Osteoclast Ultrastructure in Paget’s Disease

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The ultrastructural study of osteoclasts in biopsies from 12 patients with Paget’s disease reveals several cytological anomalies. In particular, nuclear inclusions, consisting essentially of striated filaments about 150 Å in diameter, often organized in bundles and sometimes in paraerystaline arrays, appear to be specific to the disease. Morphologically, the inclusions are remarkably similar to those observed in various cases of viral attack, and the hypothesis of the action of a possible external agent in Paget’s disease cannot be ruled out.

Key words: Paget’s disease — Osteoclast — Ultrastructure — Cytological anomalies — Nucleus.

Introduction

Although osteoclasts in general have been widely observed in light and electron microscopy [5, 11–13, 15–17] there have been, to our knowledge, no ultrastructural studies specific to Paget’s disease where marked increase in bone remodeling is known to be closely associated with the presence of particularly numerous, large and multinucleated osteoclasts [22]. These characteristics suggest that a closer examination might provide some information about osteoclast activity under abnormal conditions, and that Paget osteoclasts may eventually constitute useful material for research in the functional cytology of this type of cell.

Material and Methods

Iliac crest biopsies were taken from X-ray abnormal zones in 12 patients suffering from Paget’s disease. These patients had all been untreated and in particular had received no calcitonin. In each case the diagnostic of Paget’s disease was histologically confirmed.

Undecalcified fragments of bone tissue were fixed at 4° in 4.25% glutaraldehyde with a phosphate buffer at pH 7.2. Post-fixation was carried out in 2% osmic acid. After dehydration and passage in propylene oxide, the fragments were embedded in epon. Thin sections, cut with diamond knives, were stained with uranyl acetate and lead citrate according to Reynolds.

Results

Most of the Paget osteoclasts found in our samples are large and contain an unusually large number of nuclei (Fig. 1). Some of the cells are in close contact with bone tissue, and these will serve as a basis for our description; others appear to be completely isolated from bone.

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The Cytoplasmic Membrane. Osteoclasts are irregularly shaped, with multiple extensions and much infolding (Fig. 1). The plasma membrane shows an external coat of dense particles which probably represents the glycocalyx normally visible on the outer surface of cell membranes involved in active transport (Fig. 2). The extensions contain dense cytoplasmic material together with an occasional cell organelle.

The Ruffled Border. In contact with bone tissue, Paget osteoclasts present a modified cytoplasmic zone which constitutes the typical ruffled border. This is an organelle-free zone composed of finely granular material giving it an electron-dense aspect. The cytoplasmic membrane forms deep, narrow folds containing apatite crystals (Fig. 3). Vesicles in the neighbouring cytoplasm also contain similar crystals. Sometimes, even whole fragments of calcified tissue, membrane-bound or free, are found in the cytoplasm (Fig. 4). In the contact zone at the edge of the ruffled border, the cytoplasmic material is organized in dense bands, more or less parallel, oriented towards the bone, or arranged in a loose network according to the plane of the section (Fig. 5). In some cases, portions of the contact zone show ill-defined limits with a partial disappearance of the cytoplasmic membrane (Fig. 6).

The Nuclei. The numerous nuclei of the osteoclasts are highly polymorph. Some are smooth and avoid while others are badly deformed by multiple indentations (Figs. 1, 4, 7). The perinuclear space is sometimes dilated and contains clear vesicles; similar vesicles are occasionally visible even within the nucleoplasm (Fig. 8). Nuclear sections frequently show voluminous nucleoli and a peripheral distribution of dense chromatin (Fig. 1). In some cases the dense chromatin is so widespread that the nuclei appear to have degenerated.

In each osteoclast, several nuclei contain inclusion bodies which stand out clearly against the chromatin and the nucleoli (Fig. 1). These inclusions are essentially filament-like structures about 150 Å thick, transverse sections of which show a clear center surrounded by dense structures of about 50 Å in diameter (Fig. 9). In some cases, the inclusions consist of only a few scattered filaments, but more often several filaments are found grouped together in roughly parallel bundles with an interspace of about 150 Å (Fig. 9). Occasionally, the filaments are close-packed in para crystalline arrays with the interspace reduced to about 50 Å. A light and dark periodicity of about 50 Å gives the filaments a striated appearance suggestive of a helical form (Fig. 10).

Some inclusions are limited by an electron-transparent zone distinct from the rest of the nucleoplasm (Fig. 7), while others are associated with electron-dense, filamentous-tubular structures which form a rough peripheral limit but which may also be found among the filaments making up the inclusions (Fig. 11).

The Centrioles. As in ordinary cells, isolated centrioles are found in the neighbourhood of osteoclast nuclei, but some osteoclasts contain several additional centrioles grouped near the cell membrane (Fig. 12).

The Mitochondria. Mitochondria in some osteoclasts are predominantly long and dense (Fig. 7), while in others most appear swollen with more or less degenerate crests (Fig. 2). In a few cases, mitochondria with dark matrices, grouped together at one of the poles of the osteoclast, contain electron-dense bodies (Fig. 13).