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Original Research Article

Mast Cell Count in Atopic and Contact Dermatitis

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Abstract

Context: Mast cells are the major effector cells in immediate hypersensitivity through activation via the high affinity IgE receptor and FcεRI. Given the broad array of proinflammatory mediators secreted from FcεRI – activated mast cells and IgE elevation is seen in a majority of atopic and contact dermatitis patients. Mast cells are believed to be involved in the pathogenesis of atopic and contact dermatitis.

Aims: The present study aimed at evaluating the mast cell count with respect to morphology, distribution and quantity in atopic and contact dermatitis cases.

Settings and Design:Retrospective study in an urban tertiary care hospital.

Material and methods: The study included a total of 50 skin biopsies and mast cell count was assessed in skin biopsies from patients with atopic and contact dermatitis. The tissues were fixed in 10% formalin, processed by routine paraffin embedding technique. The sections were stained with freshly prepared toluidine blue stain. The toluidine blue stained sections were evaluated for qualitative and quantitative aspects of mast cells. Mast cells were counted per field at 40 X magnification.

Statistical Analysis Used: The test results were evaluated by student T test.

Results: Mast cells were significantly increased in skin biopsies from patients with atopic and contact dermatitis with mean mast cell count 104.94/10 high power fields.The test results were statistically significant and the p value was (<0.005).

Conclusions: This study has revealed the role of mast cells as effector cells in development of atopic and contact dermatitis.

Keywords: Mast Cells; Toluidine Blue; Atopic Dermatitis; Contact Dermatitis.

Introduction

Mast cells are the hematopoietic cells that originate from the progenitor cells in the bone marrow .

Mast cell progenitors enter the circulation and become mature mast cells after entering destination tissues under the influence of local microenvironment [1]. The mast cells are present in small numbers in normal dermis, generally concentrated about blood vessels, especially postcapillary venules [2].

Mast cells are dynamic cells playing central role in allergic inflammation, protective immune response and other inflammatory responses.

They are found in all levels of skin including dermis, around blood vessels, nerves, appendages, at dermo epidermal junction (DEJ) and also in subcutaneous tissue

[3]. We decided to quantify the mast cells to understand their significance and role as the effector cells in the pathogenesis of dermatitis. Mast cells occur in normal dermis in small numbers as oval to spindle shaped cells with centrally located granules in the cytoplasm that do not stain 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.

In the present study, we have evaluated mast cell infiltration with respect to morphology, distribution and quantity in skin biopsies of patients with atopic and contact dermatitis using simple histologic techniques.

Materials and Methods

The study was conducted in the department of Pathology M.S Ramaiah Medical college. This retrospective study included a total of 50 skin biopsies taken for diagnostic purposes from patients with atopic and contact dermatitis after informed consent. Control tissues were obtained from normal skin of 50 patients, skin which was removed as a part of radical surgery for malignancy of breast ,oral malignancy etc.Lack of pathology in these control specimens was confirmed by routine histology. The tissues were fixed in10% formalin, processed by routine paraffin embedding technique. The sections were stained with freshly prepared Toluidine blue stain. The toluidine blue stained sections were evaluated for qualitative and quantitative aspects of mast cells. Mast cells were counted at 40x magnification, in ten consecutive high power fields and the total number of mast cells was summated and expressed/10 HPF. The areas selected included dermoepidermal junction (DEJ), perivascular, peri-adnexal and areas of cellular infiltration.

Results

A total of 50 skin biopsies were obtained from patients of atopic and contact dermatitis. Control tissues were obtained from normal skin of 50 patients, skin which was removed as a part of radical surgery for malignancy of breast , oral malignancy etc. In normal skin biopsies taken as control, mast cells were seen predominantly in perivascular and peri- adnexal location. They were sparse around DEJ and in dermis.Mean Mast cell count in the control skin biopsies was 18.86/10HPF (Table 1). The age distribution of these cases ranged from 12yrs-57 yrs. Male:female-1:2.3 ,female sex predilection was seen.

In the cases with dermatitis, mast cells were found throughout the dermis and were concentrated in the vicinity of vessels and skin appendages (Figures 1,2).

They had a blue rounded nucleus, and their granules were metachromatically stained reddish purple with toluidine blue. Mast cells were significantly increased in the skin biopsies from patients with atopic and contact dermatitis and mean mast cell count in these cases were 104.94/10HPF ($p<0.005$). In majority of the cases mast cells were degranulated(70%).

