Virchows Arch [Pathol Anat] (1985) 406:197–201

Virchows Archiv A

Phagocytosis of mast cell granules by fibroblasts of the human gingiva

Yasunori Takeda
Department of Oral Pathology, School of Dentistry, Iwate Medical University
Uchimaru 19-1, Morioka, Iwate 020, Japan

Summary. Mast cell granules have been detected ultrastructurally within the cytoplasm of fibroblasts in fibrous hyperplastic lesion of the human gingiva. This finding is interpreted as phagocytosis of mast cell granules by fibroblasts. It is estimated that phagocytosis of mast cell granules occurred in four to six per cent of the fibroblasts. The result of present study suggests that mast cells play some role in fibroblast activity not only in animals as reported previously, but also in human connective tissue.

Key words: Mast cells – Fibroblasts – Phagocytosis – Human gingiva

Mast cells are found widely distributed throughout the connective tissue of most vertebrates, and they release their intracytoplasmic granules into the surrounding environment after mechanical, chemical or immunological stimuli. It is well known that the mast cell granules contain a large number of biologically active substances such as histamine, serotonin, heparin, proteolytic enzymes, prostaglandins and so on. Recently, mast cells have been shown to interact with various different cells, both in vitro and in vivo, including vascular endothelial cells (Azizkhan et al. 1980), macrophages (Lindahl et al. 1979), eosinophils (Boswell et al. 1978), epithelial cells (Barnett 1973), lymphocytes (Roszkowski 1977), fibroblasts (Norrby 1981), cancer cells (Alexander et al. 1979), and others. Furthermore, ultrastructural evidence of phagocytosis of mast cell granules by fibroblasts in vitro has been reported (Rao et al. 1983; Greenberg and Brunstock 1983; Norrby and Enestrom 1984). Such phenomenon has been termed "cell-to-cell interaction between mast cells and fibroblasts with transgranulation" by Greenberg and Burnstock (1983). However, there are few reports documenting ultrastructurally phagocytosis of mast cell granules by fibroblasts in human connective tissue.

The purpose of this paper is to report of phagocytosis of mast cell granules by fibroblasts in the fibrous hyperplastic lesion of the human gingiva.

Materials and methods

The materials examined were taken from three cases of gingival fibrous hyperplasia. This was made up histologically almost entirely of dense bundles of fibrous tissue with slight focal or diffuse perivascular mononuclear cell infiltration. Tissue was fixed in 10% neutral buffered formalin and embedded in paraffin, and thin sections were stained with haematoxylin and eosin and with 1.0% aqueous toluidine blue for light microscopy. Small segments of formalin-fixed materials were prepared for ultrastructural examination, after rinsing with neutral phosphate buffer solution. The specimens were re-fixed in 4.0% glutaraldehyde, and were post-fixed in 2.0% osmium tetroxide. They were embedded in resin after dehydration. Then ultrathin sections were cut, stained with uranyl acetate and lead citrate, and examined in an Akashi LEM-2000 ultramicroscope.

Results

Light microscopic findings

Light microscopic examination in all cases revealed a varied distribution of mast cells which were round, ovoid or elongated in shape throughout the lesion. These cells were more prevalent in the perivascular areas, and the mast cell population in these areas was approximately 80 per square millimeter.

Ultrastructural findings

Ultrastructurally, the lesion was composed of irregular- and densely-arranged collagen bundles. Varying numbers of mast cells, other mononuclear cells and fibroblasts were scattered throughout the lesion, but they were prominent in the perivascular areas. No polymorphonuclear leukocytes were found in the lesion.

