ORIGINAL ARTICLE

MAST CELL PROFILE IN DISORDERS OF SKIN PIGMENTATION

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ABSTRACT: Mast cell is a connective tissue element which is found throughout the body, particularly in association with blood vessels and nerves. Though the mast cells are distributed throughout the body. Increased proportion of mast cells are present in the skin, respiratory tract, gastrointestinal tract, uterus and urinary bladder(1) (Soter N.A. et al., 1987). An attempt is made in present study to investigate the mast cell profile through histological study of some of the disorders of skin pigmentation from the biopsies received in the Department of Pathology. 1. This study is conducted to evaluate the mast cell profile in various disorders of skin pigmentation. 2. To observe whether some disorders shown a peculiar variation.
KEYWORDS: Mast cells, Metachromatic granules, Toludine Blue.

INTRODUCTION: In 1863, von Recklinghausen described the granular cells in connective tissue. But in 1877, it was Paul. Ehrlich who termed these cells as "Mast Zellen" since he believed these cells containing granules were "overfed". Paul Ehrlich was the first person to point out that mast cells are associated with blood vessels. Nerves, inflamed tissues and glands. Increased proportions of mast cells are present in the skin, respiratory tract, gastrointestinal tract, uterus and urinary bladder.(1)

On its structural basis, mast cells can be defined as "connective tissue elements which possess cytoplasmic granules that stain metachromatically under ordinary conditions.(2) Mast cells can also be projected as tissue cells bearing high affinity binding sites for lgE, synthesizing and storing histamine and proteoglycans within cytoplasmic granules[3]. Mast cells are bone marrow derived cells that occur in normal dermis in small numbers as oval to spindle shaped cells with centrally located granules in the cytoplasm that do not stains with H & E stain. They are identifiable when stained with toluidine blue, cresyl violet. Azure-A and methylene blue – due to the presence of metachromatic granules in their cytoplasm.

MATERIALS AND METHODS: The present study was carried out in the Department of pathology. The cases were selected from the files in the Department of pathology. The study included 3 years retrospective cases and 2 years prospective cases. A careful study of the biopsies of skin lesions, received for histopathological examination along with relevant clinical data was done.

The study comprised of biopsies from the cases of disorders of skin pigmentation, which included – 6 cases of albinism, 6 cases of vitiligo, 6 cases of leucoderma, 6 cases of urticaria pigmentosa (Fig: 2), 6 cases of chronic eczema, 6 cases of junctional nevus, 7 cases of intradermal nevus and 10 cases of malignant melanoma. Ten cases of apparently normal skin (Fig: 1), from the amputation specimens / resection specimens constituted the control group.

MAST CELLS STAINING AND COUNTING: To identify the mast cells with the typical metachromatic granules. Special stain 1% aqueous toluidine blue (pH 4) was used. Toluidine blue staining method.[4]

RESULTS:

Mast cell granules – Purple
Background tissue – Blue

1. **Mast cell counting and observation:** Toluidine blue stained sections were examined under high power magnification. The number of mast cells present in 10 consecutive high power fields was counted in all the sections. Findings were tabulated and were statistically evaluated. On the basis of observations, an attempt was made to study mast cell distribution pattern in the disorders of skin pigmentation. A possible explanation for the significant mast cell alteration if any was attempted.