Table 1: Mean mast cell count in control and test skin biopsies

Skin lesions	Mean mast cell count/10high power field
Control	18.86/10hpf
Atopic and contact dermatitis	104.84/10hpf

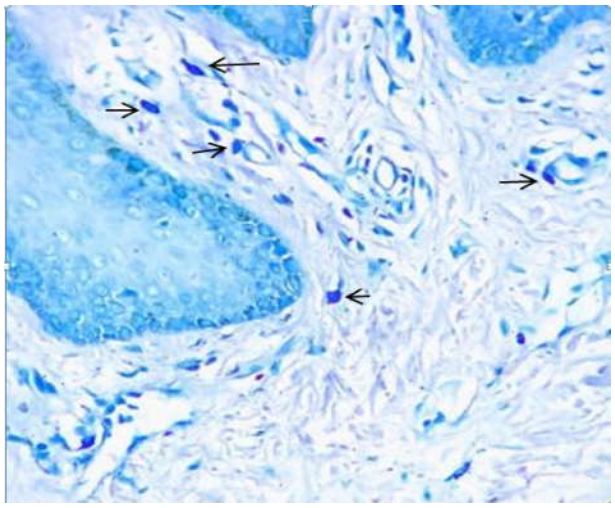

Fig. 1: Magnification 40X, Toluidine blue stained section, arrows (black) shows increased mast cells in upper dermis and around the blood vessels.

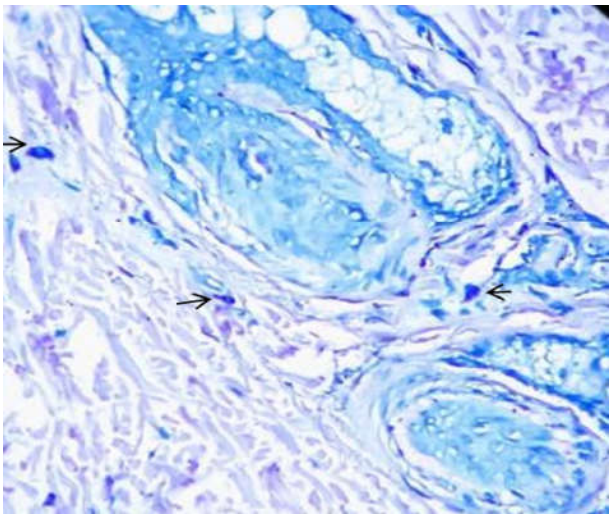

Fig. 2: Magnification 40X,Toulidine blue stained section, arrows (black) degranulated mast cells in periadnexal location

Discussion

Mast cells are well known as effector cells of IgE-mediated allergic reactions.

There is evidence of increase in the number of mast cells with degranulation in atopic and contact dermatitis, hence we decided to quantify the mast cells to understand their significance and role as the effector in the pathogenesis of dermatitis.

Mast cells are identifiable on H&E staining, but because of comparable morphology with other mononuclear cells, such as monocytes, histiocytes, lymphocytes, and melanocytes, they may require special staining for verification [4].

The high-affinity receptor for IgE (FcξRI) expressed on mast cells consists of four subunits ($\alpha\beta\gamma 2$): an IgE-binding α chain, a signal-amplifying and receptor-stabilizing β chain, and two disulfide-bonded γ chains that are the main signal transducers .

Upon encounter with multivalent antigen, IgE-bound FcåRI on mast cells become aggregated or crosslinked, leading to cell activation. Activated mast cells secrete three classes of substances: (1) preformed chemical and protein mediators, such as histamine, serotonin, heparin and chondroitin sulfates, proteases, major basic protein, acid hydrolases, cathepsin, (2) lipid mediators, such as prostaglandins, leukotrienes, and platelet-activating factor (PAF), (3) preformed and/or de novo synthesized growth factors, cytokines, and chemokines, such as tumor necrosis factor (TNF)-α , TGF-β, MIP-1α , MCP-1, VEGF, IFN-α /β/γ, GM-CSF, IL-1α /β, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-16, IL-18, IL-25, etc.

Allergic Contact Dermatitis

Allergic contact dermatitis is a common inflammatory dermatosis caused by exposure to a variety of haptenic antigens in sensitive individuals. In the sensitization phase the inflammation is initiated by the antigen being taken up by the skin antigen-presenting Langerhans cells, which then migrate to lymph nodes and present the antigen to naive T cells and activate these cells. During the elicitation phase T cells subsequently migrate to the affected skin site and are re-activated by the antigen presenting cells. This leads to a cascade of inflammatory responses, representing a type IV allergic reaction.

