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Ultrastructural analysis of periapical granulomas

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SUMMARY

A large portion of periapical granulomas is composed by cells of the mononuclear-phagocyte and lymphoid system. The ultrastructural features of the monocytes/macrophages differ in relationship to the state of activity of the cells (phagocytosis or secretion). A close correlation between cells of these two systems can be surmised by their tight contacts. An important role in the bone resorption is probably played by cytokines like IL-1 and TNF.

KEY WORDS:

Bone resorption, Cytokines, Monocytes/macrophages, Periapical lesions, Ultrastructure

RÉSUMÉ

Une grande partie des granulomes périapicaux est constituée de cellules du système mononucléaire phagocytaire et lymphoïde. Les caractéristiques ultrastructurales des monocytes/macrophages diffèrent selon le type d'activité des cellules (phagocytose ou sécrétion). Une corrélation intime entre les cellules de ces deux systèmes peut être supposée étant donné leurs contacts serrés. Un rôle important dans la résorption osseuse est exercé, probablement par l'intermédiaire de cytokines comme IL-1 beta et TNF.

MOTS-CLÉS:

Résorption des os, Cytokines, Monocytes/macrophages, Lésions périapicales, Ultrastructure.

INTRODUCTION

The mechanisms implicated in the development of pulpal and periapical lesions have not been fully elucidated (Trowbridge 1990). A large portion of periapical tissues are composed by macrophages, lymphocytes and their presence could point to a type IV cell-mediated response. The presence, moreover, of mast cells and IgE producing plasma cells could point to a hypersensitivity type I reaction. The inflammatory reactions that can take place in periapical tissues are certainly important in the destruction of the periodontal ligament and in the bone loss frequently associated with chronic periapical granulomas (Bohne 1990).

MATERIALS AND METHODS

Fourteen patients with periapical lesions underwent periapical surgery. In twelve of the patients the specimens were histopathologically verified to be

periapical granulomas, while two other cases were radicular cysts; the tissue specimens of the periapical granulomas were fixed for 6-8 hours in a 2.5% 7.2 buffered gluteraldehyde solution. The specimens were washed in sodium cacodylate buffer 0.2 M, osmicated in 1% OsO_4, dehydrated in ascending alcohol rinses and embedded in Epon 812. The ultrathin sections were stained with uranyl acetate and lead citrate and examined in a Philips EM 400 electron microscope.

RESULTS

The ultrastructural examination showed the presence of large numbers of lymphocytes (Fig. 1). These cells had a 6-9 μm diameter, presented a large round or oval-shaped nucleus with scant cytoplasm; the cytoplasm contained many ribosomes, a small Golgi apparatus, and few mitochondria. In the majority of specimens the tissue was heavily infiltrated by monocytes/macrophages.

Most of these cells were in an active state with many pinocytic vesicles, lysosomes and phagolysosomes in their cytoplasm. Other cells had, on the other hand, a smaller diameter and had, in the cytoplasm, few lysosomes, many mitochondria, a rich smooth endoplasmic reticulum and a nucleus with marginal heterochromatin (Fig. 2-4). Mast cells presented a central nucleus (Fig. 3) and numerous intracytoplasmatic granules, and were located close by fibroblasts. In the peripheral portion of the granulomas it was possible to observe fibrous tissue; here there were mast cells and lymphoid cells in close contact. In none of the periapical granulomas it was possible to observe the epithelial rests of Malassez.