Mast cells had numerous tightly-packed granules within their cytoplasm, and degranulating mast cells were frequently noted. In some parts, electron dense and spherical granules which had similar morphological features to those of the mast cell granules were detected within the cytoplasm of the spindle-shaped cells which were interpreted as fibroblasts (Figs. 1 and 2), whereas serial sections of the same cells showed no evidence that these electron dense and spherical granules had been shed into the extracellular space. Such findings were interpreted as evidence of phagocytosis of mast cell granules by fibroblasts. Some of fibroblasts containing mast cell granules in their cytoplasm were in close contact with granule-rich mast cells (Fig. 1), and some of them were not in contact with mast cells (Fig. 2). Numerous released mast cell granules were scattered around the latter type of fibroblasts (Fig. 2). It was estimated that phagocytosis of mast cell granules occurred in four to six per cent of the fibroblasts. All of granules within

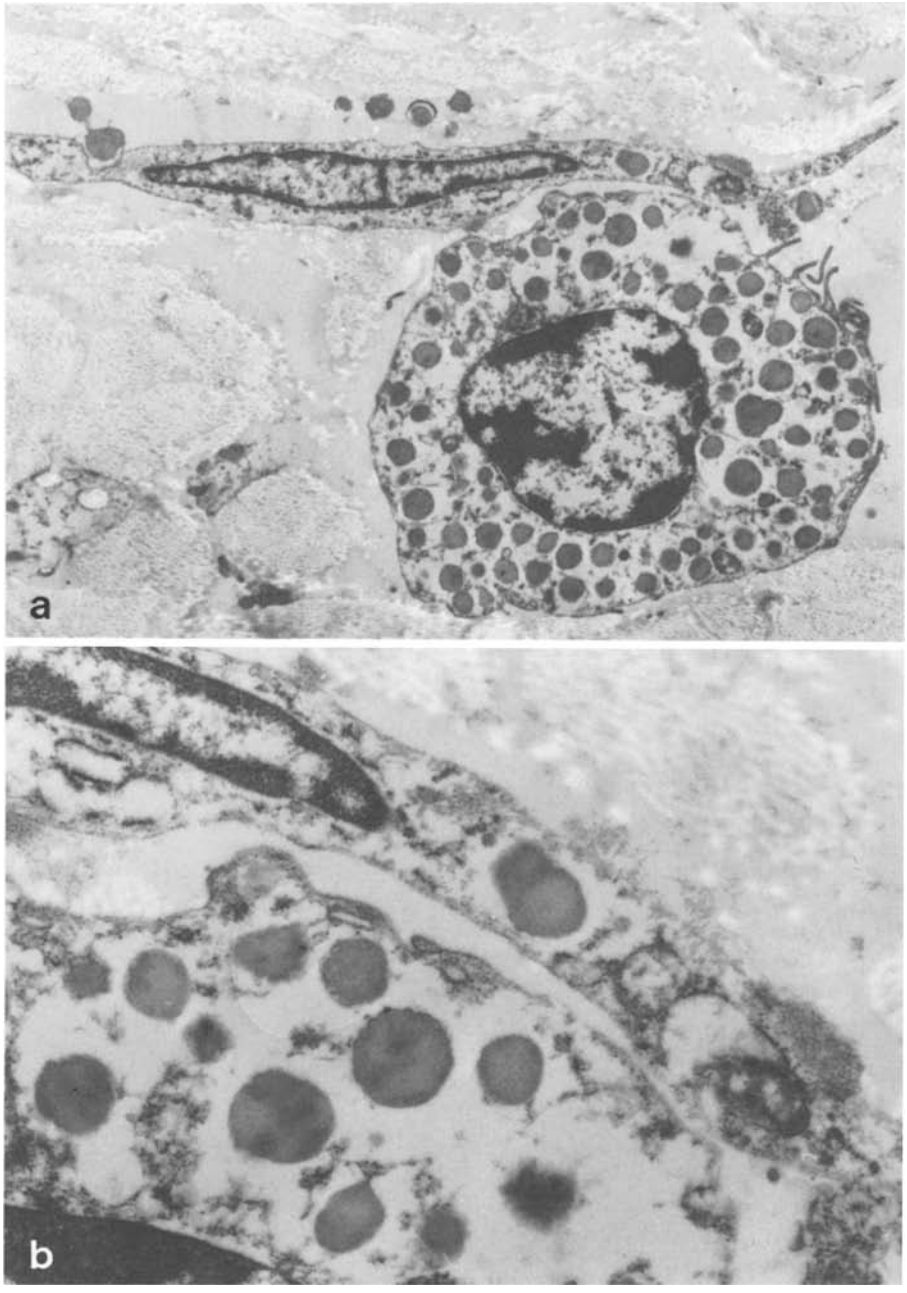

Fig. 1 a, b. Fibroblast in close contact with granule-rich mast cell, and mast cell granules can be seen with the cytoplasm of fibroblast. (**a**) × 6,670 and (**b**) × 20,600

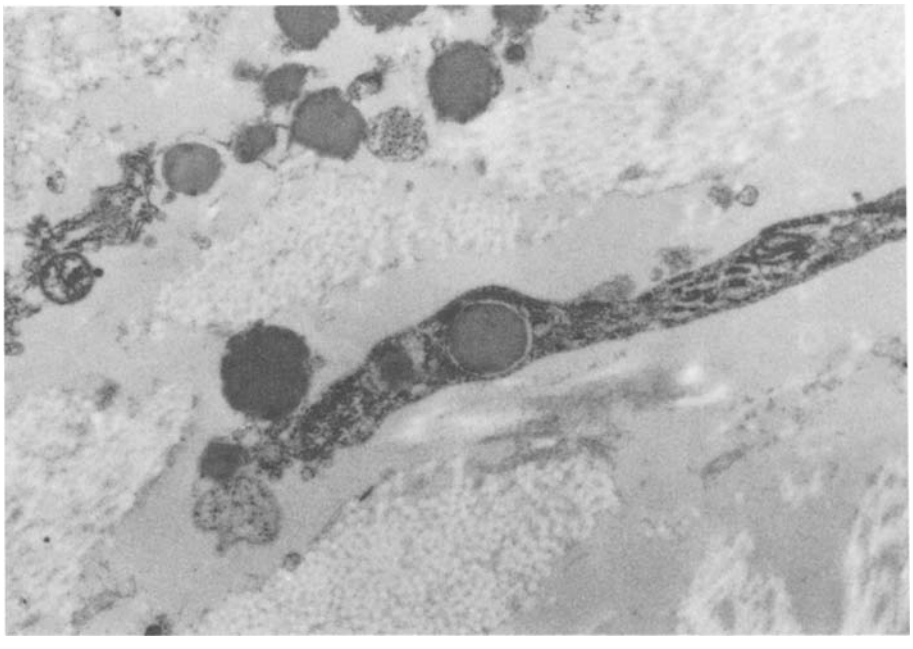

Fig. 2. Mast cell granules in the cytoplasmic process of a fibroblast. Many released mast cell granules are scattered in the surrounding area. ×16,800

the fibroblasts showed same morphological appearance. Phagocytosis of mast cell granules by vascular endothelial cells or other cells was not found.

Discussion

As yet, the precise role of the mast cells in collagen synthesis has not been elucidated. However, several good reviews of this problem have been published. Sandberg (1962) demonstrated in rats that the formation of collagen in granulation tissue was enhanced by release of mast cell granules. Watanabe et al. (1974) reported that prominent mast cell accumulation was found in the experimentally induced pulmonary fibrosis in rats, and considered that released mast cell granules would react with the septal fibroblastic cells by adsorbing on their cell surface or by being ingested, resulting in the stimulation of collagen synthesis. Furthermore, light microscopic examinations of rat skin after degranulation of mast cells induced by polyamines such as compound 48/80, anti-rat IgE, or injection of isolated mast cell granules suggested discharged mast cell granules were internalized by resident connective tissue fibroblasts (Higginbotham et al. 1956; Tannenbaum et al. 1980). Recently, confirmatory evidence of phagocytosis of mast cell granules by fibroblasts has been demonstrated ultrastructurally in vitro and in vivo by Rao et al. (1983), Greenberg and Burnstock (1983), and Norrby and Enestrom (1984).

