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Mast Cell Distribution and Its Correlation with Disease Severity in Leprosy: A Histopathological Study

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ABSTRACT

Background: Mast cells play a crucial role in inflammatory dermatoses. This study investigates mast cell distribution and its correlation with disease severity in leprosy.

Methods: A retrospective observational study analyzed 46 leprosy cases and 28 controls. Mast cell counting was performed using toluidine blue staining and high-power microscopy.

Results: Leprosy cases showed varying mast cell distributions: lepromatous leprosy (12-54 cells/10 HPF), tuberculoid leprosy (20-53 cells/10 HPF), borderline tuberculoid leprosy (22- 42 cells/10 HPF), and indeterminate leprosy (15-89 cells/10 HPF). Mast cell counts correlated with disease severity.

Discussion: This study highlights the importance of mast cells in leprosy pathogenesis and suggests their potential role in disease severity. Regional variations in mast cell distribution were observed.

Conclusion: Mast cell distribution analysis may serve as a diagnostic tool in leprosy, emphasizing the need for integrated clinical and histopathological approaches.

Keywords: *Leprosy, Mast Cells, Dermatitis, Skin Diseases, Mycobacterium leprae*

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1. INTRODUCTION

Mast cells, first identified by Paul Ehrlich in the 18th century, are dynamic immune cells that play a pivotal role in the complex interplay between protective responses, allergic inflammation, and chronic inflammatory reactions[1]. Originating from bone marrow hematopoietic tissue, mast cells are strategically positioned throughout connective tissue, including the skin, where they respond to diverse stimuli[2]. Characterized by their metachromatic granules and high-affinity IgE binding sites, mast cells regulate inflammation, influencing angiogenesis, wound healing, fibrosis, and tumor development[3,4]. Leprosy, caused by Mycobacterium leprae, is a chronic infectious disease that affects the skin, nerves, and mucous membranes[5]. The disease manifests in various forms, ranging from tuberculoid to lepromatous leprosy, depending on the host's immune response[6]. Despite advances in understanding leprosy pathogenesis, the role of mast cells in this disease remains poorly understood.

2. RESEARCH OBJECTIVES

The primary objective of this study is to investigate the distribution of mast cells in various subtypes of leprosy and assess their correlation with disease severity. Specifically, this study aims to:

- **Examine the Mast Cell Distribution**: Quantify and analyze the mast cell count in different leprosy subtypes (lepromatous, tuberculoid, borderline tuberculoid, and indeterminate).
- **Assess Disease Severity**: Correlate mast cell distribution with the clinical severity of the disease.
- **Identify Regional Variations**: Explore any regional differences in mast cell distribution within different parts of the body, particularly focusing on facial and upper extremity lesions.
- **Evaluate Mast Cell as a Diagnostic Tool**: Investigate the potential of mast cell distribution as a diagnostic marker, particularly in the early stages of leprosy (indeterminate leprosy).
- **Contribute to Pathogenesis Understanding**: Enhance the understanding of mast cells' role in leprosy's immunopathogenesis and their involvement in disease progression.

By addressing these objectives, this study will provide novel insights into the immune mechanisms at play in leprosy, ultimately suggesting potential new approaches for diagnosis and therapeutic strategies.

3. MATERIALS AND METHODS

A retrospective observational study was conducted at KIMS, Hubballi, Karnataka, from January 2015 to December 2018. A retrospective observational study was conducted at KIMS, Hubballi, Karnataka, from June 2015 to May 2018. The study included 82 leprosy cases, diagnosed based on clinical and histopathological criteria, and 42 controls. Specimens were fixed in 10% formalin, embedded in paraffin blocks, and stained with H&E and 1% toluidine blue for mast cell identification. Mast cell counting was performed under high-power microscopy, averaging 10 non-overlapping fields.

Sample Collection:

Skin biopsy specimens were collected from affected areas, fixed in 10% formalin, and embedded in paraffin blocks for histopathological examination. The samples were sectioned at 4-5 µm thickness.

Staining Procedure:

For mast cell identification, sections were stained with **toluidine blue** and **Hematoxylin and Eosin (H&E)**. Toluidine blue, known for its ability to selectively stain mast cell granules, was used to highlight the mast cells under high-power microscopy.

Mast Cell Counting:

Mast cell counting was performed under high-power field (HPF) microscopy in 10 non- overlapping fields of each section. The number of mast cells per 10 HPF was recorded for each leprosy subtype. The counting was done by two independent pathologists to ensure accuracy and minimize bias.

Data Analysis:

Statistical analysis was performed using descriptive statistics to calculate the mean and median mast cell count for each leprosy subtype. The correlation between mast cell count and disease severity was assessed using Pearson's correlation coefficient. Regional variations in mast cell distribution were noted by comparing different body regions, including the face and upper extremities.

Ethical Considerations:

Ethical approval was obtained from the institutional review board of the hospital, and informed consent was taken from all participants prior to sample collection. The confidentiality of all subjects was maintained throughout the study.

Figure1: Leprosy Study Methodology

This methodology allowed for a thorough examination of the mast cell distribution across different leprosy subtypes, providing insight into their correlation with disease severity and offering the potential for diagnostic and prognostic applications.

