Merkel cell distribution in human hair follicles of the fetal and adult scalp

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Abstract. The distribution of Merkel cells in fetal and adult terminal hair follicles of human scalp was studied immunohistochemically using cytokeratin (CK) 20 as a specific Merkel cell marker. In hair follicles of adult scalp, abundant Merkel cells were found enriched in two belt-like clusters, one in the deep infundibulum and one in the isthmus region. No Merkel cells were found in the deep follicular portions including the bulb, or in the dermis. In early fetal hair follicles (bulbous peg stage), Merkel cells were only detected in the basal layer of the developing infundibulum but not in deeper follicular areas. In later stages, Merkel cells were also present in the isthmus and bulge. No Merkel cells were seen in the dermis around developing hair follicles. Nerve growth factor receptor was not only present in nerves but was found to be widely distributed within fetal skin. In adult skin, this receptor was localized to the basal cell layers of the outer root sheath of the bulb and the suprabulbar area, but was not detectable in the areas containing Merkel cells. The present study localizing Merkel cells within the permanent hair follicle structures close to their possible stem cells suggests that they have paracrine functions.

Key words: Merkel cells – Cytokeratins – Immunocytochemistry – Nerve growth factor receptor – Hair follicles – Human

Introduction

Merkel cells, first described by Merkel in 1875, are specialized secretory epithelial cells present within several stratified squamous epithelia of many species including man (Hartschuh et al. 1986; Merkel 1875; R. Moll et al. 1984; Winkelmann and Breathnach 1973). In humans, they are disseminated within the basal layer of epidermis and oral mucosa often showing dendrites (Kidd et al. 1971; Lacour et al. 1991; R. Moll et al. 1984; Munger and Halata 1983; Turner 1983; Winkelmann and Breathnach 1973). Moreover, within the so-called Pinkus Haarscheibe, they are nerve-associated and function as touch receptor cells (English et al. 1992; I. Moll et al. 1993; Pinkus and Tanay 1968). In human fetal glabrous skin, their distribution is well established. They are clustered in a special arrangement within the epidermal ridges of palmar and plantar skin, which, in the fetus, also contain many dermal Merkel cells (Breathnach and Robins 1970; I. Moll et al. 1986; R. Moll et al. 1986; R. Moll et al. 1984).

Recent studies have shown that the intermediate (cytokeratin, CK) filaments of Merkel cells differ not only morphologically but also biochemically from tonofilaments of keratinocytes: they are composed exclusively of CKs of the simple epithelial type (CK 8, CK 18, CK 19, and CK 20; R. Moll et al. 1984, 1992). These CKs are not expressed in epidermal keratinocytes and therefore can be used as markers of Merkel cells in adult epidermis (R. Moll et al. 1982a, 1982b). The specificity of the presence of cytokeratins CK 8 and CK 18 for granule-containing Merkel cells has been demonstrated by various groups using combined immunocytochemical and electron-microscopic techniques (Lacour et al. 1991; R. Moll et al. 1984; Narisawa et al. 1992a, 1992b; Ness et al. 1987; Saurat et al. 1983). Since CK 8 and CK 18 have been shown by double immunofluorescence microscopy to be co-localized with CK 20, the latter is probably just as good a marker for Merkel cells within the epidermis as CK 8 and CK 18 (Moll and Moll 1992, 1993). Therefore, antibodies selective for these CKs have been widely used to study the distribution of Merkel cells in adult skin, oral epithelium, and various locations within fetus (Lacour et al. 1991; I. Moll et al. 1986; I. Moll et al. 1990; Moll and Moll 1992; Saurat et al. 1983). Moreover, cells positive for CK 8, CK 18 or CK 20 within human Haarscheibe show all of the well-established features of Merkel cells, including their morphology and topographical distribution (English et al. 1992; R. Moll et al. 1982a). However, fetal periderm cells, fetal basal keratinocytes, and cells of fetal and adult hair follicles may also express CK 8, CK 18, and CK 19 (R. Moll et al. 1982b). Thus, among these four
CKs, only CK 20 is exclusively restricted to Merkel cells in the entire skin of both fetuses and adults (I. Moll and R. Moll 1992; I. Moll and R. Moll 1993).

In earlier studies, Merkel cells have also been identified in human vellus and guard hair, and in hair follicles of body skin (Bonorden-Kleij and Halata 1991; Ebling 1976; Hartschuh et al. 1986; Munger and Halata 1983; Munger and Halata 1984; Santa Cruz and Bauer 1982). In the present study, selective antibodies against CK 20 have been used to analyze, at the light-microscopic level, the distribution of Merkel cells within anagen and telogen hair follicles of adult human scalp skin and of various fetal stages. Their position has been compared with the putative position of the follicular stem cells that are assumed to reside within the bulge (Cotsarelis et al. 1990). This area is claimed to express CK 19 extensively (I. Moll et al. 1986; Stasiak et al. 1989). In addition, the expression of nerve growth factor (NGF) receptor in fetal and adult Merkel cells of hair follicles has been studied.

Materials and methods

Tissues

Samples of scalp skin from six adult patients (cases 1–6) were obtained during the removal of various skin tumors; one was from an autopsy (case 7). All samples were at least 2 cm distant from the lesion to be excised. Fetal tissue samples from the scalp (case 8, 14 weeks; case 9, 15 weeks; case 10, 18 weeks; case 11, 22 weeks; case 12, 24 weeks; case 13, 26 weeks) were obtained during abortion for various medical indications or at premature delivery. All specimens were immediately snap-frozen in isopentane, pre-cooled in liquid nitrogen, and stored at −80°C until used. In some cases, formalin-fixed paraffin-embedded tissue samples were available and studied (Franke and Moll 1987; see also R. Moll et al. 1988).

Fig. 1. Immunoperoxidase staining of adult scalp skin (case 1) using antibodies against CK 20. Note that the Merkel cells of various follicles are located at the same level, corresponding to the deep Merkel cell cluster. SG Sebaceous gland; V vellus hair. ×150

Fig. 2a, b. Immunoperoxidase staining of Merkel cells (decorated by antibodies against CK 20, case 1), which are clustered within the isthmus region below the sebaceous gland (SG). The bulge area (B) is free of Merkel cells. M M. arrector pili. ×280