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# Cytologic Aspect of Fibrous Osteodystrophy in a Juvenile Siberian Husky

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**Abstract :** A 5-month-old intact female Siberian Husky dog was presented for evaluation of severely enlarged maxilla. Abnormalities in CBC, serum chemistry and urinalysis indicated purulent inflammation and renal failure. Cytologic examination of the swollen maxilla showed a mixed population of multinucleated giant cells and round to polygonal to spindle shaped cells either individualized or aggregated. Both type of cells showed moderate anisokaryosis, and anisocytosis, prominent nucleolus or multiple nucleoli, and coarse chromatin. On histopathology maxilla and turbinate were diffusely expanded and replaced by variably dense fibrous connective tissue, and the kidneys showed changes consistent with renal dysplasia. Based on these findings, the diagnosis of fibrous osteodystrophy due to renal dysplasia and fibrosis was made. Despite the supportive care, the dog continued to decline and was euthanized.

***Kew Words* :** fibrous osteodystrophy, multinucleated giant cells, Siberian Husky, dog.

## Introduction

Fibrous osteodystrophy is the skeletal lesions of increased widespread osteoclastic resorption of bone and compensatory replacement by fibrous tissue. Major causes are primary hyperparathyroidism, secondary hyperparathyroidism (nutritional or renal) and hyperparathyroidism due to a parathyroid hormone-like peptide secreting tumors in domestic animals (16). Renal fibrous osteodystrophy secondary to chronic, severe renal disease has been frequently reported in juvenile dogs of the breeds in which familial nephropathy has been described (1,2,5,9,14). Juvenile nephropathy has been encountered in more than 20 different canine breeds which includes Cocker Spaniel, Norweigian Elkhound, Lhasa Apso, Shih Tzu, Doberman Pinscher, Standard Poodle, Soft-coated Wheaton Terrier, Bull terrier, Samoyed, Chow Chow and Alaskan Malamute (14). To the best of our knowledge Siberian husky has not been previously reported associated with renal dysplasia. This report describes a dog diagnosed with fibrous osteodystrophy caused by chronic renal failure based on the abnormalities of serum chemistry, urinalysis, radiographs, cytology and histopathology with an emphasis on the cytologic aspect of fibrous osteodystrophy.

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## Case

A 5-month-old, intact female, Siberian Husky dog was examined at the Veterinary Medical Teaching Hospital, College of Veterinary Medicine, Seoul National University for a severely enlarged maxilla (Fig 1). The presenting complaints for this dog were a swollen maxilla, cachexia despite a good appetite and PU/PD of 2 month duration. Physical examination revealed inability to close the mouth, open-mouth breathing, bilateral mucopurulent nasal discharge, loose upper teeth, and erosive and ulcerative lesions on the swollen surface of the left maxilla.

**Fig 1.** Swollen maxilla of the dog.

Abnormal findings in the CBC included a mild neutrophilia and moderate left shift (segmented neutophils: 12.936 $\times 10^3$; reference interval = RI : 3.0-12.0 $\times 10^3$ and band neutrophils : 1.96 $\times 10^3$; RI : 0-0.3 $\times 10^3$) and moderate anemia (Hct 19%; RI : 37-55%). The leukogram changes were attributed to the purulent inflammation of the left swollen maxilla and nasal cavity. The regeneration of the anemia has not been evaluated. Abnormalites in serum chemistry were an increased ALP activity (435 U/L, RI 8-76), hyperphosphatemia (8.3 mg/dl, RI 2.8-6.8 mg/dl), and moderately increased BUN (48 mg/dl, RI 9-27 mg/dl), and creatinine (2.1 mg/dl, RI 0.5-1.3 mg/dl). Cystocentesis was performed to collect urine. Urinalysis by urine dipstick tests (Combur Test, Roche Diagnostics Indianapolis, IN, USA) revealed 1+ protein, 1+ occult blood, 1+ nitrite, 3+ bacterial rods, 3-5 WBCs per high power. Urine specific gravity by refractometery was 1.011. Based on the combination of azotemia, isosthenuria, and polyuria, chronic renal failure was considered, and given the juvenile dog, chronic renal failure due to renal dysplasia was top of the differential diagnoses list.

Ancillary diagnostics included plain skull radiographs, abdominal ultrasonography and fine needle aspiration cytology of the swollen maxilla. Skull radiographs revealed generalized cortical thinning and demineralization of the skull. Thickening of the maxilla and the absence of the lamina dura around the teeth roots resulted in displacement and a floating appearance of the teeth. Also, there was increased opacity to the bilateral nasal cavity with loss of turbinate detail. Abdominal ultrasonographic findings for the kidneys included an ill-defined irregular capsule, diffuse hyperechoic cortex, indistinct corticomedullary junction.

