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Pathogenesis of Psoriasis: A new angle with Mast cell

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Abstract

Background: Mast cells are bone marrow derived cells which have captured the interest of the medical fraternity since more than a century. Mast cells exhibit a constellation of biophysical functions and has been regarded as the "major cell" in inflammation and immunity. The presence of mast cells, often in an activated state or increased numbers has been noted in various cutaneous disorders.

Aims and Objectives: To study the variations of mast cells in psoriatic skin lesions. To analyse the possible pathophysiological role of mast cells in psoriasis.

Methods: A total of 100 cases of psoriasis were prospectively studied. Skin biopsies received in the Department of Pathology Dr. BR Ambedkar Medical College/Hospital, Bangalore were fixed in 10% formalin and routinely processed. 3-5 µ thin sections were cut and stained with Haematoxylin and Eosin. All sections were stained with Toluidine blue to selectively identify and count mast cells.10 control sections were studied. Mast cell variations in terms of morphology, distribution and count were studied in psoriasis. Mean mast cell count were calculated and statistically analysed using student's *t* test.

Results: Mast cells revealed a varied morphology and distribution often exhibiting an activated state and statistically significant increase (P value< 0.0001) in mast cell numbers in psoriasis when compared to the normal skin control

Conclusion: This study highlights the definitive pathophysiological contribution of mast cells in psoriasis and suggests that mast cells are of primary importance in these lesions and their presence does not merely represent a secondary event.

Keywords: Mast cells, Metachromasia, Psoriasis, Mast cell profile, Toluidine blue, Student's *t* test.

Introduction

Psoriasis is one of the most common dermatological diseases affecting upto 1%-2% of total population.[2] Mast cells and their granules have captured the interest of investigators from variety of scientific disciplines over the last century[1]. Mast cells which reside in connective tissue matrices and epithelial surfaces are "effector cells" that initiate inflammatory responses[2]. The development of staining techniques for histologic sections led to the initial definitive description of mast cells by a medical student named PAUL EHRLICH over a 100 years ago[1].

By structure, mast cells measure 8-15 µm in diameter are round, oval or fusiform in shape. The most characteristic features of mast cells is the presence of numerous (500-800/cell dense), metachromatic granules, which may mask the bean-shaped nucleus[3]. The suggestion that mast cells participate in different disease processes stems from morphologic data demonstrating either a change in mast cell numbers or a change in their ultrastructure[1]. An increase in mast cells is seen in a variety of Inflammatory Dermatoses. Riley, reviewed that in acute inflammation there is decreased number of mast cells, in contrast chronic inflammation is accompanied by numerical increase in mast cells[4,5].

Since, not many studies have been done in this context a great deal of lacunae exists in understanding the role of mast cells in variety of lesions. Thus, the present study is conducted to highlight the possible pathophysiological role of mast cells in psoriasis with respect to alterations in morphology, distribution and quantitation's.

Aims and Objectives

1. To study the alterations in mast cells in terms of morphology, distribution and number in psoriasis.
2. To study the possible pathophysiological role of mast cells in psoriasis.

Materials and Methods

The material obtained for this prospective study were skin biopsies received from the Department of dermatology Dr. BR Ambedkar Medical College/Hospital, Bangalore. A total of 100 cases of psoriasis were evaluated for mast cell variations. 10 biopsies of normal skin were evaluated as control.The tissues were fixed in 10% buffered formalin, routinely processed and embedded in paraffin. 3-5 µ thin sections were cut and were stained with Haematoxylin and Eosin and with modified Johnson's methodto visualize mast cells.

Mast cells were counted at 400x magnification in 10 consecutive fields. Fields of study included epidermis, superficial dermis, deeper dermis, perivascular and periappendegeal areas. Counts were expressed as number of mast cells per 10 relevant high power field (hpf.). The mean mast cell count was calculated, tabulated and analysed statistically using student's *t* test and results expressed as mean mast cell counts + standard error of mean (SEM)/10hpf.

