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Mast Cell Intercellular Interactions of Involuting Infantile Hemangiomas

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Mast cell intercellular interactions are presented in the present article as well as their significance in infantile hemagioma (IH) involution. The influence of mast cells (M) upon endothelial cells, fibroblasts and myofibroblasts and the processes associated with endothelial thrombosis, microthrombosis, together with stromal hyalinosis and fibrosis recognizes the leading role of mast cells in tumor regression phenomenon.

Key words: Mast cells, hemangionas, endothelial cells, stromal cells, apoptosis.

Introduction

Infantile hemangiomas (IH) are the most common tumors in early childhood, whose molecular pathogenesis still remains unclear [1]. Recent hypothesis [2] suggest block of endothelial development in early development, hence suppressed proliferation and initiation of regression.

Many reports show presence of mast cells M in vascular proliferations. The interaction of M from one side and endothelium with fibroblasts from the other is a complex and reciprocal process [10], which leads to involutive changes in IH presented with hyalinosis and fibrosis. Mediators of M play certain role in this process too [6].

Piling up data for IH, together with the investigations on M, related to angiogenesis, tissue remodelling and fibrosis, evoke further questions still waiting to be answered.

Material and Methods

Ten IH are fixed in 10 % neutral formalin and embedded in paraffin. Tissue cuts (5 μm) are stained with hematoxyline and eosin and toluidine blue.

Tissue from 3 of the IH has been selected for ultrasrtucture and samples achieved by routine tissue processing (each 0,05 μm in thickness) have been inspected on electron transmission microscope "Phillips" CM 12 /STEM.

Results

Stained with hematoxyline and eosin MC present with centrally placed nuclei and evenly distributed chromatin. The cytoplasm is intensively pinkish, appreciating well its composition from bright granules. The toluidine blue staining provides a better vision of M and particularly of their granules in the cytoplasm, as well as in the stroma after cellular degranulation and in close proximity with stromal cells and blood vessels.

Most of the mast cells are located close to capillaries and stromal cells. The endothelium of the capillaries demonstrates apoptotic change — pyknosis of the nuclei (Fig. 1). On ultrastructure nuclear debris and lipofuscin granules are readily seen (Fig. 2). Some