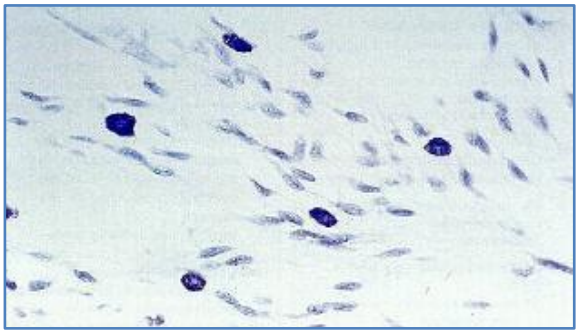

Fig. 1: Normal Mast cell 40x, Toludine blue stain

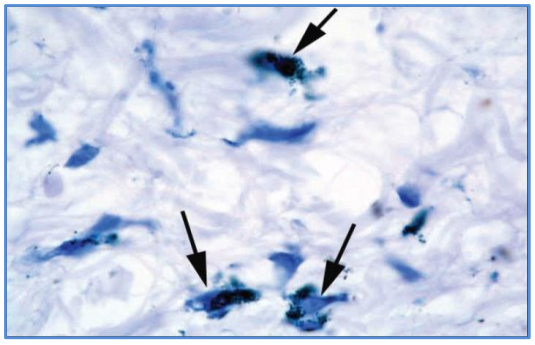

Fig. 2: Urticaria pigmentisa. Mast cell (arrow) 40x Toludine blue stain

DISCUSSION: Mast cells with their large battery of mediators and substances are known to play a vital role in health as various disease state in human beings. The present study of mast cell profile in disorders of skin pigmentation is a preliminary effort to probe into the mast cell distribution in Albinism, Vitiligo, Leucoderma, Urticaria Pigmentosa, Chronic eczema, Intradermal Nevus, Junctional Nevus and Malignant melanoma. Although, the number of cases in the present study are not very large. It appears to be adequate to draw certain logical conclusions.

This is to be specially emphasized that the literature on mast cells in hypopigmented and hyperpigmented skin lesions assorted from Medlar Medline. Interenet, index medicus has been scant. This study is a sincere attempt to probe the facets of mast cells alterations in these disorders of skin pigmentation.

There does seem, however, to be a consensus that mast cells are advanced cells with unique growth requirements. They remain differentiated and viable in C-Kit ligand, also known as stem cell factor (SCF). Other cells early in differentiation also respond to this factor although, as they mature and differentiate they down regulate C-Kit and depend on lineage-specific growth factors. This aspect of mast cell biology may account for their many preserved biological activities

of other immune cells including lymphocytes, monocytes and neutrophils. Mast cells phagocytes, process antigen, produce cytokines and release vasoactive substances.

They exhibit an array of adhesion molecules, immune response receptors and other surface molecules that empower the mast cells with an advanced capability to react to multiple non-specific and specific stimuli.[5]

The mast cells adhere not only to matrix but to other cells as well. The biological consequences of these interactions include mast cell trafficking. Inter digitation of lymphocytes and mast cells membranes has been observed in inflamed tissues. Activated mast cells from heterotypic aggregates with T-lymphocytes. These observations suggest a functional relationship between mast cells and lymphocytes that relates to direct contact between these cells.[5]

The activation of mast cells not only causes the release of performed granule associated mediators, but initiates the de novo synthesis of lipid derived substances. Of particular importance are the cyclocoxygenase metabolites of arachidonic acid, because these products possess potent inflammatory activity. The mast cells are particularly well placed to enhance venular permeability at tissue sites by inducing the generation of histamine, PGD2, LTC4, LTB4 AND PAF[5] (Metcalfe D., et al, 1997). Several growth factor cytokines are known to affect the growth and differentiation of mast cell including IL-3, IL-4, IL-9 IL-10, SCF and NGF.

In the present study, the age range in patients with albinism was 10 to 60 years, with a mean age of 33years. In vitiligo the age ranged from 17 to 39 years, with a mean age of 26.16 years. In leucoderma patients, the age ranged from 14 to 30 years, with a mean age of 23.16 years in patients with 26.83 years. In chronic eczema, the age ranged from 14 to 46 years, with a mean age of 24 years. In patients with intradermal nevus. The age ranged from 26 to 65 years. With a mean age of 39.3 years. In malignant melanoma, the age range was 48 to 65 years, with a mean age of 52.8 years the present observation of age rnage in malignant melanoma cases is similar to that of criado-PR, et al, 1999.[6]

The Male: Female (M:F) ratio in the cases of albinism, vitiligo, leucoderma, urticaria pigmentosa, chronic eczema. Intradermal nevus and junctional nevus did not show wide variation except in cases of malignant melanoma where the M:F ratio was 7:3. In the present study, the mast cells count range in normal skin was 32-45 cells per 10 HPF, with a mean of 39.4.

The cases of albinism in the present study showed, mast cell count ranging from 56-80 cells per 10 HPF. With a mean of 67 cells. The mast cell count was significantly increased in albinism ($P<0.001$). When compared with the count of normal skin sections.

