Review Article

Merkel Cells: A Review on Role of Merkel Cells in Histology and Disease

Nandhini G. Ashok, Abilasha Ramasubramanian
Department of Oral Pathology, Saveetha Dental College, Chennai, Tamil Nadu, India

Abstract

The basic objective of this review is to understand the role of Merkel cells (MCs). MCs are neuroendocrine cells present in the epidermis of basal layers of vertebrates. The origin of MCs is controversial. They act as mechanoreceptors. MC carcinoma is known to be aggravating primary cutaneous neoplasm. Diagnosis of this is based on their staining. Radiation therapy and chemotherapy are given for such patients.

Keywords: Merkel-cell carcinoma, Merkel cells, neuroendocrine cells

Introduction

Merkel cells (MCs), otherwise known as Merkel–Ranvier cells, are neuroendocrine cells that are found in the skin of vertebrates near the nerve endings. They are nonkeratinocytes that act as touch receptors through the tactile meniscus.

History

They were first described by Friedrich Sigmund Merkel in 1875 and named " Tastzellen" (touch cell) assuming a sensation with the skin.[1] Clusters of Merkel nerve endings in glabrous skin were called "touch corpuscles." These terms indicated Merkel's assumption of them to be mechanoreceptors. Later, they were simply called MC.[2]

Origin

MC origin is found to be controversial. One hypothesis proposes that they are derived from neural crest cells.[3] This hypothesis believes that they migrate into the mammalian epidermis during the embryonic period.[2] The other one postulates that they originate from epidermal progenitors.[3]

The presence of desmosomal contacts between MC and keratinocytes is interpreted as support for the ectodermal origin hypothesis.[2]

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Location

MCs are found in the skin and some parts of the mucosa of all vertebrates. In mammalian skin, they are clear cells found in the stratum basale (at the bottom of sweat duct ridges) of the epidermis approximately 10 μm in diameter. They also occur in epidermal invaginations of the plantar foot surface called rete ridge. Most often, they are associated with sensory nerve endings, when they are known as Merkel nerve endings (also called a MC-neurite complex) [Figure 1]. They are associated with slowly adapting somatosensory nerve fibers.[2]

Structure

MCs are oval epidermal cells found in the basale layer below a row of columnar cells. They appear individually or in clusters. They are different from the other clear cells. They measure about 10–15 μm. They have a dense-core granules containing numerous neuropeptides and cytoskeletal elements consisting of cytokeratin and desmosomes.[4] They have finger-like projections on their surface which are of different and varying sizes and lengths to interdigitate with the neighboring

Address for correspondence: Dr. Nandhini G. Ashok, Department of Oral Pathology, Intern, Saveetha Dental College, Chennai - 600 077, Tamil Nadu, India.
E-mail: doc.nandhiniashok@gmail.com

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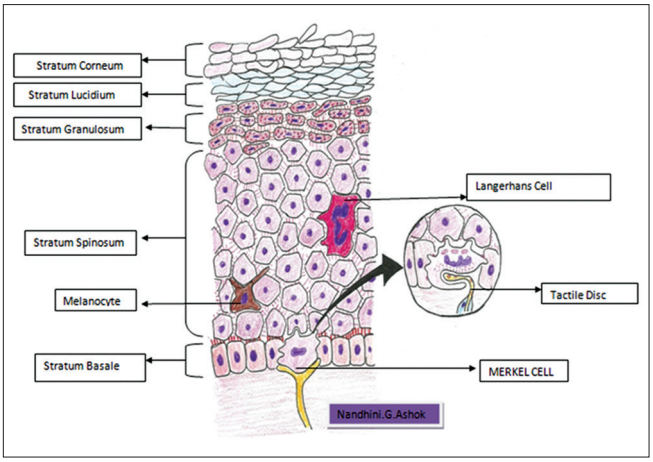

Figure 1: Location of Merkel cell

keratinocytes. The nucleus is large and lobulated. The nerve terminal contains mitochondria.

Function

They function as mechanoreceptors through their Merkel nerve endings. MCs play in light-touch responses have been the center of controversy for over 100 years.[5] They can be divided into innervated and noninnervated type.[1] The MCs are also believed to have a neuroendocrine function. Recent immunohistochemical demonstrations of neuropeptides in MCs of several mammals[6-9] support the classical concept that the MC is directly involved in mechanoreception[10-12] presumably through the release of these neuropeptides as messenger substances.[9]

Identification

MCs are difficult to identify by routine light microscopy but have been identified by electron microscopy and specific antibodies.[13] FM dyes were used for long-term staining of live MCs since quinaerine was lost quickly from the intracellular spaces, and MCs became difficult to identify.[14] They are also identified with eosin and hematoxylin staining.

Merkel-Cell Carcinoma

MC carcinoma (MCC) is an uncommon type of skin cancer which was described for the first time by Toker in 1972. MCC is a rare but aggressive human skin cancer that typically affects elderly and immunosuppressed individuals, a feature suggestive of an infectious origin.[15] It is also known as cutaneous APUDoma, primary neuroendocrine carcinoma of the skin, primary small-cell carcinoma of the skin, and trabecular carcinoma of the skin.[16] They are caused by polyomaviruses. Polyomaviruses are small circular DNA viruses encoding a T-antigen oncoprotein locus. T-antigens are expressed from variably spliced viral transcripts that target tumor suppressor and cell cycle regulatory proteins including retinoblastoma tumor suppressor protein (Rb).[17]

It mostly affects the elderly and people who have weak immune systems. The mortality rate is about 25%. Studies show that MCC cases have tripled over the past 20 years and half the patients with advanced stages live only 9 months.

