

Merkel Cells - Pathophysiology- A Review

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ABSTRACT

The objective of this review is to know about the function, theoretical background and clinical importance of merkel cells. Origin of merkel cell is believed to be the neural crest derivative. Whereas others said it is derived from fetal epidermal keratinocytes. Merkel cells are situated in the basal layer of oral epithelium. Merkel cell, unlike melanocyte and langerhans cell is not dendritic. They are concentrated in touch sensitive area, hairy skin and mucosa. This review gives information about the origin, distribution, staining and ultrastructure and functions of merkel cells.

Keywords: Markel cells, Pathophysiology, Epithelium.

INTRODUCTION

Merkel cells are found on the basal cells of the oral epithelium. It is a specialized neural pressure-sensitive receptor cell. It responds to touch sensation. Most commonly seen in masticatory mucosa. They are absent in lining mucosa. They differ from other non keratinocytes in that they are non dendritic... its nucleus shows characteristic rodlet and also contains numerous electron dense granules. They migrate from neural crest cells. They are sensory and respond to touch.

Origin

They are derived from two hypotheses- 1. Neural crest origin hypothesis, 2. Epidermal origin hypothesis. Moll *et al.*, (1990) also showed that MCs when xenografted from human epidermis to on the dermis of nude mice that had been deprived of nerve elements.^{1, 2, and 3} this shows they are epidermal derived. Merkel cells are associated with neural elements. They are stem cell differentiated and are do not have mitotic activity.

Distribution

They are found in some parts of mucosa and skin. They are about 10 μ m in diameter and are found in the stratum basale layer of the epidermis. It has sub adjacent nerve tissue and are associated with the neural cells. It is a specialized neural pressure sensitive receptor cells. Most commonly seen in the masticatory mucosa and are absent in lining mucosa. They are concentrated in the hairy skin, glabrous skin and in certain mucosal sites.⁴there is density variation distribution of these cells. They are found dense in the palmar aspect of the hand, the feet and the plantar aspect of the toes. In oral cavity they are found in dense in lip, anterior part of hard palate and the gingiva. These regions are involved in tactile perception and also they are abundant in the sun exposed regions of the skin.

Staining

In H & E staining the merkel cells are hardly identified. They can be viewed by special staining techniques probably periodic acid Schiff. The dense

granules present stains positively for neuroendocrine markers- chromgranin A, neuron specific enolase and synaptophysin. These markers are adjuvant for diagnosis. Substance-p sometimes shows variable positivity. In light microscope, CK-20 shows higher specificity⁵ sometimes they can be identified by incorporation of fluorescent dyes.

Ultrastructure

They are found on the basement membrane. They are non-dendritic, sparse desmosomes and tonofilaments. They show characteristics electron dense vesicles and associated nerve axon. The nucleus shows a deep invagination and characteristic rodlet. They also contain numerous electron dense granules located exclusively in the cytoplasm. Between axon terminals and merkel cells the type of junction is intermediate. The function of this granules are non known and are stained by PAS. They shows spine like protrusions sometimes called microvilli. They measure 2.5 mm in length and 80-120 nm in diameter.⁶ Cytoplasm contains intermediate filament cytoskeleton and have low microscopic density.

Possible functions

There are three main functions of merkel cells

1. Somatosensation
2. Endocrine function
3. Chemo sensation

Somatosensation

They form complex with afferent somatosensory to form slowly adapting touch receptors. They are sensory cells that transduce mechanical stimuli and then via neurotransmission they communicate with the afferent sensory. They are sensitive receptor cells.⁷

Endocrine function

Since they secrete variety of amines and polypeptide hormones they have endocrine

functions. They store hormones in cytoplasmic granules that are visible by electron microscopy. It was shown that the morphology of secretory granules of endocrine cells were similar to dense core granules of merkel cells⁸

Chemosenation

They have nociceptive function mediated by free nerve endings. Pain is transmitted via free nerve endings. Substance-p and calcitonin gene related peptide responds to physical or chemical irritation. They are the mediator for nociceptive information⁹

Merkel cell carcinoma

They are aggressive malignancy with poor prognosis. They are diagnosed clinically at the time of clinical presentation. They are mostly blue or red, non tender, solitary, dome shaped nodule which are firm. Differential diagnosis for this include-basal cell carcinoma, squamous cell carcinoma, pyogenic granuloma. Diagnosis through routine H & E and immunohistochemistry. Histologically they involve full thickness of dermis. They are found mainly in elderly patients with the risk of lymphatic metastasis. Mortality-25% common in head and neck region and in extremities and greater prediction of periorcular region. They are composed of small, round malignant cells¹⁰. In most cases it can be caused by merkel cell polyoma virus. Histopathologically they are of three types-trabecular type, intermediate type and small cell type

CONCLUSION

These cells are located in the basal cells and are electron dense granules. Most studies focus on neuroendocrine functions of merkel cells and their possible transformation into malignant merkel cell carcinoma.

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