There are only a few studies addressing the function of mast cells in allergic contact dermatitis in humans. An early work examined allergic contact dermatitis reactions to dinitrochlorobenzene and urushiol (the antigen responsible for poison ivy contact dermatitis) and noted the presence of mitotic mast cells three days after the application of the allergens, as well as an increase in the number of these cells. In addition, mast cells noted to have undergone degranulation [5]. Most of our knowledge on the role of mast cells in allergic contact dermatitis is derived from studies of mouse models, in which skin reactions are induced by topical application of haptens. A number of studies demonstrated an increase in the mast cell density at the reaction sites. For example, in one study the investigators topically applied picryl chloride on days 4, 11, 18, and 25, and after the 4th application noted a significant increase in the number of mast cells [6]. These additional cells could originate from the bone marrow or from division of cells originally residing in the skin.

Degranulation of mast cells is also a regular finding in the lesional skin in the mouse models.This is observed at the sites of allergic contact sensitivity induced by a variety of haptens, including oxazolone, picryl chloride, trinitrochlorobenzene [7-8]. In a time course study, Kerdel et al [8], noted there was modest degranulation of mast cells between 1 and 6 h and extensive degranulation at 12 h, after antigen challenge, in mice sensitized with 0.1% tinitrochlorobenzene (TNCB) and then challenged with 1% TNCB. In summary, allergic contact dermatitis in humans is associated with an increase in the number of mast cells and activation of these cells and these findings are noted also in mouse models. In addition, it would be of interest to test whether mast cell inhibitors are useful for treatment of allergic contact dermatitis, in conjunction with other modes of therapies.

Atopic dermatitis (AD)

Atopic dermatitis is a relatively common chronic inflammatory skin disease characterized by intense pruritus and eczema, and is often associated with allergic asthma, rhinitis and food allergies. Various studies indicated that AD has a complex etiology, with involvement of multiple immunologic and inflammatory pathways. About 80% of AD patients show high levels of total and specific IgE antibodies to a variety of allergens, especially those in food and inhalant antigens, such as chicken egg, dust mites, pollens, and molds. Serum IgE levels in AD patients tend to be higher than those in other allergic diseases. Previous studies have shown a strong correlation between the serum. IgE levels and severity of AD. IgE-dependent allergic reactions are therefore thought to contribute to the development of AD. However, the involvement of IgE in the pathogenesis of AD remains controversial. Mast cells have also been shown to represent

key effector cells of acute AD lesions and contribute significantly to chronic AD.In acute AD lesions, mast cell population is normal in number but shows degranulation [8]. In contrast, there is a significant increase in their number, especially in areas of lymphocytic infiltration in the papillary dermis, in chronic AD lesions [10]. Elevated concentrations of histamine have been detected in the skin and plasma of patients with AD [11].

In AD skin, both IL-4 and IL-13, key cytokines for the development of the Th2 response, are increased. Mast cells have been shown to be the major source of these cytokines [12]. A recent report revealed that IL-4 and IL-13 are expressed by 66% and 20% of mast cells in AD skin, respectively [13]. Mast cells can contribute to Th2 polarization in the skin of AD patients through these cytokines. Mast cells also produce IL-5, which is likely to contribute to eosinophil infiltration in the AD skin [14]. Moreover, mast cells are found to be in close association with endothelial cells in the lesional skin and there is evidence suggesting that they stimulate vascular proliferation, probably via the release of proangiogenic factors [15]. Thus, these cells can promote inflammation indirectly through increasing the vasculature at the inflammatory sites. The current view is that AD, like other allergic disorders, results from complex interactions between a number of genetic and environmental factors.

There have been several reports about a significant association between the polymorphism of mast cellrelated genes and AD. One such report has demonstrated a strong association between gene polymorphism in the β chain of high-affinity IgE receptor (FcξRI) and AD [16]. Such polymorphism can result in increased surface expression of this receptor as well as amplification of intracellular signaling, resulting in increased IgE-dependent mast cell activation. Chymase, which is a chymotrypsin-like serine protease stored in mast cellgranules that hydrolyzes a variety of substrates, such as angiotensin I, metalloproteases, lipoproteins, and procollagen, is increased in the AD skin [17]. A recent discovery is a drug targeting IgE, Omalizumab, which has shown promise in the treatment of AD. Omalizumab is a humanized monoclonal antibody that binds to IgE at the same location recognized by FcξRI and it is thus able to effectively inhibit IgE binding to mast cells.In view of information supporting mast cells as critical effector cells in both acute and chronic AD lesions, therapies targeting mast cells might prove useful for treatment of AD.

Conclusion

Mast cells are found to be increased in number in many immunological skin diseases, including contact dermatitis, atopic dermatitis.This study has revealed the role of mast cells as effector cells of allergic reactions, which might also be true in the development of skin lesions in atopic and contact dermatitis.However, little is known about their potential role in modulating the course of atopic and contact dermatitis disease progression. Mast cell density, distribution and morphology may be useful in identifying various allergic skin lesions, understanding their evolution and modifying treatment protocols.

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Conflict of Interest: Nil

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