast cells^{4,6}. The diverse array of uterotonic and inflammatory mediators makes them powerful mediator cells with the potential to regulate uterine contractility and cervical ripening, respectively¹³.

A statistically significant difference (p value <0.001) of the mean mast cell count among the various myometrial lesions were observed with the highest value of 40.02 ± 25.34 mast cells/10HPF in the leiomyoma and lowest value of 4.67 ± 3.06 mast cells/10HPF in the cases of carcinoma. Mean number of mast cells observed in adenomyosis and myometritis were $7.10 \pm 4.70/10$ HPF and $15.00/10$ HPF respectively. Gousuddin et al¹⁴ and Barauh and Dam¹⁵ also reported similar trends for leiomyoma & adenomyosis. Compared to the adjacent normal myometrium (65.70 ± 30.96) a decrease in the mast cell count was observed for all the myometrial lesions. Several authors have previously analysed the presence of mast cells in the uterine smooth muscle tumours in addition to the normal myometrium. The number of mast cells in the leiomyoma reported by various authors has varied considerably. Fox & Abel¹⁷ in their study on mast cells in uterine myometrium and leiomyomatous neoplasms observed that 46% of leiomyomas contained 0-1 mast cells/ 10 mm fields, 30% had 2-7 cells, 10% 8-13 cells and 14% 14 or more cells. They concluded that the average values for leiomyomatous tumours were significantly below those of normal myometrium. Similar findings were also observed in the present study. On the other hand, Maluf and Gersell¹⁸ observed that the mast cell counts were consistently higher in the leiomyomas than in myometrium in ratios varying from 3:1 to 12:1. A decreasing trend in the mean number of mast cell with advancing age in adenomyosis and leiomyoma as well as the normal myometrium was also observed. These findings were consistent with Orii et al.¹⁶ who also reported decreasing number of mast cells in leiomyomas with increasing age concomitant with the general atrophy of the uterus that occurs with the ageing and particularly following menopause. These observations lend evidence to the proposition that there exists an inverse correlation between the mast cell count and advancing age which may be attributed to the role of estrogen and progesterone at the physiologic levels. However, some authors^{17,18} are of the view that there is no difference in the mast cell population in the leiomyomas between the patients in reproductive and postmenopausal age groups. All three cases of of invasive endometrial adenocarcinoma and one case of myometritis were observed in postmenopausal age group.

D'souza et al¹⁹ suggested that malignant stroma is not a favorable field for mast cells and that presence of mast cells would indicate the benign nature of the lesion¹. Further studies conducted by Orii et al, Zhu et al and

Erol et al also reported that the mast cell density was lower in the malignant than in benign lesions of the uterus^{16,20-21}. They suggested that presence of mast cells would indicate benign nature of endometrial lesions and this may be important in assessment of malignant and premalignant lesions. Similar trend was also observed in the present study for the myometrial lesions. However, Maluf and Gersell¹⁸ observed that mast cells were irrelevant to discriminate between the benign and malignant smooth muscle tumors.

Conclusion

Based upon the observations of this study, progressively decreasing mast cell count from benign to malignant lesions in myometrium was observed. It is suggested that mast cell count appears inversely proportional to the degree of dysplasia and may act as a good prognostic indicator of the benign nature of the lesions.

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