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A Cross-sectional Study of Mast Cell Distributions in Uterine Leiomyoma and its Adjacent Myometrium.

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KEYWORDS

Mast cells;
Uterine leiomyoma;
Adjacent myometrium;
Histopathology;
Toluidine blue stain;
Targeted therapy;
Diagnostic markers.

ABSTRACT:

Introduction: Mast cells, discovered by Paul Ehrlich, drive inflammation, angiogenesis, wound healing, fibrosis, and benign/malignant lesion development. Tumour-associated mast cells at peri- and intratumoral sites secrete histamine, tryptase, VEGF, TNF-α, TGF-β, and interleukins, exerting protumorigenic or antitumorigenic effects. In uterine pathology, they localise to myometrium and smooth muscle tumours, associating with smooth muscle cells, fibroblasts, and collagen. Their role in leiomyoma pathogenesis is debated, with conflicting protumorigenic versus suppressive evidence.

Materials and Methods: This prospective comparative study at ACS Medical College and Hospital, Chennai (Jan–Dec 2025), analysed 40 hysterectomy specimens. Paraffin sections were stained with H&E and toluidine blue; mast cells were counted per 10 high-power fields (40×) in leiomyoma versus adjacent myometrium.

Results: Seventy percent of cases occurred in the age group 41–50 years. Leiomyoma mast cell density (23.35 ± 17.84/10 hpf) was significantly lower than myometrium (41.13 ± 23.74/10 hpf; $p < 0.001$). Among 14 degenerated cases, 13 had hyaline (myometrial mean: 35/10 hpf) and 1 myxoid (20/10 hpf) degeneration.

Conclusion: Higher adjacent myometrial mast cells suggest they promote leiomyoma growth via the tumour microenvironment, aiding benign versus malignant distinction and identifying therapeutic/diagnostic targets.

1. Introduction

Mast cells are key innate immune cells that originate in the bone marrow and are found in various connective and mucosal tissues throughout the body. Mast cells are like the Swiss Army knives of the immune system - they're involved in tons of processes, and researchers are still uncovering their many roles in health and disease (1,2). These cells are master multitaskers, involved in everything from allergic reactions and tissue inflammation to angiogenesis, growth, repair, and cancer progression.

Mast cells' impact on uterine and cervical health is still unclear. Some studies say they fuel tumour growth by promoting new blood vessels, while others suggest they might actually slow down cancer growth – it's a mixed bag (3,4). In cervical neoplasia, mast cell density is reportedly reduced in malignant versus normal epithelium (5,6). Although uterine cancer data suggest protumorigenic potential, clinical observations and experimental models also support antitumor host responses. Their precise influence on uterine fibroids warrants clarification, which motivates this investigation. Given the paucity of literature on mast cell distribution across different types of fibroid degeneration, this study comparatively assesses their infiltration in fibroids and adjacent myometrium, and checks how mast cell counts change with different degeneration patterns.

2. Aims and Objectives

- To evaluate the role of mast cells in the pathogenesis of uterine leiomyoma.
- To analyse mast cell distribution in uterine leiomyoma relative to adjacent myometrium.

3. Materials and Methods

The current study included 40 samples of uterine hysterectomy specimens that were sent from the Department of Obstetrics and Gynaecology at A.C.S. Medical College and Hospital, Chennai, for histopathological testing. The histopathological analysis was done in the Department of Pathology at the same hospital. It was a year-long study, spanning January to December 2025. The study was approved by the Institutional Human Ethics Committee with the reference number (No.1334/2024/IEC/ACSMCH Dt. 13.12.2024).

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Two samples each of fibroid tissue and surrounding muscle tissue were taken, fixed in formalin, and embedded in paraffin. These were then sliced into 4µm sections and stained with Haematoxylin & Eosin for routine check and 1% toluidine blue to highlight mast cells, which showed up purple/red due to the stain (figure). Mast cells were counted in 10 high-power fields (40X) per slide in areas with the most mast cells. Counts were compared between fibroid and adjacent myometrium, and between degenerative and non-degenerative fibroids. The types of degeneration in fibroids were also noted. Average mast cell counts and standard deviations were calculated for fibroids, adjacent myometrium, and degenerative vs non-degenerative fibroids.