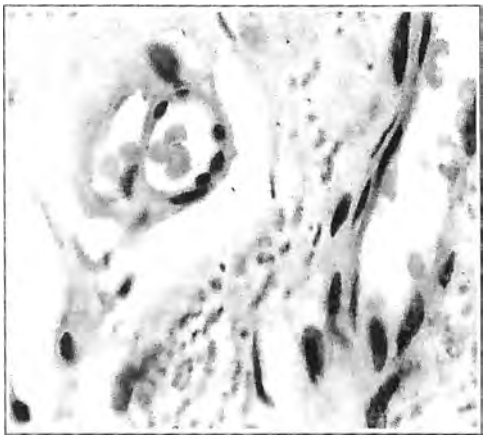

Fig. 1. Endothelial apoptosis (arrow) and mast cells (arrowhead). HE, × 200

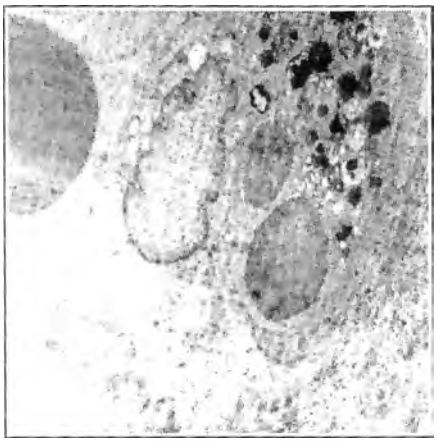

Fig. 2. Nuclear endothelial apoptotic debris. Electron microscopy. × 8000

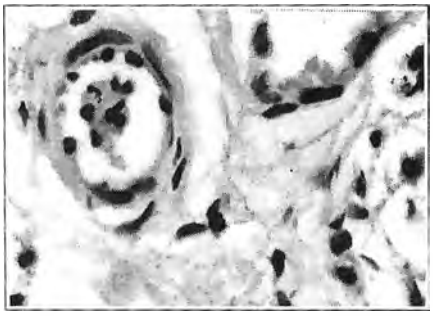

Fig. 3. Microthrombosis (arrow) and mast cells (arrowhead). HE, × 400

Fig. 4. Two types mast cells — oval (arrowhead) and elongated (arrow). HE, × 200

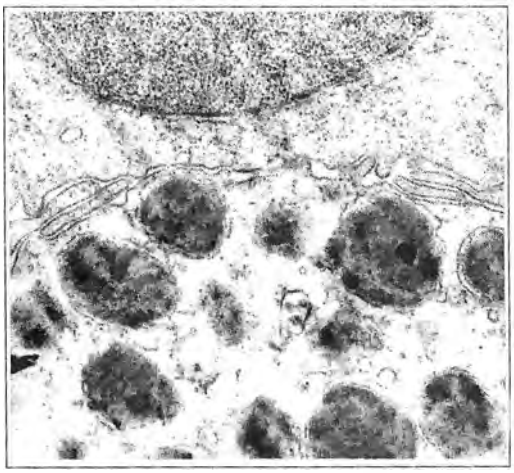

Fig. 5. Mast cell rich in granules in immediate proximity to stromal cell and finger-like cytoplasmatic protrusions between two cell types. Electron microscopy. × 18 000

Fig. 6. Mast cells (arrowhead) and stromal cells and perivasal hyalinosis (arrow). HE, × 400

of the capillaries close to the Ms display thrombotic aggregates and microthrombosis (Fig. 3). Expressed hyalinosis surrounds many of the blood vessels (Fig. 4).

Electron microscopy demonstrates the abundance of secretory granules in the cytoplasm of the mastocytes neighboring stromal cells. In cells intercellular regions, in between the cellular membrane of closely opposed cells, a finger-like cytoplasmic projections are seen (Fig. 5).

The stroma shows fibrosis, inflammatory cells, fibroblasts, myofibroblasts — the cytoplasm of the latter being rich in profiles of rough endoplasmic reticulum and myofilaments. Pinocytic vesicles are also present.

The observed mast cells display two morphological varieties— the classical "oval" and elongated (Fig. 6).

The underneath tissue shows inflammatory reaction.

Discussion

Phases of IH development (evolution) are dependent on changes in stroma and endothelium. Important role in the vascular changes has been attributed to apoptois. Nuclear pyknosis of endothelium is its earlier change. On ultrastructure nuclear debris and lipofuscin granules are readily seen (direct and indirect apoptotic features), as were shown in some of our previous works [4, 5].

Some of the capillaries in involuting IH display thrombotic aggregates and microthrombosis close to apoptotic endothelium, which suggests their relation with programmed cell death.

Next to endothelium in apoptosis, multiple mast cells are found which further puts their role in the above mechanism, a phenomenon already described by H a s a n et al. [7].

The interaction between endothelium and M is a complex and reciprocal process, not solely dependent on apoptosis. In view of this, large numbers of M are seen close to capillaries, even corresponding with the endothelium. Such a proximity is

not by chance—M survive lacking exogenous factors in an endothelium medium which suggests that endothelium compensates these factors in their "lifetime" [9].

Significant numbers of M are found in late stages of IH when fibrosis and hyalinosis prevail, which suggests M influence on these two processes as well. In proof of that are the ultrastructural cytoplasmic outpouching of M and neighboring stromal cells in involuting IH, similar to those depicted by D e t h l e f s e n et al. [3]. They can be accepted as contact expression, activating collagen synthesis of the stroma.

Other morphological expression of such functional influencing is probably the M changed appearance. Some of the M are different from the common oval shape. These elongated M are found alongside the classical M situated to stromal cells. The first description of the two M forms in both proliferative and involuting phases of IH belongs to P a s y k et al. [11]. It has been suggested that this change explains different functional capacities: M a k l o u f and I s h a k [8].

In conclusion — the present study demonstrates the morphological changes in IH. They are mainly related to M and M-cellular interactions which supports the thesis for the great importance of these multifunctional cells in IH regression.

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