4. RESULTS

Leprosy cases showed varying mast cell distributions across subtypes:

- Lepromatous leprosy (n = 27): 12-54 cells/10 HPF (median: 14)
- Tuberculoid leprosy (n = 27): 20-53 cells/10 HPF (median: 24)
- Borderline tuberculoid leprosy (n = 18): 22-42 cells/10 HPF (median: 28)
- Indeterminate leprosy (n = 10): 15-89 cells/10 HPF (median: 15)

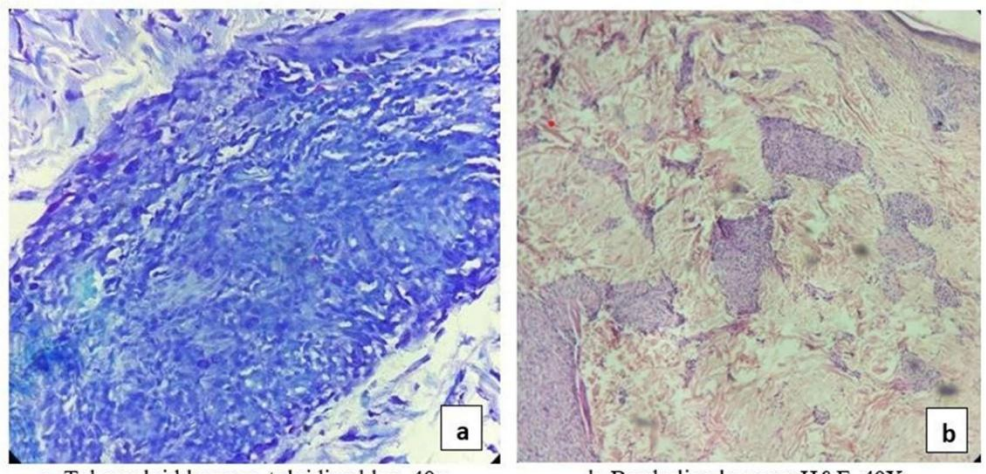
Mast cell counts correlated with disease severity, with higher counts observed in more severe forms of leprosy. Regional variations in mast cell distribution were noted, with higher counts in the face and upper extremities.

Table 1: Mast Cell Distribution in Leprosy Subtypes

Leprosy Subtype	Mast Cell Count (cells/10 HPF)	Median
Lepromatous	12-54	**14**
Tuberculoid	20-53	**24**
Borderline Tuberculoid	22-42	**28**
Indeterminate	**15-89**	**15**

Table 2- Comparision of age and sex distribution of leprosy with other studies.

Study	Age (mean)	Sex ratio
Present study	38.0	**3.6:1**
Cree I A et al9	36	**16:6**
SERIES 1		
SERIES 2	38	**28:7**
Vijaya v mysorekar et al10	-	**1.2:1**
Shwetha et al11	-	**2:1**



a. Tuberculoid leprosy, toluidine blue, 40x b. Borderline leprosy, H&E 40X

Figure 1: Mast Cell Distribution in Leprosy

5. DISCUSSION

This study supports the notion that mast cells play a crucial role in leprosy pathogenesis[7,8]. The significant correlation between mast cell counts and disease severity suggests that mast cells may contribute to disease progression[7,8]. Regional variations in mast cell distribution may indicate specific mast cell responses to M. leprae infection[7].

This study's findings align with previous research on leprosy demographics and mast cell distribution. Consistent with Cree et al. and Vijaya V Mysorekar et al., our study showed a male predilection and similar age incidence[9,10]. The high prevalence of borderline tuberculoid leprosy and male dominance also corroborates Meenakshyee M Joshi and Shwetha et al.'s studies[3,11]. India's socioeconomic factors may contribute to the increased leprosy prevalence. Notably, our study found the highest mean mast cell count in indeterminate lesions and borderline tuberculoid leprosy, with no statistically significant difference. This is consistent with Aroni et al.'s observations[12]. The high mast cell counts in indeterminate leprosy, also reported by Vijaya V Mysorekar et al., suggests that mast cells may increase as a protective mechanism in the initial stages of leprosy, potentially aiding in diagnosis[10]. These findings underscore the importance of mast cell analysis in understanding leprosy pathogenesis and diagnosis. However, further research is necessary to elucidate the mechanisms underlying mast cell involvement in leprosy.

6. CONCLUSION

The present study provides valuable insights into the role of mast cells in leprosy, highlighting their potential diagnostic significance. The findings demonstrate a correlation between mast cell distribution and disease severity, with the highest mean mast cell count observed in indeterminate lesions. Consistent with previous research, our study underscores the importance of mast cell analysis in understanding leprosy pathogenesis. The results suggest that mast cells play a crucial role in leprosy, particularly in the initial stages, and may serve as a diagnostic marker for indeterminate leprosy. Furthermore, the study highlights the need to consider socioeconomic factors contributing to the increased prevalence of leprosy in developing countries. Future research should investigate the mechanisms underlying mast cell involvement in leprosy and explore the therapeutic potential of targeting mast cells in leprosy treatment, ultimately aiming to improve diagnostic accuracy and develop novel therapeutic strategies.

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