A Case of Osteoblastoma of the Mandible with Immunohistochemical Findings of Bone Related Proteins

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Introduction

Osteoblastoma is a benign primary bone forming tumor of osteoblast like cells accounts for 1% of all bone tumors. The occurrence of the skull and jaw bones are quite rare and account for only 15% of all osteoblastoma and less than 1% of all tumor of the maxillofacial region.

Clinical Summary

A 19 years old female patient came to consult at the Okayama University Dental Hospital with a complaint of dull aching pain and swelling at the left side of the mandible. Radiaographic examination revealed a well-defined mixed radiolucent radiopaque lesion at the left retromolar area with no sclerotic border. The lesion was well-separated from the teeth and the mandibular canal. Complete resection of the lesion was done under general anesthesia.

Histological findings

Microscopically, the lesion is composed of irregular trabeculae of woven bone and osteoid lined by osteoblast like cells and multinucleated giant cells. The osteoblasts are plump with abundant eosinophilic cytoplasm, enlarged and eccentrically placed nuclei and prominent nucleoli. The perinuclear zones are also evident. Although the cells are active, they are benign with neither atypia nor mitotic activity and they resemble their normal counterparts(Fig.1). Multinucleated giant cells are of osteoclastic type with associated Howship's lacunae. The woven bone trabeculae have prominent irregular cement lines and entrapped osteocytes. The stromal tissue is loose with many thin-walled blood capillaries. The lesion is diagnosed as osteoblastoma.

Electron microscopic findings

The tumor cells are with eccentric, irregular and indented nuclei. They resemble normal osteoblasts except for the markedly dilated endoplasmic reticulum and the very well-developed golgi apparatus at the juxtanuclear position(Fig.2). The giant cells are also similar to the osteoclasts with many mitochondria, vesicles, lysosomes and the ruffled borders near the bony surface. The stroma contains collagen fibres with evident of initial calcification. Overall, there are no greate structural changes of the cell and matrix.

Immunohistochemical findings

Immunohistochemical analyses of the bone related proteins were performed to clarify the role of these proteins in the pathogenesis of osteoblastoma as follow; goat polyclonal antibodies to BMP 2-7 (Santacruz, USA) and mouse monoclonal antibody to osteopontin(IBL-America) by goat and mouse vectrostatin elite ABC kit(Vector) and rabbit polyclonal antibody to osteocalcin(Cosmo Bio, Japan) by PAP method (Dako). Generally, the tumor osteoblasts show positive immunoreaction to BMP proteins except BMP-3, localized perinuclear staining

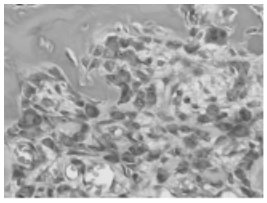

Fig.1 HE x40

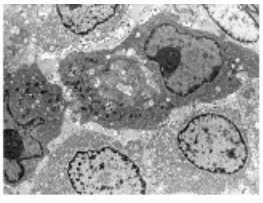

Fig.2 Electron micrograph

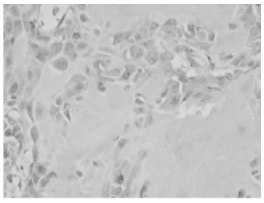

Fig.3 BMP-2

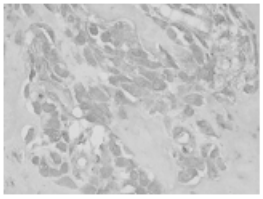

Fig.4 BMP-5

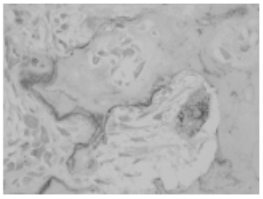

Fig.5 Osteopontin

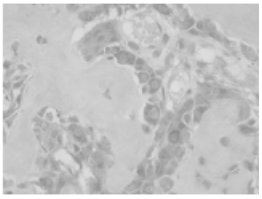

Fig.6 Osteocalcin

for BMP-2(Fig.3), 4, 7 and diffuse cytoplasmic staining for BMP-5(Fig.4), 6.

Strong immunoreactivity to osteopontin(Fig.5) is seen in mineralization fronts and cement lines and variably localized in the osteoblasts and osteocytes. Osteoclasts also show granular cytoplasmic staining for osteopontin. Osteoblasts show diffuse cytoplasmic staining to osteocalcin(Fig.6).

Conclusion

The exact etiology of osteoblastoma is not yet clear but the possibility of reactive lesion with abnormal repair or remodeling process may be considered. The immunohistochemical results show that BMPs as well as osteopontin and osteocalcin produced by the tumor cells are responsible for differentiation and recruitment of cells and mineralized tissue formation. It is possible that the tumor cells produce BMPs for a prolong period of time, inducing the mesenchymal cell differentiation to osteoblasts that in turn produce bone matrix and account for progressive growth of tumor mass. Osteopontin immunoreactivity was seen at the reversal lines, mineralization fronts and the osteoclasts suggest that it is responsible for both bone formation and resorption of osteoblastoma. Abnormal mineralization of woven bony trabeculae and moderate number of osteoclasts may be due to the production of osteocalcin in an attempt to inhibit excessive mineralization.