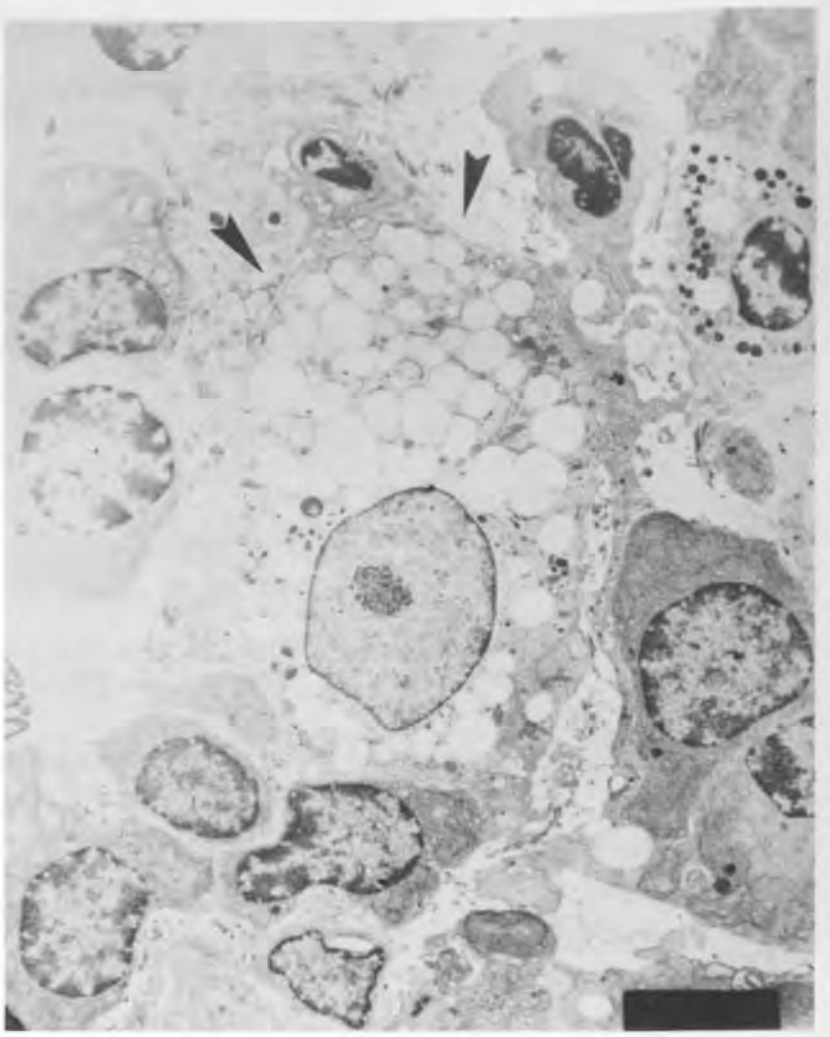

Fig. 2: It is possible to observe a macrophage with large cytoplasm with pinocytic vesicles, lysosomes and phagolysosomes (arrowheads); nearby are present lymphocytes (6400×).

Fig. 2: On peut remarquer un macrophage avec un cytoplasme abondant contenant des vésicules de pinocytose, des lysosomes et des phagolysosomes (flèches): en proximité il y a des lymphocytes (6400×).

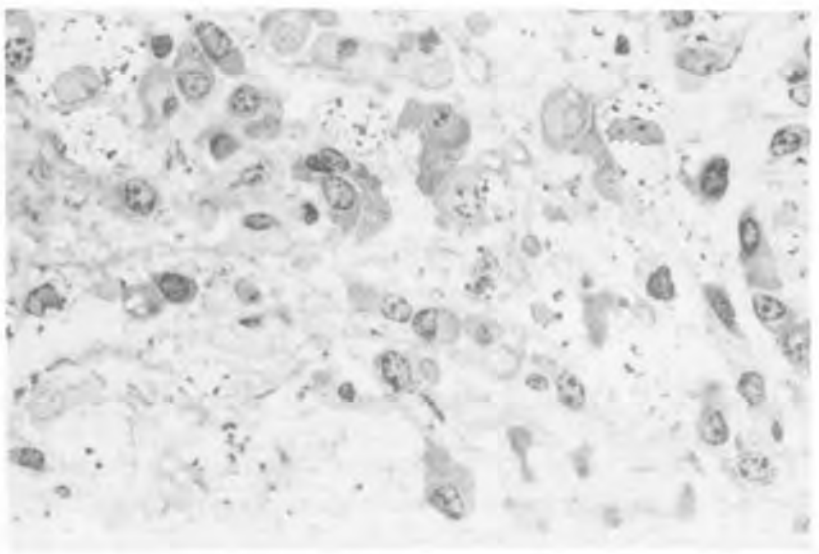

Fig. 1: Semithin section. A richly vascularized connective tissue is infiltrated by monocytes/macrophages and lymphocytes (Toluidine blue: 1000×).