Inclusion criteria: All hysterectomy cases with uterine fibroids were included.

Exclusion criteria: Cases where the tissue was autolysed, necrosed, or had very little myometrial tissue were excluded from the study.

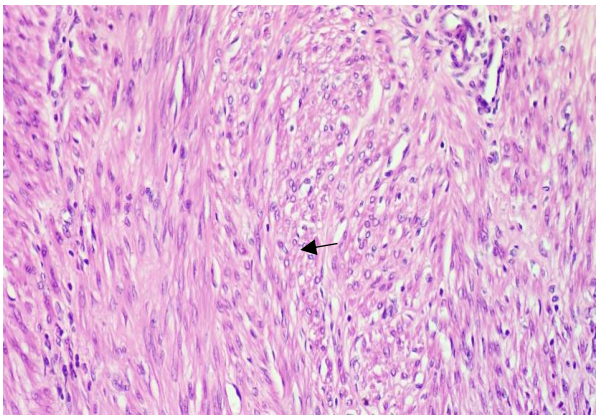

Figure 1: Mast cells within adjacent myometrium (H & E stain, x100).

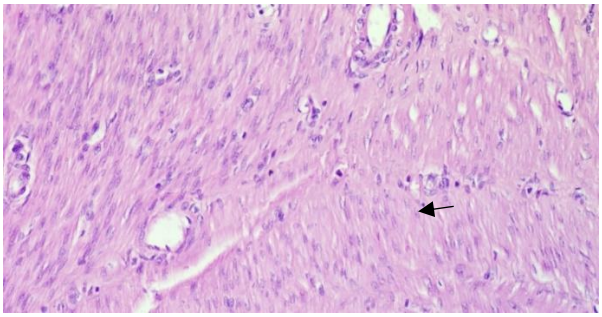

Figure 2: Mast cells within leiomyoma. (H & E stain, x100).

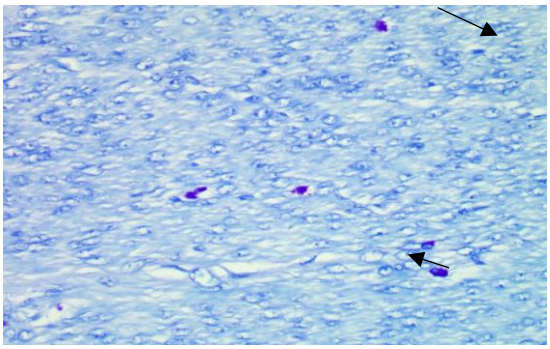

Figure 3: Mast cells within adjacent myometrium (Toluidine blue stain, ×400).

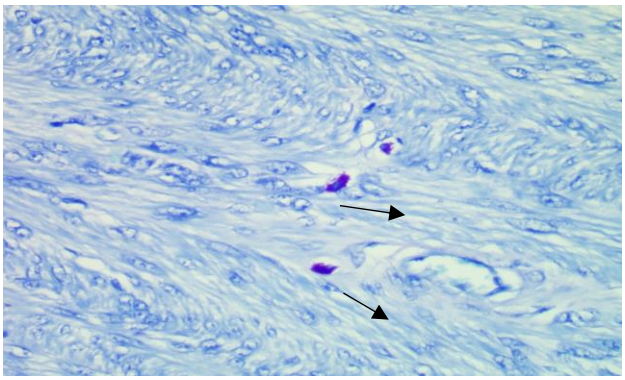

Figure 4: Mast cells within leiomyoma. (Toluidine blue stain, ×400).

	Group	Number	Mean ± SD	p-value
Mast cells	Leiomyoma	40	23.35 ± 17.84	0.000
	Adjacent myometrium	40	41.13 ± 23.75	

4. Statistical Analysis

Data collection and entry were performed using Microsoft Excel 2021, followed by statistical analysis in SPSS version 28.0 (Statistical Package for the Social Sciences). Mast cell counts are presented as mean ± standard deviation (SD), and intergroup comparisons utilised the independent samples t-test, with statistical significance set at $p < 0.05$.

