MAST CELL: A REVIEW

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Abstract

Mast cells (MC) are large spherical or elliptical mononuclear cells found in a variety of tissues including skin, submucosa or connective tissue of various organs & mucosal epithelial tissues & also in dental pulp. These cells display a diversity of roles in extracellular matrix degradation, angiogenesis and innate and acquired immune responses, due to their ability to release specific products such as chymase, basic fibroblast growth factor, tryptase, heparin, histamine, tumour necrosis factor, interleukins, chemokines and lipid mediators. This article briefly reviews the hallmarks related to the discovery, characterization and role of mast cells.

Key Words: Cells, Mast Cell, Staining

Introduction

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] A mast cell (mastocyte) is a resident cell of areolar connective tissue (loose connective tissue) that contains many granules rich in histamine and heparin. Although best known for their role in allergy and anaphylaxis, mast cells play an important protective role as well, being intimately involved in wound healing and defense against pathogens.[3] 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.[4]

In oral mucosa and skin, they are distributed preferentially about the micro-vascular bed, being in close proximity to the basement membranes of blood vascular endothelial cells and nerves.[5] Mast cells are relatively small cells, which are round or oval in shape, having a diameter of about 12-15µm. Their numerous cytoplasmic granules frequently obscure the small, round nucleus. In some sections, these cells seem to have degranulated, so that many of the granules are located outside the cells. These metachromatic granules are easily detected by stains such as toluidine blue.[6]

Origin

In 1879, Ehrlich further discovered mast cell with basophilic granules which appeared to originate in the bone marrow and stated that mast cells are tissue basophils and basophils were blood mast cells. Michael D in 1938 stated that mast cells arise from a multipotent CD 34+ precursor in the bone marrow and circulate in the peripheral blood as agranular monocyte appearing cells. After migrating into the tissues these immature mast cells assume their typical granular morphology.[7]

Development of Mast Cells

Mast cells appear at different stages of embryonic development in different organs. Hence it is difficult to assess the embryology of mast cells. In human embryo no mast cells could be demonstrated between 15th to 60th days of intra uterine life. Mast cells with sparse metachromatic granulation appear in the tissue of human embryos after the 2nd month. Some of these cells have 2 nuclei, but mitoses has been noted only once.[8] In the 5th and 6th months old human foetus mast cells are demonstrable in the kidney, liver, spleen, skin and muscles, but are of smaller size than in adults.[9]

It is now accepted that mast cells arise from pluripotent haematopoietic stem cells in the bone marrow. It was demonstrated by Kitamuray and co-workers.[10]

There is a developmental basis for the possibility that cells of the neural crest derivation (including melanocytes) may continue to differentiate in the adult organism from pluripotent mesectodermal stem cell origin.

Mast cells entering circulation are small in number. Before they can be identified morphologically from circulation, mast cell precursors enter in peripheral tissue, where they express their final phenotype under influence of stem cell factor (SCF) and other locally produced cytokines.[11]

Structure

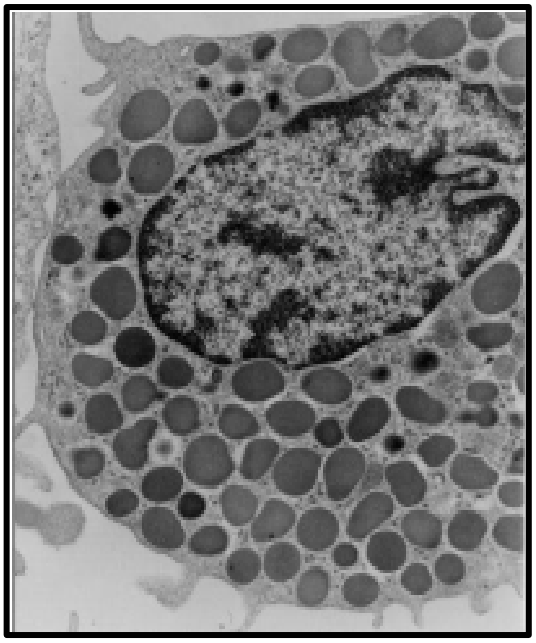

Figure 1: Ultrastructural finding of a resting human mast cell showing a monolobed nucleus, narrow surface folds and numerous electron dense cytoplasmic granules. Original magnification X 15000.

A typical mast cell has a mean diameter of almost 8-15µm. The mast cells are irregular in outline with clear cut cytoplasmic processes extending from them. The cytoplasm is packed with granules and show very few small mitochondria. The most characteristic subcellular components of mast cells are their secretory granules. They vary in size from 0.2 to 0.8µm and are bounded by a unit membrane. The shape of these granules has varying patterns, such as scrolls, whorls and particulate or lamellar structure.[12] (Figure 1)

In oral mucosa & skin the granules in mast cell have complex form with the amorphous region located next to crystalline region. The crystalline region ranges in configuration & three types of mast cell population is identified.

