

## Osteoid Osteoma like Osteoblastoma in Proximal Humerus of a Dog

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### Abstract

Osteoid osteoma and osteoblastoma are uncommon benign bone tumors which originate from osteoblasts in animals. Both tumors have similar characteristics. Osteoid osteoma is well described in humans, but there known to be only two cases in domestic animal species. Differentiating the diagnosis of osteoid osteoma from osteoblastoma by using immunohistochemistry was aimed in this study. A 12-year-old mix breed female dog was brought to the clinic with complaints of swelling in proximal forelimb and progressive loss of motion. Animal was died during surgery. In necropsy, tissue samples were taken from the mass and fixed in %10 formalin. Samples were stained with hematoxylin and eosin, Masson's trichrome and Alizarin Red S. For revealing of cell differentiation, ABC-P method was applicated to adhesive section by using BMP6, S100, vimentin ve p53 markers. Macroscopically, proximal humerus was swollen. Cut section was generally lytic within bone residues. Soft tissue was haemorrhagic and edematouse. Microscopically, osteoblasts and hypervascular nidus were surrounded by large sclerotic and mineralized bone tissue. Large lytic areas were also observed. Masson's trichrome revealed sclerosis and Alizarin Red S revealed osteoid matrix. Immunohistochemically, BMP6 was moderately reacted in osteoid matrix and S100 was moderately reacted with nerve fibers in nidus. Vimentin had strictly positive reaction in fibrocytes. P53 was negative in osteoblasts.

In conclusion, this case is the third reported in domestic animals and the second in dogs. Also osteoid osteoma is evaluated for the first time by immunohistochemistry in animals.

**Keywords:** Dog; Immunohistochemistry; Osteoblastoma; Osteoid osteoma; Pathomorphology

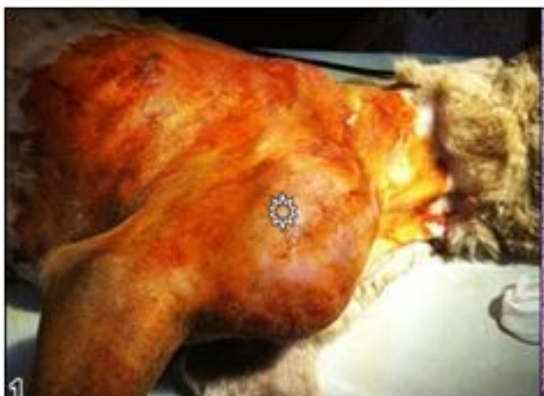
### Case Description

Osteoid osteoma and osteoblastoma have been variously regarded as both similar and distinct entities in the past [1]. It is suggested that these two entities should be classified as a single entity in the future [1]. Currently, WHO classifies these tumors separately [2].

Osteoid osteoma was firstly described by Jaffe in 1935. Osteoid osteomas are benign, painful, small sized osteogenic tumors of young patients [3-5]. Typically, long bones are affected, and it is primarily located within the cortex [3,4]. It is composed of a small "nidus (lytic lesion)" measuring from a few millimeters to 1.5-2 cm, which exhibits various portions of calcification and is surrounded by reactive sclerosis and periosteal reaction [4,6]. Histopathologically, osteoid osteoma is composed of anastomosing bony trabeculae of various widths and bony trabecule is rimmed by a single layer of osteoblasts, sclerotic bone and vascular osteoid tissue [4,5,7]. Cartilage tissue and mitotic figures are usually absent [4,7]. Osteoblastoma has identical histological and immunoprofiles to osteoid ostoma [1]. On the other hand, osteoblastoma often extends to extraskelatal soft tissue structures, mostly recures after surgery, may even metastasize and has more extensive lytic and sclerotic areas than osteoid osteoma [7,8]. Additionally, osteoid osteoma has a smaller size of 2 cm in diameter while osteoblastoma is 2 to 10 cm [3,6]. In veterinary medicine, there were two reports of osteoid osteoma; affecting the mandible of a cat and the humerus of a dog [8,9]. In this case report, we aimed

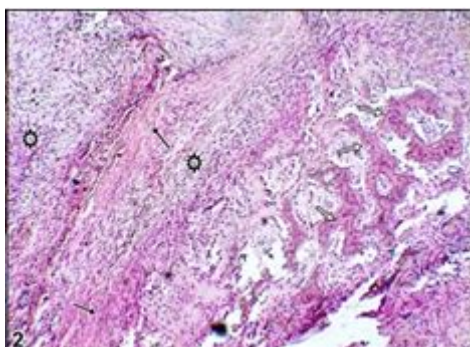
differentiating the diagnosis of osteoid osteoma from osteoblastoma by using immunohistochemistry in a dog.