Results

Mast cells in normal skin: In skin, mast cells are usually found in the dermis with some accentuation around the superficial vascular plexus and appendages. On an average, there are approximately 7000 mast cells/mm 3 of skin.

Mast cells in psoriasis: an increase in the mast cell density especially around the sebaceous glands is prominent and is believed to play a role in the pathogenesis. In early relapsing and acute eruptive psoriasis the psoriatic tissue alterations appears to have been initiated by degranulating mast cells as well as by macrophages which later invaded the epidermis.

The superficial dermis of lesional psoriatic skin contained more mast cells than either normal or non lesional psoriatic skin.

Morphology: The mast cells were round to ovoid in the normal skin biopsies, taken as control. In psoriasis majority of the mast cells were spindly and degranulated.

Distribution: Mast cells were mainly distributed in the upper dermis and around the blood vessels and dermal appendages in the normal skin (control). In cases of psoriasis, mast cells were increased in number throughout the dermis but were more pronounced in the papillary dermis (upper dermis). Characteristically in psoriasis increased intraepidermal mast cells were observed.(Table 1)

Mast Cell Counts: The control group showed a mean mast cell count of 41.83 + 1.76 / 10 hpf.(Table 2)

Mean mast cell count in psoriasis was 119.56 + 1.1/10 hpf which when compared to controls was statistically significant ($p<0.0001$). (Table 3)

Table 1: Mast cell distribution

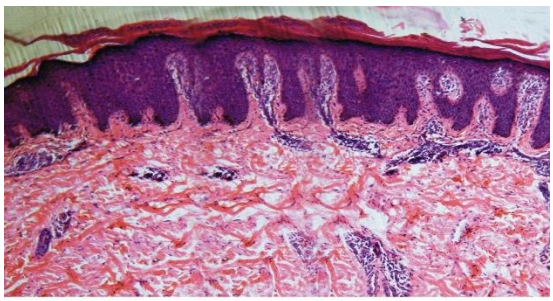
Sl. No.	Distribution	Grade
1	Epidermis /intraepidermal	+ + + + +
2	Superficial dermis	+ + + +
3	Deeper dermis	+ + +
4	Perivascular	+ +
5	Periappendegeal	+

Table 2: Mean Mast cell count in control group

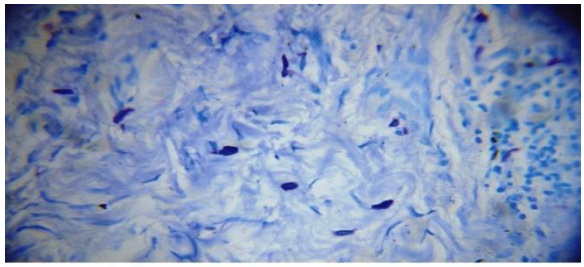
Sl. No.	Stain	No. of cases	Mean MC count/10 hpf + SEM
1	Toluidine Blue	10	41.8+1.76

Table 3: Mean Mast cell count in psoriasis

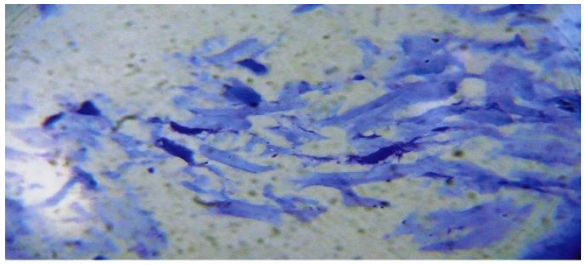
Sl. No.	HP Diagnosis	No. of cases	Range	Mean MC count + SEM
1	Psoriasis	100	110-140	119.56



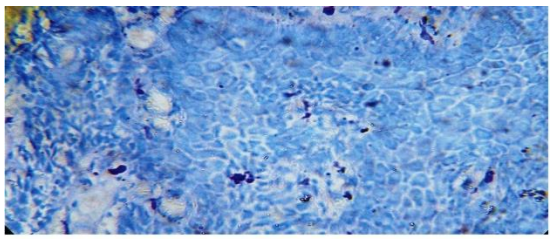
Psoriasis
(H & E Stain - 10 X)