5. Results

A total of 40 uterine leiomyoma cases were analysed, with the majority (70%) occurring in women aged 41-50 years.

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Age Group(years)	Number	Percentage%)
31 – 40	7	17.50%
41 – 50	28	70%
51 – 60	5	12.50%
Total	40	100%

Table 1: Age distributions

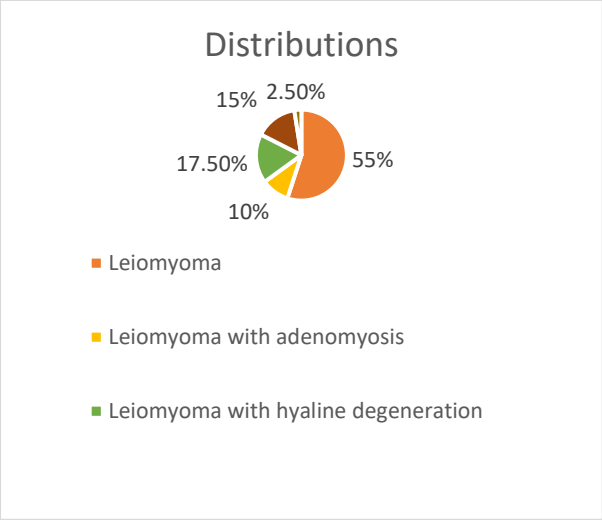

Chart 1: Distribution of leiomyoma and other associated pathology.

The mean mast cell count was lower in leiomyoma, which is 23.35 ± 17.84, than in the adjacent myometrium, which is 41.13 ± 23.74, and this difference was statistically significant ($p < 0.001$).

Table 2: Comparative analysis of mast cells in leiomyoma versus adjacent myometrium

Table 3: Mast cell comparison in leiomyoma and adjacent myometrium across degenerative vs. non-degenerative groups

	Degeneration	Number	Mean ± SD	p-value
Mast cells of leiomyoma	Non Degenerative	26	24.77 ± 18.15	0.500
	Degenerative	14	20.71 ± 17.61	
Mast cells in the adjacent myometrium of the leiomyoma	Non Degenerative	26	44.92 ± 24.85	0.171
	Degenerative	14	34.07 ± 20.55	

Out of the 14 cases that showed degeneration, 13 had hyaline degeneration, and one case had myxoid degeneration. This included 7 leiomyoma cases with hyaline degeneration and 6 cases exhibiting both adenomyosis and hyaline degeneration. The case with myxoid degeneration also had adenomyosis. Mean mast cell counts within the adjacent myometrium were 35 per 10 hpf for cases with hyaline degeneration and 20 per 10 hpf for the case with myxoid degeneration. [Table 4].

Table 4: Mast cell distribution in adjacent myometrium according to degeneration patterns

Degeneration	Number of cases n(%)	Average
Hyaline Degeneration	13 (92.86%)	35.15
Myxoid Degeneration	1 (7.14%)	20.00