Fine needle aspirates were obtained from the swollen maxilla for cytologic examination and the smears were stained with Diff-Quik (International Reagents Corp., Kobe, Japan). The cytologic preparations from the lesions were moderately cellular and contained a mixed population of multinucleated giant cells and round to polygonal to spindle shaped cells either individualized or loosely grouped (Fig 2). The giant cells were extremely variable in size, approximately 20 - 200 μm in diameter, and had multiple nuclei from 2 to about 40. Cytoplasm was moderately basophilic, and in variable quantity. Nuclei showed moderate anisokaryosis, and had one to 2 or 3 round nucleoli. Chromatin was either vesicular or reticular. Non-giant cells were pleomorphic, showed variable N : C ratios, and a basophilic cytoplasm. Nuclei were round to oval and central or eccentric. There were one to 4 prominent nucleoli, that were occasionally of unequal size. Chromatin was coarsely reticular. Some cells had perinuclear clear zones in their cytoplasms. Rare mitotic figures were present. Amorphous extracellular eosinophilic material was also found infrequently along with rare inflammatory cells (Fig 3). Based on the findings of multinucleated cells mixed with variably shaped mesenchymal cells, the provisional diagnosis were malignant fibrous histiocytoma. Differential diagnoses were osteosarcoma, fibrosarcoma and giant cell tumor of bone. Given the the young age of the dog and the clinical presentation, fibrous osteodystrophy, and exuberant reactive/benign proliferation of mesenchymal cells were also considered.

On postmortem examination the snout and maxilla were swollen and the nasal cavity was severely compressed. A homogeneously tan, firm tissue obscured the maxilla, turbinates and nasal septum. Dental attrition was present and the remaining teeth were malaligned. The kidneys were tan, shrunken and firm. On cut surface there was dilatation of the renal pelvis, marked cortical atrophy and an irregular corticomedullary junction. No other significant gross abnormalities were found.

On histopathologic examination the maxilla and turbinates were diffusely expanded or replaced by dense fibrous connective tissue (Fig 4). Bony trabeculae were thin and rimmed by oestoblasts and numerous osteoclasts were scattered in the fibrous stroma (Fig 5). The resorptive cavities were increased. Similar changes were present in the mandible. Atrophied and

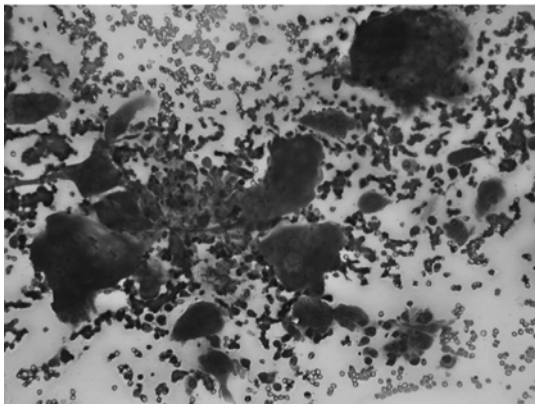

**Fig 2.** Aspiration smear from the swollen maxilla. Diff-Quik, × 40 objective.

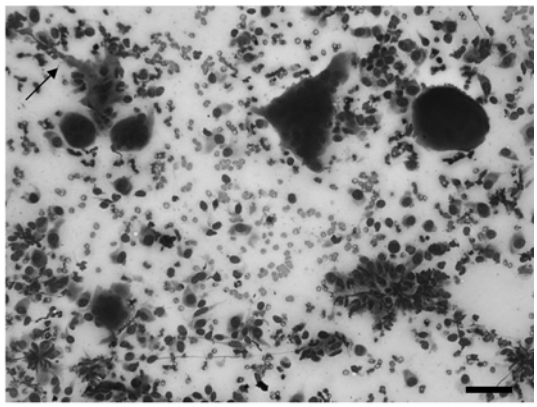

**Fig 3.** Aspiration smear from the swollen maxilla. Note the presence of extracellular matrix in the upper left corner (arrow). Plump spindle, spindloid or round mesenchymal cells were found along with multinucleated cells. High N: C ratio, increased cytoplasmic basophilia, mild to moderate anisocytosis and anisokaryosis were noted (Diff-Quik, × 40 objective, Bar = 40 μm).

