Scanning electron microscopic observation of the brown tumor of the head of mandible

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ABSTRACT

Brown tumors are tumor-like, expansile osteolytic lesions of bone which are seen in both primary and secondary hyperparathyroidism. They generally resolve after surgical treatment of the parathyroid adenoma. Here, we report a case of brown tumor of the mandible of a cadaver with its scanning electron microscopic observation and review of literature.

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Brown tumors are tumor-like lesions of bone which are seen in both primary and secondary hyperparathyroidism. They are expansile osteolytic lesions of bone, occurring in hyperparathyroidism. They are more commonly seen in primary hyperparathyroidism (PHP) and tend to regress after the removal of parathyroid adenomas.[1] They are less common in secondary hyperparathyroidism (SHP) but have been reported in literature. The entire spectrum of bone lesions associated with hyperparathyroidism was firstly described by Von Recklinghausen as osteitis fibrosa cystica in 1891. Jaffe was one of the first authors who introduced the term "brown tumor" describing the osteolytic and cellular lesions in bone, seen in hyperparathyroidism.[2-4] In this article, we present a brown tumor case of the head of mandible that is investigated by scanning electron microscopy. Light and transmission electron microscopic observation of brown tumors are present in literature but scanning electron microscopic evaluation of this tumor is very rare.

Case Report. The bone specimens were obtained from a 63-year-old male cadaver who had diagnosis of primary hyperparathyroidism. The mass removed from the cadaver was dark brown in color (not reddish due to formalin fixation) and well circumscribed from the bone tissue. During the scanning electron microscopic (SEM) analysis, brown tumor was detected on the head of mandible. Accordingly, subperiosteal and mild resorption of the mandibular surface were demonstrated. Here brown tumor was photographed and demonstrated by using SEM technique for the first time. First, the specimens were directly mounted on metal stubs, then sputtered with a 100 Angstrom thick layer of gold in a Bio-Rad sputter apparatus. The specimens were examined with a JEOL SEM (SEM ASID-10) in 40-80 KV. In this study, typical results such as bone resorption findings which are similar to the brown tumor studies with light microscopy were obtained. In light microscopic examination with hematoxylin-eosin stain, typical findings of brown

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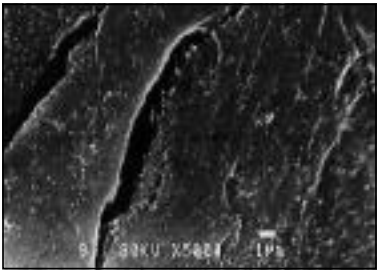

Figure 1 - Subperiostal and mild resorption of the mandibular surface.

tumor, namely, multinucleated giant cells and spindle shaped stromal cells were present. On the samples taken from the facial bones which were examined with SEM, subperiosteal and mild resorption of the mandibular surface of head of mandible were detected bilaterally **(Figure 1)**. No additional pathognomonic findings have been observed by scanning electron microscopy. These findings were shown for the first time in the literature using SEM, which serves as a 3 dimensional demonstration technique.

Discussion. Brown tumors of the facial bones are rarely seen. They are classically associated with PHP, but are being reported with an increasing frequency in SHP as the patient care standards get better, for example increasing life expectancy of patients on hemodialysis for chronic renal failure.[1,5]

Previous reports have documented the presence of brown tumors involving the maxillary and sphenoid sinuses, orbits, temporal bones, maxilla and palate. The "brown tumors," so called because of the reddish-brown color of their tissue, occur both in patients which suffer from PHP and SHP, undergoing long term dialysis or with endstage renal disease. In the head and neck, the lesions develop chiefly in the mandible and maxilla.[5,6] Menard et al[7] referred to a brown tumor of the mandible in a report; a female patient who underwent hemodialysis due to uncontrolled severe SHP.[7] Many multiple brown tumors were associated and reported by Zamurovic et al.[8] Histological sections have confirmed the diagnosis of brown tumor with remarkable capillary proliferation.[7] The most frequently seen oral signs in PHP are loss of the lamina dura (40%), osteoporosis of the mandible and brown tumors of the mandible (4%).[9] The mandibular location of these tumors frequently constituted the first sign of the disease.[10] In the head and neck, the lesions develop chiefly in the mandible and maxilla. Histological differentiation between the brown tumor and the giant-cell granuloma, aneurysmal bone cyst and reparative granuloma may be impossible, therefore, the role of the imaging procedures for different diagnosis is of great importance.[11] Special attention should be given to locate the presence of smaller multiple cystic areas in bones, generalized osteoporosis, subperiosteal bone resorption, especially of distal phalanges and the distal end of the clavicle and disappearance of the lamina dura. All these signs indicate hyperparathyroidism and lead to the diagnosis of "brown tumor."[1,11]

Osteitis fibrosa cystica is a relatively rare entity. The concomitant existence of an ameloblastoma of the mandible was reported. The clinical and standard radiological appearances of the ameloblastoma mimicked a brown tumor in the context of hyperparathyroidism. Ameloblastoma may present cystic components and is, of course, most frequently located in the jawbones, particularly at the angle of the mandible. An expansive lesion with cortical thinning and scalloping at the margins is typical in ameloblastoma; roentgenograms of the edentulous mandible showed multiloculated expansive hypodense lesion at the right angle, with cortical disruption at the superior edge.[8] Osteoid tissue is formed but with poor bony trabecular formation. Cysts may develop as a result of bleeding and tissue degeneration. The hemorrhagic stroma gives the mass the characteristic brown color which is surgically and histologically observed. Histological studies of these lesions demonstrated osteoclastic giant cells, fibroblasts and lipid-laden macrophages in a dense stroma with hemorrhage and hemosiderin deposition with an important capillary proliferation.[12]

The most frequently seen cells are multinucleated giant cells and fibroblasts. The giant cells have similar ultrastructural features to osteoclasts such as numerous mitochondria, dilated rough endoplasmic reticulum, and short filopodia. However, the ruffled borders that are typical in osteoclasts are not seen. In that manner, the giant cells of brown tumor are inactive osteoclasts. The presence of myofibroblastic differentiation of the fibroblasts reminded us that brown tumor represents a reparative cellular process which is similar to giant cell granuloma of bone.[2]

There are a few studies using electron microscopy to investigate cases of brown tumor. Okada et al,[13] reported that ultrastructure of many of the giant cells was similar to that of osteoclasts, except for the ruffled cell border and mononuclear spindle cells containing many cytoplasmic microfilaments that had enlarged processes that

enfolded the giant cells, indicating that these cells were fusing. Based on their findings using transmission electron microscopy, Okada et al, conclude that giant cells were not the proliferative elements of the lesion.[13] To our knowledge, brown tumors have not been investigated with scanning electron microscopy (SEM) before. However, SEM is a valuable method which enables one to explain the morphology of biological and non biological substances, with its high power magnification feature.[14] Thus, this case is of importance in the aspect of giving SEM morphological features of brown tumor.

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