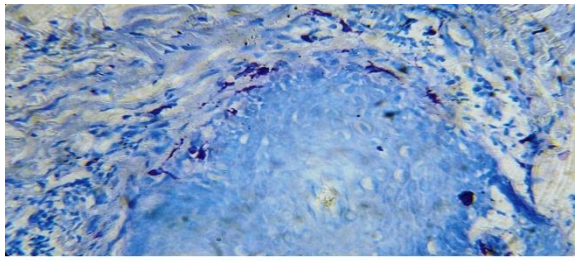
Round To Oval MC
(TB - 400X Magification)



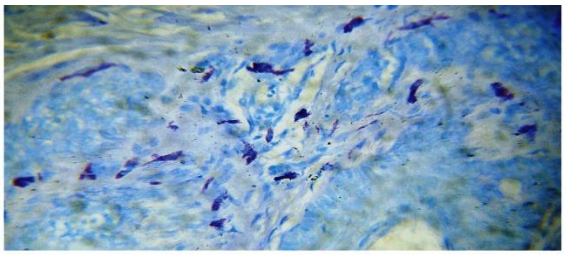
Spindly And Degranulated MC
(TB Stain - 400X Magnification)



Intra Epidermal MC In Psoriasis
(TB Stain - 400X Magnification)



MC In Papillary Dermis
(TB Stain - 400X Magnification)



Increased No Of MC in Psoriasis (TB Stain - 400X Magnification)

Discussion

Psoriasis is a chronic relapsing and a remitting skin disorder, the pathogenesis of which needs to be updated by detailed studies to formulate new effective therapies, and hence this study.

Mast cells have traditionally been considered as "effector" cells in allergy and inflammation. The physiological role of mast cells in the skin is not well known however, there is a growing evidence suggesting that mast cells are also essentially involved in inflammatory patho mechanism.

The present study on mast cell profile in psoriasis is a preliminary effort to probe into the possible role of mast cells in the pathogenesis of psoriasis. This study on mast cell variations encompasses a detailed observation of mast cell alterations in terms of morphology, distribution and number.

David E Elder who stated that psoriasis is a common chronic inflammatory skin disorder[6]. Psoriasis is one of the most common of all skin diseases, with an incidence of 1-2%[7].

The present study revealed varying shapes of mast cells. Majority of the mast cells in the control group were round to ovoid. This study is consistent with that of Eady R.A.J et al; 1979 who reported that mast cells in normal dermis were round to oval with regular granules.[8]

In psoriasis majority of the mast cells were degranulated. This finding is consistent with that of Brody I (1984). He studied mast cell degranulation in psoriatic lesions and stated that mast cell degranulation is an early and constant feature in the evolution of acute eruptive guttate psoriasis.[9]

In this study, in normal skin (control) mast cells were distributed mainly in the upper dermis and around the vascular and appendegeal structures. DAVID WEEDON who stated that in the skin, mast cells are usually found in the dermis with some accentuation around the superficial vascular plexuses and appendages[3].

In psoriasis a good number of epidermal mast cells were noted. This observation is consistent with Ikka T. Harvima (2008) et al; who stated that even though mast cells can only, rarely be seen in the epidermis of the healthy looking skin, the presence of mast cells in close association with the epidermis of the psoriatic lesion is a typical feature and sometimes mast cells are present even inside the lesional epidermis[10].

Mast cells were mainly distributed in the superficial dermis in psoriasis than around appendageal structures. This finding is consistent with S. Toyry et al; 1983 who stated that superficial dermis of lesional psoriatic skin contained more mast cells than the normal skin[11].