Treatment

Treatment is generally based on the stage of the disease. There are four major treatments for MCC: (1) surgical excision of the primary lesion, (2) lymph node surgery, (3) radiation therapy, and (4) chemotherapy. Depending on how well a patient tolerates the treatments, surgery, radiation therapy, and chemotherapy may be given at the same time or one after the other.

Surgery is usually the first treatment that a patient undergoes for MC cancer. Lesions usually appear purple–red in color, and there is little else to distinguish this variant of skin cancer from other types. Its identity usually comes as a surprise after surgery and pathologic examination. Radiotherapy is commonly used to treat MC cancers. Adjuvant radiotherapy is effective in reducing the recurrence rate and in increasing the survival of the patients.

Follow-up Care

MCC is optimally cared for by a team of doctors from dermatology, surgery, medical oncology, and radiation oncology. Most recurrences of MCC and most deaths from this disease occur within the first 3 years. Patients should have regular appointments for skin and lymph nodes examinations every 3–6 months for the first 3 years. Computed tomography (CT) scans are sometimes performed every 6 months for a few years after a high-risk diagnosis. Unfortunately, by the time MCC is visible on a CT scan; curative treatment is no longer possible. Therefore, scans are not routinely recommended.

Conclusion

The importance and function of MCs were only described years later after its discovery. They can be studied under light and electron microscopy. However, till today, their origin is still under argument. Their main function is to act as mechanoreceptors although the Merkel nerve endings. MCC is another grade of skin cancer which is near to the highest grade of skin cancers. The only best treatment is by radiation therapy or chemotherapy.

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Conflicts of interest

There are no conflicts of interest.

References

1. Moll I, Roessler M, Brandner JM, Eispert AC, Houdek P, Moll R,

et al. Human Merkel cells – Aspects of cell biology, distribution and functions. Eur J Cell Biol 2005;84:259-71.
2. Halata Z, Grim M, Bauman KI. Friedrich sigmund Merkel and his "Merkel cell", morphology, development, and physiology: Review and new results. Anat Rec A Discov Mol Cell Evol Biol 2003;271:225-39.
3. Winkelmann RK. The Merkel cell system and a comparison between it and the neurosecretory or APUD cell system. J Invest Dermatol 1977;69:41-6.
4. Lucarz A, Brand G. Current considerations about Merkel cells. Eur J Cell Biol 2007;86:243-51.
5. Maricich SM, Wellnitz SA, Nelson AM, Lesniak DR, Gerling GJ, Lumpkin EA, *et al.* Merkel cells are essential for light-touch responses. Science 2009;324:1580-2.
6. Hartschuh W, Grube D. The Merkel cell – A member of the APUD cell system. Fluorescence and electron microscopic contribution to the neurotransmitter function of the Merkel cell granules. Arch Dermatol Res 1979;265:115-22.
7. Hartschuh W, Weihe E. Fine structural analysis of the synaptic junction of Merkel cell-axon-complexes. J Invest Dermatol 1980;75:159-65.
8. Hartschuh W, Weihe E, Yanaihara N, Reinecke M. Immunohistochemical localization of vasoactive intestinal polypeptide (VIP) in Merkel cells of various mammals: Evidence for a neuromodulator function of the Merkel cell. J Invest Dermatol 1983;81:361-4.
9. Hartschuh W, Reinecke M, Weihe E, Yanaihara N. VIP-immunoreactivity in the skin of various mammals: Immunohistochemical, radioimmunological and experimental evidence for a dual localization in cutaneous nerves and Merkel cells. Peptides 1984;5:239-45.
10. Iggo A, Muir AR. The structure and function of a slowly adapting touch corpuscle in hairy skin. J Physiol 1969;200:763-96.
11. Horch KW, Whitehorn D, Burgess PR. Impulse generation in type I cutaneous mechanoreceptors. J Neurophysiol 1974;37:267-81.
12. Parducz A, Leslie RA, Cooper E, Turner CJ, Diamond J. The Merkel cells and the rapidly adapting mechanoreceptors of the salamander skin. Neuroscience 1977;2:511-21.
13. Ness KH, Morton TH, Dale BA. Identification of Merkel cells in oral epithelium using antikeratin and antineuroendocrine monoclonal antibodies. J Dent Res 1987;66:1154-8.
14. Fukuda J, Ishimine H, Masaki Y. Long-term staining of live Merkel cells with FM dyes. Cell Tissue Res 2003;311:325-32.
15. Feng H, Shuda M, Chang Y, Moore PS. Clonal integration of a polyomavirus in human Merkel cell carcinoma. Science 2008;319:1096-100.
16. Rapini Ronald P, Jean L , Jorizzo Joseph L. Dermatology: 2-Volume Set. St. Louis: Mosby; 2007.
17. DeCaprio JA, Ludlow JW, Figge J, Shew JY, Huang CM, Lee WH, *et al.* SV40 large tumor antigen forms a specific complex with the product of the retinoblastoma susceptibility gene. Cell 1988;54:275-83.