In cases of vitiligo, mast cell count ranged from 60-101 cells/ 10 HPF, with a mean of 78.50 cells. The mast cell count was significantly increased in vitiligo ($p<0.001$) when compared with the count in normal skin sections. The mast cell density was more in the superficial dermis.

Preliminary ICMR studies on vitiligo indicate that mast cells increase predominantly during re-pigmentation with highly dentritic melanocytes. These cells appear positive for serotonin. Further study is being conducted to study this interesting relationship (ICMR Bulletin, 1990)[7]. The ultraviolet light irradiation which is being used as a treatment modality in vitiligo may account for the increased mast cell count in the present study of vitiligo cases. The ultraviolet irradiation, in doses conducive to mild cutaneous inflammation, initially decreases and then increases the mast cells count.[8]

In case of leucoderma, the mast cells count ranged from 68-91 cells/10 HPF, with a mean of 78.83 cells. The mast cell count was significantly increased in leucoderma ($p<0.001$).when compared with the count in normal skin sections.

On comparison of mast cells distribution in cases of albinism versus vitiligo cases and in cases of leucoderma versus vitiligo cases, no statistical significant difference ($p>0.1$) was seen in either studies. The comparison of mast cell distribution in cases of albinism versue leucoderma cases showed significant difference ($p<0.05$) with increased count in leucoderma cases.

The literature on the mast cell distribution in the cases of albinism, vitiligo and leucoderma is scant, as assorted from Medlar, Medline, Internet and index Medicus.[9]

In urticaria pigmentosa cases, the mast cell count ranged from 161-202 cells / 10 HPF with a mean of 183 cells. The mast cell count was significantly increased in urticaria pigmentosa ($p<0.001$) when compared with the count of normal skin sections.

The present observation is similar to that of Bohac, 1906;[10] woringer, 1955 and[11] Marney SR Jr, 1992.[12] It is postulated that the mast cell is responsible for interactions with inhaled, ingested and injected antigens that comprise IgE-mediated allergic reactions, abnormally high numbers of mast cells in a localized area of skin result in urticaria pigmentosa.

On comparision of the mast cell distribution in cases of urticaria pigmentosa versus chronic eczema, significant statistical difference ($p<0.1$) was seen in urticaria pigmentosa. In cases of urticaria pigmentosa verusus intradermal nevus, significant statistical difference ($p<0.001$) was seen with increased count in urticaria pigmentosa. The comparison of cases of urticaria pigmentosa versus junctional nevus cases for the mast cell distribution showed significant statistical difference ($p<0.001$) with the mast cell count more in urticaria pigmentosa. And the mast cell distribution in cases of urticaria pigmentosa versus malignant melanoma cases showed no statistically significant difference ($p>0.1$) between the two groups.

In chronic eczema cases, the mast cell count ranged between 139-184 cells / 10 HPF with a mean of 163 cells. The mast cell count was significantly increased in chronic eczema ($p<0.001$) when compared with the count in normal skin.

The present observation is similar to that of Wiedmann and Niebauer, 1959.[13] It is stated that considerable alterations in the mast cells density occur as a consequence of inflammation, and the direction of the changes appears to depend mainly upon the intensity and chronicity of the lesions.

In comparison of mast cells distribution in cases of chronic eczema versus intradermal nevus, there was statically significant increase ($p>0.05$) in chronic eczema. The mast cell distribution in cases of chronic eczema versus junctional nevus showed no statistically significant difference ($p>0.1$) between the two groups. On comparison of the mast cells distribution in cases of chronic eczema versus malignant melanoma showed no statistically significant difference ($p>0.1$) between the two groups.

In intradermal nevus cases, the mast cell count ranged from 128-161 cells/10 HPF with a mean of 143 cells. The mast cell count was significantly increased in intradermal nevus ($p<0.001$) when compared with normal skin sections.

In junctional nevus cases, the mast cell count ranged from 139-164 cells/ 10 KPF with a mean of 152 cells. The mast cell count was significantly skin sections.

The present observation of increased mast cell count in nevi is similar to that of Rheindorf, 1905 and[14] staffel, 1906[15]. They assumed that mast cells can be transformed into pigment cells. There are no other latest studies available on this observation.

