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Transmission electron microscopy study of benign giant cell tumor of bone

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Giant cell tumor of bone is still one of the most obscure and intensively examined tumors of bone. The World Health Organisation has classified it as "an aggressive, potentially malignant lesion", which means that its evolution based on its histological features is unpredictable and there are still many unanswered questions with regard to both its treatment and prognosis. In the report a detailed investigation of the ultrastructure of benign giant cell tumor of bone in five cases is presented.

Key words: giant cell tumor of bone, ultrastructural characteristics.

Introduction

Giant cell tumor of bone (GCTB) is defined as a primary intramedullary bone tumor composed of mononucleated cells and osteoclast-like multinucleated giant cells and presenting as a locally aggressive lesion with unpredictable behavior [2, 3, 4, 8]. It accounts for around 5% of primary bone tumors [8]. Nearly 50% of cases occur in the region of the knee, but other frequent sites are the distal part of the radius, the proximal humerus and fibula, and the pelvic bones [8]. It is usually situated in the epiphysis, and may later also affect the metaphysis. It appears most often in the third and fourth decade of life with a slight predilection for females. The definite treatment of GCTB varies from intralesional curettage followed by bone grafting and/or bone cement packing to wide resection [2, 3, 4, 8].

The aim of this study is to investigate the ultrastructural characteristics of giant cell tumor of bone.

Materials and Methods

We examined material from 5 patients with benign GCTB (3 female and 2 male). A musculoskeletal pathologist verified all tissue specimens for the pathologic diagnosis.

Electron microscopy preparation protocol: Tumor tissues were fixed in 3% glutaraldehyde for 2 h. After that the tissue samples were postfixed in 1% OsO_4 in PBS

for 2 h. Then the slices were dehydrated and embedded in Durkupan (Fluka, Buchs, Switzerland). All slices were processed with disectional microscope and cut with ultramicrotome (LKB, Stockholm-Bromma, Sweden). Finally, they were mounted, covered, contrasted and examined with an electron microscope Hitachi 500.

Results

Our study revealed different cell types:
Multinucleated, osteoclast-like giant cells:

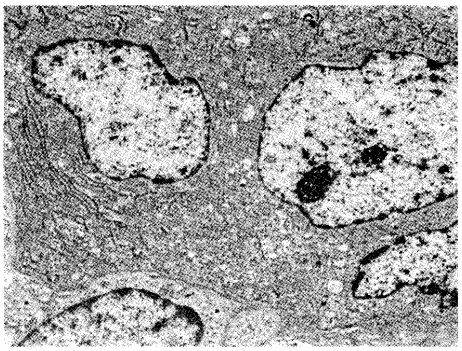

Fig. 1. Electron micrograph of multinucleated, osteoclast-like giant cell x 6000.

Ultrastuctural study of GCTB revealed large multinucleated, osteoclast-like giant cells with round or ovoid form. They had numerous nuclei with oval or irregular shape. The nuclear chromatin is finely granular and arranged in clusters in the peripheral nuclear area. The cytoplasm contained a large number of mitochondria, distinct lysosome-like bodies and large vacuoles (Fig. 1). In some instances, pseudopode-like vili covering parts of cell surface were found. Degenerating multinucleated giant cells were also observed. The cytoplasm of these cells consisted many vacuoles. Mitochondria in stages of degeneration were detected.

Fig. 2. Electron micrograph of mononuclear spindle-shaped cell x 15000.

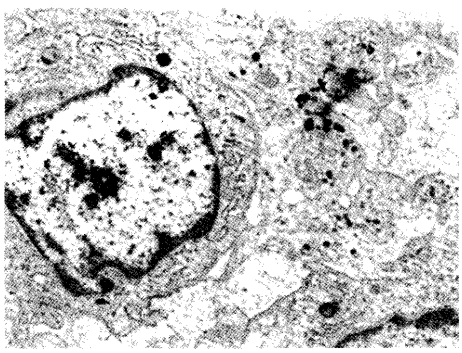

Fig. 3. Electron micrograph of mononuclear polygonal cell x 7000.

Mononuclear spindle-shaped cells

The mononuclear spindle-shaped tumour cells resemble fibroblastic cells at the ultrastructural level. Their nuclei displayed a very delicate chromatin structure, clearly visible heterochromatin in the peripheral nuclear area. The cytoplasm contained expanded rough endoplasmic reticulum, free ribosomes, polysomes and irregularly shaped mitochondria (Fig. 2).

Mononuclear polygonal cells

The ultrastructural features of the mononuclear polygonal cells are similar to those of macrophages. Their nuclei are oval with low chromatin density. The cytoplasm had relatively abundant rough endoplasmic reticulmn, well developed Golgi apparatus, variable number of mitochondria, lysosomes, vesicles, and free ribosomes (Fig. 3).

Other cells resembling lymphocytes and monocytes were also detected. They were characterized by with scanty rough endoplasmic reticulum, few mitochondria and a small Golgi apparatus.

Discussion

In 1818 Sir Astley Cooper first described GCTB as an expansive lesion of the fibular head and named the lesion "fungus medullary exostosis". He documented the natural history, gave detailed anatomic descriptions, and provided the first pathologic drawings of this lesion [1]. In 1845 Lebert described the first microscopic observations of GCTB presented by multinucleated giant cells and fusiform cells and termed it "tumeur fiblastique" [6]. The first electron microscopic description of GCTB was reported by Miller and Monteleone in 1957. The authors concluded that the giant cells were highly differentiated because of the large number of organelles they contained [7]. Since then, several reports have appeared, all in the Japanese literature, the majority of them emphasizing the variety of stromal cells and the ultrastructural similarity of giant cells to osteoclasts [5]. Later, however it was accepted that the multinucleated giant cells differ from osteoclasts of normal bone in their degree of multinucleation and the presence of pseudopode-like vili covered the cell surface [5, 9]. The majority of mononuclear tumor cells of the GCTB have the ultrastructural features that are seen in adult connective tissue cells. In conclusion, we defined ultrastructurally three main cell types: multinucleated osteoclast-like giant cells, mononuclear spindle-shaped cells that resemble fibroblastic cells and polygonal cells similar to macrophages.

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