Fig. 1: Section semi-fine. Tissu conjonctif richement vascularisé, infiltré par des monocytes/macrophages et des lymphocytes (Toluidine blue: 1000×).

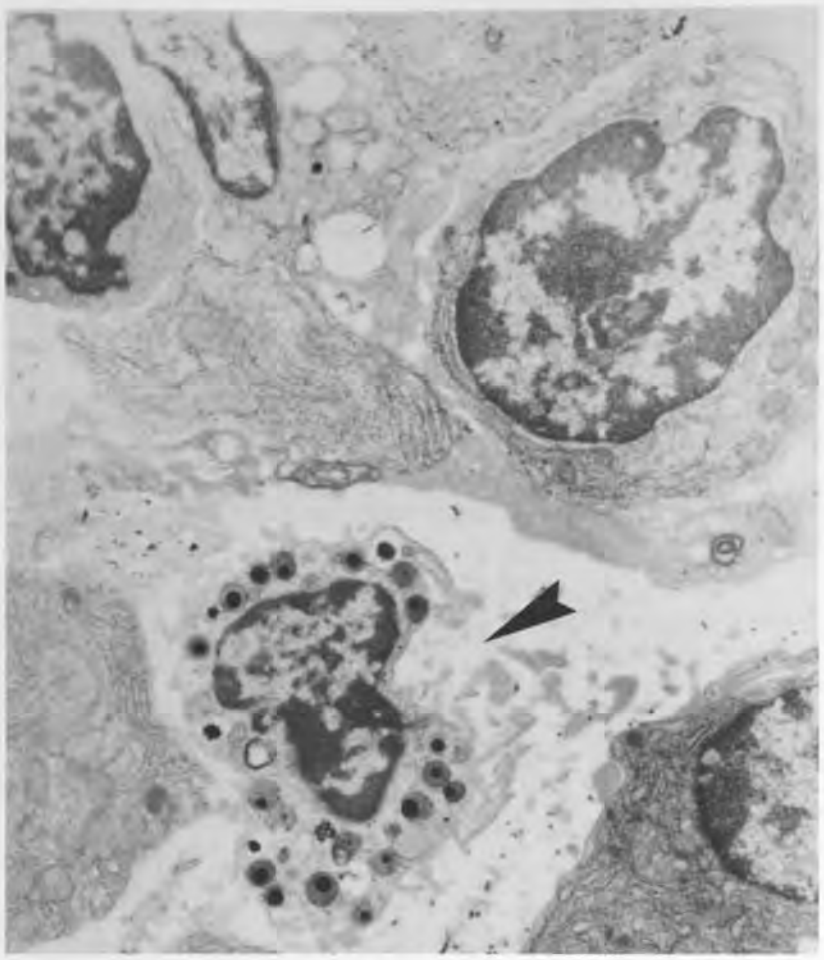

Fig. 3: Mast cells with a nucleus in central position (arrow) (7200×).

Fig. 3: Mastocytes avec le noyau en position centrale (flèche). (7200×).