Light Microscopy: Mast cells on Haematoxylin and Eosin staining, resemble large eosinophils in that the abundant cytoplasm is filled with eosinophilic granules. Nucleus is ovoid and not lobulated usually[12]. Immature mast cells are spindle shaped resembling fibroblasts or histiocytes in routinely stained sections with few or no cytoplasmic granules. Granules are well shown by staining with Alcian blue at pH 2[13]. Cytoplasm may sometimes show pigment granules as mast cells take up a variety of foreign substances (lipids or metals) through the process of mastopexis[14]. On special staining with Toluidine Blue or Geimsa mast cells show up as large rounded avoid or spindly shaped cells. They lack a basal lamina and may have short pseudopodia, because they are wandering cells[15].

The granules are refractile, water-soluble and they exhibit metachromasia[16].

Electron Microscopy: Electron Microscopy is essential to detect the pre granular and degranulating stages which are likely to be overlooked on light microscopy. There has been recurrent interest in the observation that mast cells occasionally contain melanin granules ("Dual Granulation").[17] Electron Microscopic studies have confirmed the occasional presence of melanization of mast cell granules[18]. The most characteristic subcellular components of mast cells are their secretory granules. They vary in size from 0.2 to 08 µm and are bounded by a unit membrane[19]. The shape of these granules have varying patterns, such as scrolls, whorls and particulate or lamellar structure[20].

Physiology of Mast Cells: Most of these mediators are stored in the mast cell granules, but a few mediator like platelet activating factors (PAF) and cytokines (TNFα) are newly generated in response to inflammation[20]. The mediators thus released into the surrounding tissues satisfy the local and systemic requirements, which led to regard mast cells as first aid kits distributed throughout the body[21].

Staining Reactions: Most of the conventional staining methods fail to visualize mast cells on light microscopy. The most characteristics feature of mast cell is based on the presence of dense metachromasia of their granules[22].

Metachromasia: It is histochemically defined as the staining of a tissue component in such a way that the absorption spectrum of the resulting tissue –dye complex differs sufficiently from that of the original

dye and from its ordinary tissue complexes to give a marked contrast in colour.[23]

Special Stains: As Routine Haematoxylin & Eosin Stain are not able to demonstrate the presence of granules special stains have to be used. Mast cells stand out prominently in sections stained with toluidine blue at about pH 4. For a selective stain alcian blue at pH1 is preferred[24,26].

Counting: Toluidine blue stained sections allows highly selective staining of mast cells with the background being under stained, hence increasing the prominence of the mast cells which facilitates their counting in low power[25].

A.C. Markey 1989 studied human cutaneous mast cells in normal skin. The authors counted mast cells in 10 sequential fields along both levels of dermis under 100x objective[22].

A. Naukkarinen et al (1991) who quantitatively analysed mast cells in cutaneous psoriasis and lichen planus and stated that a common morphological character to both of these dermatoses is a prominent dermal inflammatory reaction where mast cells are increased in number as compared with the number in a healthy skin[28].

C. Schubert and E. Christopher's (1984) stated earliest indications of relapse in psoriasis were endothelial alterations followed by increased appearance of mast cells around the post capillary venules which showed signs of degranulation[27].

Mast cell degranulation appears to be a common denominator in the pathways of most of the inflammatory dermatoses including psoriasis[7].

A number of investigators have demonstrated that on degranulating, these mast cell release a range of both performed and newly synthesized cytokines and chemokines, including TNF-alfa which activates endothelium and induces expression of adhesion molecules resulting in increased vascularity in psoriasis[10].

The present study highlights definite participation of mast cell in psoriasis and hence documents significant alterations in mast cell profile in terms of morphology, distribution and numbers.

Conclusion

The present study documents significant alterations in mast cell profile in psoriasis in correlation with morphology, distribution and quantification. Mast cells thus prove their definite role in modulating and amplifying the inflammatory responses in psoriatic skin lesions. Understanding the role of mast cells thus provides important insights into the pathogenesis of Psoriasis. Perhaps a future extended and sophisticated study in various biochemical and molecular parameters may offer light to understand the course of this disease, their trigger mechanisms and provides insights to formulate new more effective treatment strategies.

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