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Characterization of factor XIIIa+ dendritic cells in dermatofibroma: Immunohistochemical, electron and immunoelectron microscopical observations

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Summary

Background: Previous studies indicate that FXIIIa+ proliferative cells are the cells constituting DFs, however, in spite of the high incidence of DFs, there is a little information in the literature regarding ultrastructural characteristics of the FXIIIa+ dendritic cells on DFs.
Objectives: In this study, we examined the fine structures and potential heterogeneity among the subgroup of factor XIIIa (FXIIIa) positive dendritic cells consisted of eleven cases of dermatofibroma (DF).
Methods: Immunohistochemical, electron microscopical, and immunoelectron microscopical techniques were utilized.
Results: We demonstrated (i) the immunohistochemical labeling of FXIIIa and CD68 in the DFs. The reactivity was stronger in histiocytic lesions than in fibroblastic lesions. On the other hand, the labeling of HHF35 was mainly in fibroblastic lesions. (ii) The fibroblastic and histiocytic cells on DFs displayed the same basic fine structures; moderate or abundant rough endoplasmic reticulum (RER), lipid droplets and/or bundles of myofilaments in varying proportions. Macular adherence connections between neighboring cells were common. (iii) They also showed the similar features to dermal dendritic cells (DDC), which have been well characterized with long cytoplasmic processes, abundant RER, fibronexus-like plaques and pinocytotic vesicles. (iv) FXIIIa expressions were found within the cytoplasm of both fibroblastic and histiocytic cells in association with the nucleus by immunoelectron microscopy. The labeling was stronger in the histiocytic cells and the cells expressing elongated cytoplasmic processes than in the fibroblastic cells.

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Conclusion: The FXIIIa+ dendritic cells might be an essential cell of DF, and might have potential to develop HHF35+ fibroblastic or CD68+ histiocytic cells, under appropriate stimuli. The FXIIIa+ dendritic cells might be originated from DDC.

1. Introduction

The resident interstitial cells of the human dermis were widely believed to be fibroblasts, and were described as spindle-shaped, based on the observation of paraffin- or plastic-embedded sections. However, in 1986, Headington [1] designated the cells, which showed highly dendritic configuration when stained with nicotinamide adenine dinucleotid diapholase or adenosine triphosphatase on frozen sections, as ''dermal dendrocytes''.

Moreover, Cerio et al. [2] demonstrated that factor XIIIa (FXIIIa) labeled highly dendritic dermal cells located particularly in the upper reticular and the papillary dermis. They concluded that FXIIIa+ cells in human skin represented a specific population of dermal dendritic cells (DDCs), a subset of the monocyte-macrophage system, and were a population distinct from Langerhans cells. In 1990, Nickoloff and Griffiths [3] reported by double-labeling immunofluorescence studies that FXIIIa+ spindle-shaped or dendritic cells in normal and diseased skin were bone marrow-derived monocyte/macrophages, but not mesenchymally derived fibroblasts.

Recent studies of mesenchymal cells of the dermis, using antibodies to FXIIIa and CD34, have demonstrated immunophenotypic heterogeneity amongst the normal DDCs of the dermis [4,5].

Dermatofibroma (DF), also known as benign fibrous histiocytoma, represents one of the most common fibrohistiocytic tumors of the skin. Histopathologically, DF is characterized by the presence of different cell types consisting of fibroblastic cells, histiocytic cells, and even multinucleated giant cells, in varying proportions. DF can be divided into fibrous lesions composed of almost entirely of fibroblastic cells and collagen fibers, and cellular lesions composed of a significant numbers of histiocytic cells including foam cells. It was controversial whether the primary cell in DF was a fibroblast or a histiocyte until the immunohistological studies was introduced [7,8]. The immunohistological studies conduced by Cerio et al. [9] have clearly demonstrated that most of the cellular components of DF reacted with FXIIIa, suggesting DDC as the origin of DFs.

These data indicate that FXIIIa+ proliferative cells are the cells constituting DFs, however, in spite of the high incidence of DFs, there is a little information in the literature regarding ultrastructural characteristics of the FXIIIa+ dendritic cells on DFs [10].

Recently, Sueki et al. [11] reported that DDC had some unique ultrastructural characteristics differed from dermal fibroblasts. There have been no previous reports describing the ultrastructural similarities of DDC to the cells of DFs.

In order to further study of phenotypic characteristic of FXIIIa+ dendritic cells on DFs, we studied eleven DFs immunohistochemically, and electron- and immunoelectron microscopically.

2. Materials and methods

2.1. Case selection

Eleven DFs were found to have typical histological diagnostic features. All cases were subjected for immunohistochemical and electron microscopical investigations. Moreover, one case (case 8) was investigated by immunoelectron microscopical methods.

2.2. Immunohistochemical staining

Specimens were prepared routinely for histological study. Immunohistochemical studies on the formalin-fixed and paraffin-embedded tissue specimens were performed using a streptavidin-biotin-peroxidase technique. The following antibodies were used; polyclonal antibody to FXIIIa (Hoechst, Middlesex, UK) diluted in 1:1000, monoclonal antibody to CD34 (Immunotech S.A., Marseille, France) diluted in 1:50, monoclonal antibody to CD68 (DAKO, Glostrup, Denmark) diluted in 1:200, monoclonal antibody to smooth muscle actin (HHF35; Enzo Diagnostics, Farmingdale, USA) diluted in1:200.

Neoplastic cells from within these tumors with positive staining were evaluated semiquantitatively using a technique similar to that employed by Altman et al. [6]. The average number of immunopositive cells in 10 high-power fields ($\times$40) was estimated, and scored using the following system: (0) no tumor cell staining; (1) $<$10% tumor cell staining; (2) 10—25% tumor cell staining; (3) 25—