A 12-year-old mix breed, female dog was brought to the clinic with complaints of swelling in proximal forelimb and progressive loss of motion. The swelling was firmness in palpation and it was thought to be a tumorigenic mass. Surgery was decided. During operation, animal was died following pulmonary and cardiac arrest. In necropsy, tissue samples were taken from the mass and fixed in 10% formalin. Tissue samples were processed routinely and embedded in paraffin. Paraffin blocks were sectioned at 4 µm. Samples were stained with hematoxylin and eosin, Masson's trichrome and Alizarin Red S. Immunohistochemistry was performed according to a standard avidin-biotin-complex peroxidase (ABC-P, Dako) method by using BMP6 (1:50 dilution, Santa Cruz Biotechnology), S100(1:200 dilution, Dako), vimentin (Sigma, 1:200) and p53 (1: 500, Dako) markers as primary antibodies. As chromogen, 3,3'-diaminobenzidine (DAB, NovaCastro) was selected and Harris's haematoxylin were used for counterstaining. Control sections were stained by normal mouse sera. Clinically, the health condition of the animal was normal in apperance. However, there was a painful swelling detected in right forelimb during clinical examination. At radiography, there were no prominent extra osteoid structures except structure of regional bones. Macroscopically, periphery of proximal humerus was swollen. This swelling was 12 cm in diameter (Figure 1).

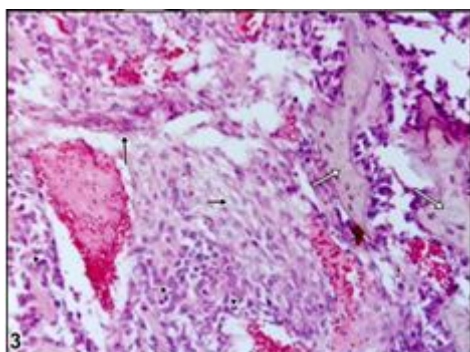


**Figure 1:** Preoperative appearance of right proximal humerus of the dog.

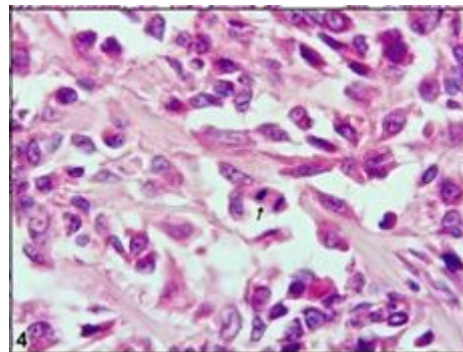
Cut section was generally seen as lytic within bone residues. Soft tissue was haemorrhagic and edematous. Microscopically, neoplastic osteoblasts and hypervascular nidus were surrounded by largely sclerotic and mineralized bone with very rare mitotic figures (Figures 2-4).



**Figure 2:** Nidus (white arrows), sclerotic areas (black arrows) and neoplastic osteoblastic cells in areas (asteriks), x40, H&E.

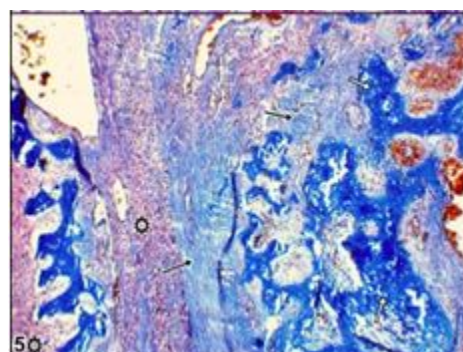


**Figure 3:** Nidus (white arrows), sclerotic areas (black arrows) and neoplastic osteoblastic cells in areas (arrow heads), 100X H&E.

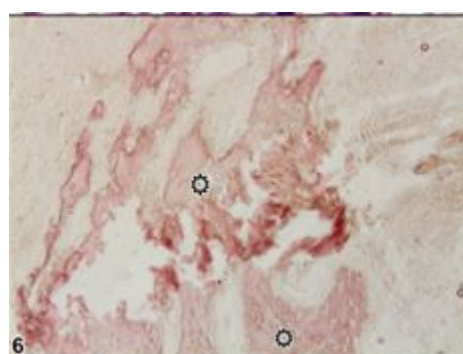


**Figure 4:** Rare mitotic figures in neoplastic osteoblastic cells, 400X H&E.

Large lytic areas were also attended. Masson's trichrome staining differentiated sclerotic areas in tumors and Alizerin Red S differentiated osteoid matrix (Figures 5 and 6).