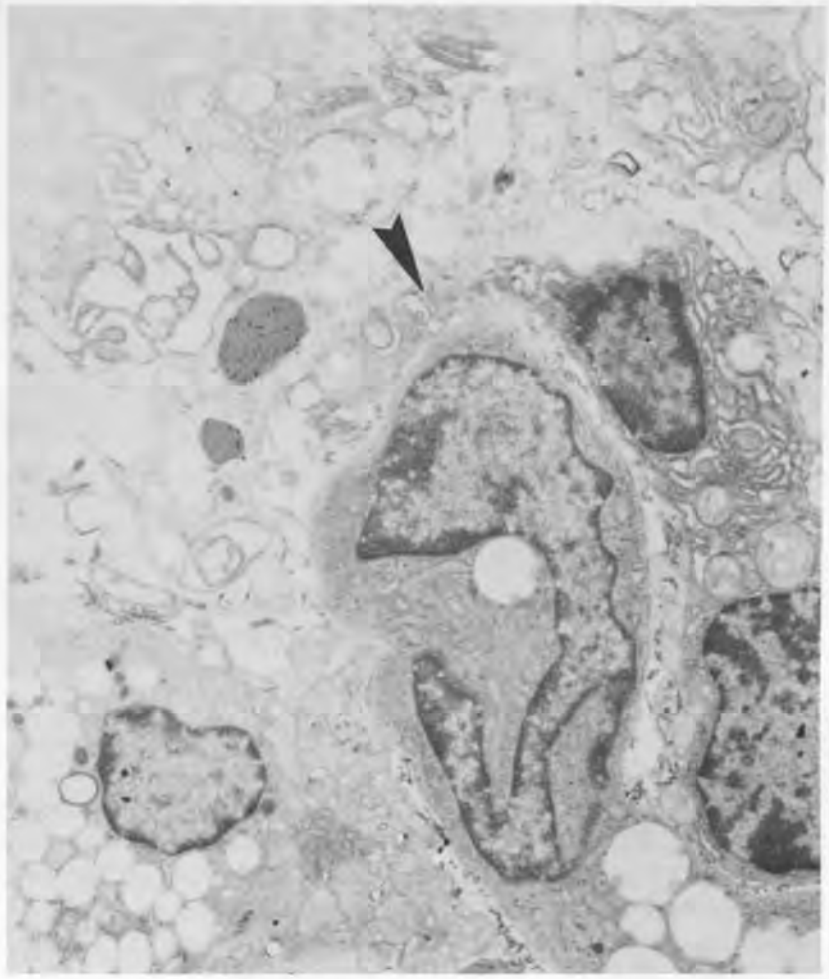

Fig. 4: Monocyte-macrophage with a large quantity of rough endoplasmic reticulum (arrow) (7200×).

Fig. 4: Un monocyte/macrophage avec un réticulum endoplasmatique rugueux abondant (flèche) (7200×).

DISCUSSION

Ultrastructural examination of periapical lesions showed the presence of richly vascularized connective tissue, heavily infiltrated by inflammatory cells. Most of the inflammatory cells were monocytes/macrophages, lymphocytes and plasma cells.

The presence of a chronic inflammation due to bacteria within the radicular canal can be surmised by the presence of these cells. Monocytes/macrophages presented different ultrastructural features, probably due to varying functional states. Most of the cells presented in the cytoplasm many pinocytic vesicles, lysosomes and phagolysosomes and were probably in a active phagocytic state. Other cells had a smaller diameter with a cytoplasm rich in mitochondria and rough endoplasmic reticulum, suggesting a protein synthetic activity.

Monocytes/macrophages were in tight contact with lymphocytes. These cells were probably implicated in the production of chemotactic and growth factors and cytokines. In previous works from our laboratory we have shown that monocytes/macrophages were present in periapical lesions with a large cellular component, whereas they were almost absent in the areas or in the lesions with a prevalent fibrous component (Piattelli et al, 1991; Artese et al., 1991). The cells of the mononuclear-phagocyte system are, in fact, pluripotent cells that can become active when subjected to external stimuli. An active macrophage is a cell constituted by a large cytoplasm with many lysosomes, phagolysosomes, mitochondria and an increased membrane activity with an higher capability for bacteria destruction. This active state can be caused either by lymphokines, produced by activated T lymphocytes, or stimulation by microbial products (i.e. endotoxin). Macrophages are very important in cell-mediated immune response and in their active state secrete a large quantity of products that play a role in inflammation (i.e. IL-1, TNF, Interferons): IL-1 β and TNF are implicated in bone resorption (Stashenko et al., 1989, Moerig et al., 1991), and they probably play an

important role in the progression of periapical lesions (Artese et al., 1991; Bando et al., 1993). The regulation of these secretion products can be modulated by cellular interactions: in our cases it has been possible to evidence very close contacts between cells of the mononuclear-phagocytic and lymphoid systems. A close relationship seems to exist between cells of the immune system and mast cells. It has been demonstrated that secretion products of T lymphocytes increase the in vitro growth of mast cells and that the migration of basophils is also modulated by interleukins. Histamin could then suppress the production by T lymphocytes of IL-2 and interferon gamma. Mast cells probably are a part of a negative feed-back mechanism to block the development of the immune response (Piattelli et al., 1991).

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