On comparison of mast cell distribution in cases of intradermal nevus versus juncitonal nevus. There was no statistically significant difference ($p>0.1$) Between the two groups. On comparison of intradermal nevus versus malignant melanoma cases, the mast cell distribution showed statistically significant increase ($p<0.001$) in malignant melanoma. The comparison of malignant melanoma cases versus junctional nevus cases for the mast cell distribution showed statistically significant increase ($p>0.001$) in malignant melanoma. This observation is similar to that of Schadendori et al, 1995[16] and higher in melanoma when compared with benign nevi.

In malignant melanoma cases, the mast cell count ranged from 151-187 cells / 10 HPF, with a mean of 171-7 cells, the mast cell count was significantly increased in malignant melanoma ($p<0.001$) when compared with normal skin sections. This observation is similar to that of Cawley and Hochligeti, 1961.[17] The distribution of mast cells was more at the tumor margins than compared within the lesion. This observation is similar to that of[18] Bonney, 1908. Similar observation was also noted by tabor[19] toth et al, 2000 and they postulated that melanomas show a strong immune-reactivity for IL-3, which is a potent mast cell chemotactic factor, whereas benign nevi showed no such immune-reactivity. The mast cells are suggested to play a crucial role in the vascularization by the release of angiogenic factors (VEFG) and may account for tumour progression and poor prognosis.

As early as 1914. Jacobi stated that the mast cells were common in the vicinity of pigmented regions. The common occurrence of simultaneous mastocytosis and pigmentation in various condition including urticaria pigmentosa, suggests some relationship between melanin formation and the mast cells.[20]

On comparison of the mast cell distribution in the cases of hyperpigmented skin lesions versus cases of hypopigmented skin lesions. There was a statistically significant increase ($P<0.001$) in hyperpigmented lesions (ICMR Bulletin, 1990). In 1954, Cottenot stated that the mast cells play an important role in cutaneous pigmentation since their number is increased in many dermatoses associated with hyperpigmentation.

It is thought that the action of tyrosinase is normally inhibited by SH-groups and that the mast cells may use up the available SH-for the synthesis of sulfated mucoplysaccharides, thereby removing a natural inhibitor of tyrosinase in melanogenesis. This study is a sincere attempt to probe the facets of mast cell alterations in the disorders of skin pigmentation. A careful review of literature on mast cells in hyper and hypo pigmented skin lesions has documented paucity of references.

The present study of mast cell pattern in the disorders of skin pigmentation highlights, that.

1. Mast cells can be documented in the skin tissue.
2. The mast cell alterations do occur in the disorders of skin pigmentation.
3. Mast cell count in hypo pigmented skin lesions was significantly increased as compared to normal skin.

4. Mast cell count in hyper pigmented skin lesions was significantly increased as compared to normal skin.
5. Mast cell count was significantly increased in urticaria pigmentosa, chronic eczema and malignant melanoma than compared to other diseases in hyper pigmented skin lesions.
6. Mast cell count was significantly increased in malignant melanoma as compared to benign nevi.
7. Mast cell count was significantly increased in hyper pigmented skin lesions as compared to hypo pigmented skin lesions.
8. Mast cell profile any be an additional diagnostic / grognostic parameter in these lesions.
9. Possible explanatory mechanisms for the above alterations have been suggested.

SUMMARY AND CONCLUSIONS: The present study of "Mast cells profile in disorders of skin pigmentation" included total cases of 53. Out of these; 6 cases of albinism, 6 cases of vitiligo, 6 cases of leucoderma, 6 cases of urticaria pigmentosa, 6 cases of chronic eczema, 7 cases of intradermal nevus, 6 cases of junctional nevus and 10 cases of malignant melanoma.

The mast cell count was performed per 10 HPF. Analyzed tabulated and statistically evaluated. A comparative evaluation of mast cells in disorders on skin pigmentation was performed.

The results of the present study trigger a speculation that mast cell modulation may present a role in therapeutic application of hypo pigmented / hyper pigmented lesion. Agents which increase mast cells and their degranulation may help in hypo pigmented skin lesions Conversely, mast cell inhibitors might prove useful in hyper pigmented skin lesions or malignant melanomas. Further sophisticated research on mast cells in pigmented skin lesions is required to elucidate these facts.

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