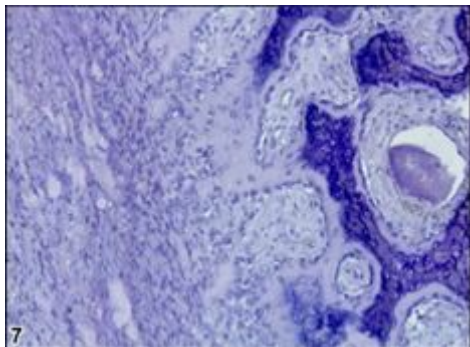
**Figure 5:** Nidus (white arrows), sclerotic areas (black arrows) and neoplastic osteoblastic cells in areas (asteriks), 40X Masson's trichrome staining.



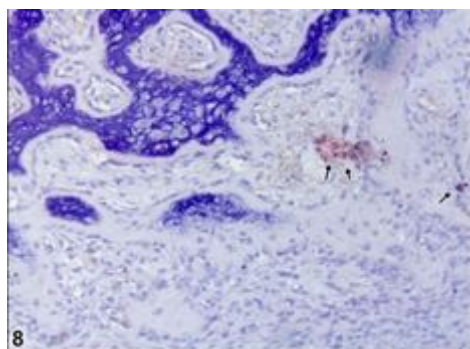
**Figure 6:** Osteoid nidus, 100X Alizerin Red S staining.

Immunohistochemically, BMP6 was moderately reacted in osteoid matrix and S100 was moderately reacted with nerve fibres (Figures 7 and 8).



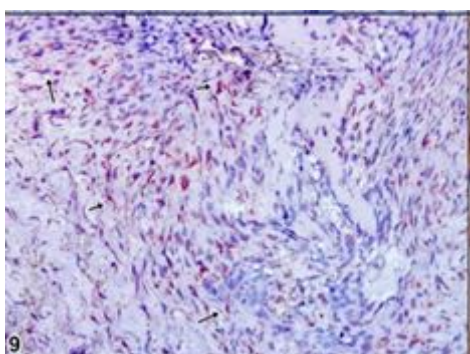


**Figure 7:** P53 negativity, 100X ABC-P.

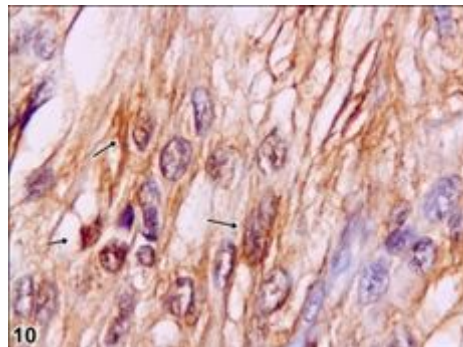


**Figure 8:** Mild BMP-6 positivity around nidus, 100X ABC-P.

Vimentin gave strictly positive reaction in fibrocytes in especially sclerotic areas of the tumor, P53 was negative in osteoblasts and other cells such as fibrocytes and bone residual cells (Figures 9 and 10).



**Figure 9:** Strict vimentin positivities in sclerosed areas, 100X ABC-P.



**Figure 10:** Moderate S100 positivities in neoplastic osteoblastic cells, 400X ABC-P.

It has been reported that, nerve fibers that express S100 are present in the reactive zone around the nidus and/or in the nidus itself, in approximately 25% of osteoid osteomas [10]. These fibers have not been observed in any other tumors, which suggests that the nerve supply of osteoid osteoma might serve as a marker in diagnostically difficult cases [10]. However, any documentation could not be found on the basis of veterinary literatures regarding osteoblastoma. In this case, S100 was moderately reacted with nerve fibers within nidus. Due to this reaction, it is thought that the tumor can be pertain with osteoid osteoma even though it is rarely expressed in this kind of tumors. But, some morphological features thought that the tumors can be osteoblastoma. On the other side, among benign bone tumors, bone morphogenetic proteins (BMPs) are expressed in osteoid osteomas and osteoblastomas and effect reactive bone formation [11]. Also in this case, BMP6 was mildly reacted in osteoid matrix and results similar to the previous knowledge were observed. An immunohistochemical assay demonstrated that BMP-2-4 was expressed in the cytoplasm of the osteoblastic cells in osteoid osteoma [12]. However, p53, which is known as malignancy showing marker, was negative in the current case even though there were rare mitotic figures in osteoblastic cells. Thus, it was thought that the tumor had low or no malignancy [13].

In conclusion, the tumor was diagnosed as osteoid osteoma because it was smaller than 2 cm in diameter, rarely shown mitotic figures, had p53 negativity showing no malignancy in neoplastic cells. Also, the case showed that BMP6 and S100 were useful for revealing presence of osteoid matrix and differentiation [13,14]. Osteoid osteoma was evaluated before only in a dog to best of our knowledge [5]. But, immunohistochemistry has not been used for describing in such kind of cases. Thus, we believe that immunohistochemistry has been immensely recommended to the researchers for providing differentiation of the dilemma in such kind of cases.

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