6. Discussion

Mast cells are derived from bone marrow hematopoietic progenitors and reside in vascularized tissues throughout the body. Mast cells were first identified by Paul Ehrlich in 1878 during his doctoral studies, identified by their metachromatic granules when stained with aniline dyes [7]. Over the past two decades, research has elucidated their multifaceted roles in homeostasis and pathology, extending beyond immediate hypersensitivity[7]. Mast cells help with physiological events like inflammation, making new blood vessels, healing wounds, forming scars, and changing tissues[8]. They are also involved in diseases like asthma. Mast cells contribute to tissue growth and development in both normal and neoplastic contexts across various anatomical sites[9]. Upon activation, mast cells degranulate, releasing an array of mediators including histamine, tryptase, chymase, VEGFs, TNF-α, MMPs, FGFs, TGF-β, and various interleukins [10]. These mediators can either help or inhibit cancer growth. Certain cancer cells overexpress stem cell factor (SCF), which recruits, proliferates, and activates mast cells to release their mediators [10]. Studies demonstrate mast cells' intimate association with tumour angiogenesis. A primary mechanism linking mast cells to malignancy involves their secretion of pro-angiogenic factors[11]. Peritumoral stroma harbours mast cells that secrete pro-angiogenic proteins and enzymes[12]. They predominantly localise at tumour margins adjacent to stroma, vasculature, and lymphatics, potentially promoting neoplastic proliferation, invasion, and neovascularisation [9]. Tumour-infiltrating mast cells may reflect an attempted host defence, deploying TNF-α and granzyme B for cytolytic activity against neoplastic cells. Their accumulation in certain malignancies likely represents a broader chronic inflammatory response[10]. Cajal noted an

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intimate association of mast cells with certain epithelial tumours, implying a role in host defence mechanisms[13]. The human uterus, particularly its smooth muscle layer (myometrium), exhibits higher mast cell density than most other tissues. These mast cells localise near smooth muscle cells and within the surrounding connective tissue. Jiang L et al. suggested that mast cell density could distinguish leiomyomas from leiomyosarcomas. Limited research has investigated mast cell associations with leiomyomas, particularly those exhibiting degenerative changes[14,15,16]. However, Abeyratne NV et al. observed reduced mast cell density in uterine fibroids exhibiting hyaline degeneration [17]. This is why one of the main goals of this study was to examine how mast cells are spread in different types of degeneration in leiomyoma and in adjacent myometrium, thus making this study unique.

The current investigation identified a statistically significant reduction ($p < 0.001$) in mean mast cell counts within uterine leiomyomas compared to adjacent myometrium. The mean mast cell count within uterine leiomyomas measured 23.35 per 10 high-power fields (HPF), compared to 41.13 in adjacent myometrium. These results match earlier studies showing similar mast cell proportions (Table 5).

Table 5: Comparison of various studies in the literature with the present study.

Study	Place and year of publication	Mast cell count per 10 hpf
D. Shobha et al.,[2]	Kuppam, Andhra Pradesh, 2023.	Leiomyoma: 11.65±15.81 Adjacent myometrium: 37.16±23.01 (p-value <0.0001)
Apurva V et al., [14]	Muzaffarnagar, India, 2016	Leiomyoma: 40.02±25.34 Adjacent myometrium: 65.70±30.96 (p-value <0.0001)
Erol AY et al., [15]	Turkey, 2011	23.2±7.8 in the stroma (p-value=0.987) 41.4±17.1 in the myometrium (p-value=0.810)
Present study	Chennai, Tamil Nadu, 2026	Leiomyoma: 23.35 ± 17.84 Adjacent myometrium: 41.13 ± 23.75 (p-value = 0.000)

Uterine leiomyomas with degeneration exhibited a mean mast cell count of 20.71 per 10 HPF in the lesion, versus 34.07 in adjacent myometrium. Particularly, the adjacent myometrial mast cell density showed a decreasing trend in degenerated cases.

Direct quantitative comparisons of mast cell counts remain challenging owing to the restricted cohort of leiomyoma specimens analysed and the limited tissue sections evaluated, potentially missing heterogeneous distribution patterns. Higher mast cell counts in the myometrium adjacent to leiomyomas highlight their role in tumour angiogenesis [10].

7. Limitation(s)

The study was limited by the small number of leiomyoma cases analysed. Also, microscopic mast cell assessment depends on subjective pathologist interpretation, potentially causing result variability.

8. Conclusion(s)

Mast cells were more abundant in the muscle layer adjacent to the fibroid, suggesting they might promote tumour growth. Their presence could indicate a non-cancerous tumour, aiding cancer diagnosis. Mapping mast cell distribution can reveal their role in tumour development. This insight could lead to new avenues for targeted therapies or diagnostic markers, leveraging mast cells' role in the tumour microenvironment.

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