In addition, it is well known that mast cell accumulations in various degrees occur in the human neoplastic and non-neoplastic lesions with more or less prominent fibrous component. Furthermore, Arnold and Huth (1978) and Janin-Mercier et al. (1981) have demonstrated ultrastructurally that active fibroblasts are in close contact with degranulating mast cells in the human lesions. However, there have been no reports documenting phagocytosis of mast cell granules by fibroblasts in the human lesion. Although the present ultrastructural examination of fibroblasts in fibrous hyperplastic lesion of the human gingiva was derived from materials fixed originally in 10% neutral buffered formalin, internalized mast cell granules in fibroblasts were evident. Such findings are interpreted as phagocytosis of mast cell granules by fibroblasts, and thus, mast cells may play some role in fibroblast activity in not only animals as reported previously, but also in human connective tissue.

References

Alexander P (1979) The mast cell: In: Pepys J, Edwards A (eds.) its role in health and disease. Pitman Med Publ Co, London, p 137

Arnold W, Huth F (1978) Electron microscopic findings in four cases of nasopharyngeal fibroma. Virchows Arch [Pathol Anat] 379:285–298

Azizkhan RG, Azizkhan JC, Zetter BR, Folkman J (1980) Mast cell haparin stimulates migration of capillary endothelial cells in vitro. J Exp Med 152:931–944

Barnett ML (1973) Mast cells in the epithelial layer of human gingiva. J Ultrastruct Res 43:247–255

Boswell RN, Austen KF, Geotzl EJ (1978) Intermediate molecular weight eosinophil chemotactic factors in rat peritoneal mast cells: Immunologic release, granule association, and demonstration of structural heterogeneity. J Immunol 120:15–20

Greenberg G, Burnstock G (1983) A novel cell-to-cell interaction between mast cells and other cell types. Exp Cell Res 147:1–13

Higginbotham RD, Dougherty TF, Jee WSS (1956) Fate of shed mast cell granules. Proc Soc Exp Biol Med 92:256–261

Janin-Mercier A, Bourges M, Fonck-Cussac Y, Bussieres JL, Leblanc B, Delage J (1981) Eosinophilic fasciitis. Ultrastructural study of an early biopsied case. Virchows Arch [Pathol Anat] 394:177–184

Lindahl U, Pertoft H, Seljelid R (1979) Uptake and degradation of mast-cell granules by mouse peritoneal macrophages. Biochem J 182:189–193

Norrby K (1981) On the 48/80-induced secretion of tissue mast cells and its mitogenic effect on nearby cells in the intact rat. Virchows Arch [Cell Pathol] 38:57–65

Norrby K, Enestrom S (1984) Cellular and extracellular changes following mast-cell secretion in avascular rat mesentery. An electron-microscopic study. Cell Tissue Res 235:339–345

Rao PVS, Friedman MM, Atkins FM, Metcalfe DD (1983) Phagocytosis of mast cell granules by cultured fibroblasts. J Immunol 130:341–349

Roszkowski W, Plaut M, Lichtenstein LM (1977) Selective display of histamine receptors on lymphocytes. Science 195:683–685

Sandberg N (1962) Accelerated collagen formation and histamine. Nature 194:183

Tannenbaum S, Oertel H, Henderson W, Kaliner MA (1980) The biologic activity of mast cell granules. 1. Elicitation of inflammatory responses in rat skin. J Immunol 125:325–335

Watanabe S, Watanabe K, Ohishi T, Aiba M, Kageyama K (1974) Mast cells in the rat alveolar septa undergoing fibrosis after ionizing irradiation. Lab Invest 31:555–567

Accepted January 21, 1985