1. Cells deeper in connective tissue (except that in close vicinity to blood vessels) are round /oval in shape & dark purple in colour. The cell borders are well defined & nucleus is not visible due to granules making the nucleus & is called as intact cells.
2. In the superficial connective tissue, immediately below infiltrate in Oral Lichen Planus and near the blood vessels the mast cells appear flattened / irregular & cytoplasm appears granular. The cell borders are not defined & the nucleus is only partially appreciable; these cells are called spreading cells.
3. The third type called degranulated cells found within the infiltrate & appeared paler as the staining has changed from metachromatic violet to light pink, the nucleus blue in colour and well defined.[13]

Masts cells are classified according to protease content. MCT type contain tryptase only and are located in the respiratory and intestinal mucosa, where they localize around T lymphocytes. MCTC contain both tryptase & chymase and are predominantly found in connective tissue areas such as skin, conjunctiva and synovium.[14]

Staining

Mast cells on Haematoxylin and Eosin staining, resemble large eosinophils,in that the abundant cytoplasm is filled with eosinophilic granules. Granules stain less brightly than those of an eosinophilic leucocyte. Nucleus is ovoid and not lobulated usually. The cytoplasm of the cells is generally pink, the nucleus is purplish or blue and the cytoplasmic granules are dark blue or even blackish.[15]Immature mast cells are spindle shaped resembling fibroblasts or histiocytes in routinely stained sections with few or no cytoplasmic granules.[16]

On special staining with Toluidine Blue mast cells show up as large rounded ovoid or spindly shaped cells.(Figure 2)They lack a basal lamina and may have short pseudopodia, because they are wandering cells. The granules are refractile, water-soluble and they exhibit metachromasia.[17]

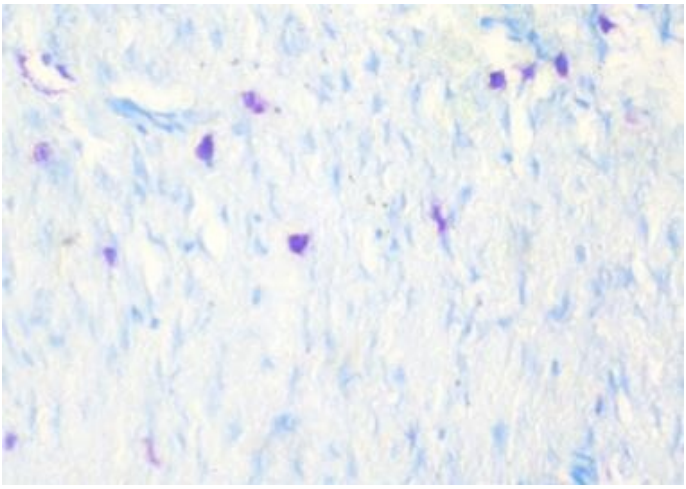

Figure 2. Photomicrograph showing mast cells in periapical granuloma 40X magnification

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 pH 1 is preferred. For selective staining of mast cells one can use chrysodin, Bismark brown or a modification of Astra blue technique. One can also stain the metachromatic granules and the rest of the cell (nucleus, cytoplasm) in contrasting by Fuelgen and Methyl green or Fuelgen and Bismark brown technique. By this method one can see mitotic figures in mast cells very clearly. Granules are well shown by staining with alcian blue at pH 2.They are positive also for chloracetate esterase (unlike eosinophilic granules).[18]

Role of Mast Cells

Apart from being prominently involved in allergic reactions, mast cells are critical for the maintenance of tissue integrity and function. This correlates with their ubiquitous presence in nearly all tissues. Their central role in immunological as well as non- immunological processes is further reflected by the large number of mediators by which mast cells may influence other cells. These mediators allow mast cells to regulate either local tissue functions or host defense by acting as innate immune cells, by interacting with the specific immune system, or by inducing and regulating inflammation.[19]

Since mast cells are located at the border of the body and environment, they are perfectly equipped with their mediators to orchestrate the immune system. They can recruit other immune cells to the site of injury and control the function of various cells such as eosinophilic granulocytes, T and B lymphocytes, thereby being implicated in the protection of the organism against bacterial, parasitic and viral infections. This role can be achieved precisely because mast cells are able to release selective mediators without degranulation (differential release). Otherwise, activation would always lead to

allergic or anaphylactic reactions.[20]

In addition, mast cells essentially regulate homeostasis. In this connection, they contribute to wound healing as well as tissue remodelling, e.g. in hair follicles and bones. Mast cells promote homeostasis by degrading certain endogenous toxins such as endothelin-1 or neurotensin released in response to bacterial infection by means of their potent proteases. Similarly, mast cells are involved in the control of exogenous toxins such as venoms and bacterial toxins.[21]

Mast cells can participate in direct killing of organisms by phagocytosis and reactive oxygen species production, and can produce antimicrobial peptides, such as cathelicidins, both constitutively and in response to lipopolysaccharide or lipoteichoic acid exposure. These peptides were found to mediate killing of Group A streptococci (GAS) in vitro and in vivo. Additionally, similar to neutrophils, mast cells have been found to produce extracellular traps that encompass and kill organisms, such as GAS, in vitro. Although these microbicidal responses may be important in some infections, the relatively small number of mast cells in tissues suggests that indirect effects of mast cells in coordinating host innate and adaptive responses may be more important in the balance of host defence.[22]

Conclusion

Mast cells serve a critical role in the development of inflammation in the oral mucosa and the dental pulp, both in the early, vaso-inductive events and in the transition from acute to chronic inflammation. Because of the unique properties of mast cells, these cells are ideally poised to serve as "gatekeepers" of the microvasculature in the oral cavity. An appreciation of the multiple interactions among mast cells, endothelial cells, nerves, and other immune system provides a basis for therapies for targeting mast cell responses. Hence, this overview aims to understanding mast cells and their role.

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