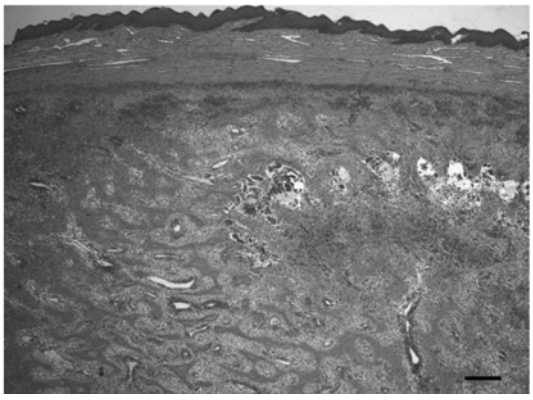

**Fig 4.** Maxilla. Thin cortical bone and replacement of normal bone structure due to fibrous tissue (H&E, Bar = 200 μm).

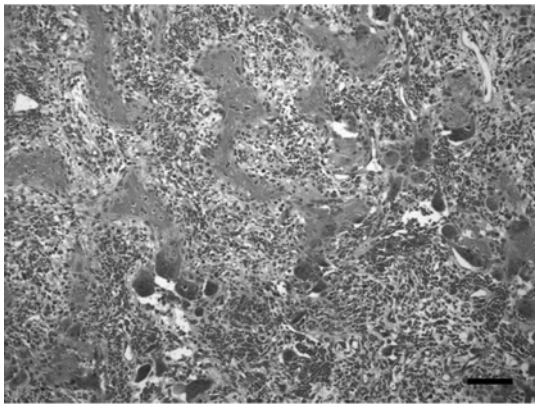

**Fig 5.** Maxilla. Note numerous multinucleated giant cells. The bone trabeculae were thin and surrounded by osteoblasts and multinucleated cells (HE. Bar = 100 μm).

immature glomeruli, dilation of many renal tubules and Bowman's space and persistent mesonephric ducts were present in the kidneys. There was marked interstitial fibrosis and a mild lymphoplasmacytic interstitial nephritis. No other significant microscopic findings were found. Radiographically, thin cortex with demineralization of the skull was noted but histopathology was not performed. Gross and microscopic changes of the parathyroid were unremarkable. The histologic diagnosis was maxillary and mandibular fibrous osteodystrophy due to renal dysplasia and fibrosis.

## Discussion

Fibrous osteodystrophy causes extensive osteoclastic resorption of bone and replacement by fibrous tissue. Among species, dogs are most commonly affected with renal osteodystrophy, and bone disease is more likely to be recognized clinically in growing dogs (16). Dogs showed bone pain, loss of teeth and deformity of the maxilla or mandible as in this case report. In this patient the proliferation of fibrous tissue was quite exuberant and the normal structure of the maxilla and nasal turbinate were destroyed, which might in part explain the dog's open mouth breathing. In previous reports, not all the affected animals developed these bony changes, and it is uncertain why clinical signs vary among individuals. Metabolic bone disease should be suspected in patients especially young animals with bone lesions when there is concurrent renal disease (16). A high serum PTH level or histological evidence of chief cell hyperplasia in the parathyroid gland should confirm the diagnosis (11).

Histologically fibrous osteodystrophy is characterized by the presence of osteoclast-like multinucleated giant cells mixed with a proliferation of fibroblasts. It is difficult to recognize fibrous osteodystrophy by cytology alone because these features can also be found in a few benign bone lesions like giant cell granuloma and aneurysmal bone cyst (3,7,10,17). In veterinary medicine, there has been no reported cytologic descriptions of fibrous osteodystrophy as well as other benign bone lesions, and in human medicine a mixed population consisting of mononuclear stromal cells and multinucleated giant cells were reported in fine needle aspiration cytology of giant cell granuloma, aneurysmal bone cyst and brown tumor of hyperparathyroidism (human counterpart of renal fibrous osteodystrophy) (3,10,11). Because these lesions are indistinguishable from each other in cytologic evaluation, clinical and radiologic findings were essential for the diagnosis. As fibrous osteodystropy the presence of multinucleated giant cells in aspirate smears should be evaluated in the context of a patient with severe chronic renal failure and high serum PTH level, which is also true to canine patients (11).

Differential diagnoses also contain tumors such as the giant cell variant of malignant fibrous histiocytoma, giant cell osteosarcoma, giant cell tumor of bone and fibrosarcoma (4,6,10,13,15). Among these, giant cell tumor of bone and the giant cell variant of malignant fibrous histiocytoma would be the primary considerations because these tumors show a large number of multinucleated giant cells on histology. Multinucleated giant cells could be found in increased number in some aspirates of fibrosarcoma or osteosarcoma although these cells are not a predominant population. It is challenging because both the giant cells and non-giant mesenchymal cells in this case showed mild to moderate dysplastic changes such as prominent nucleoli, increased number or size of nucleoli, increased N : C ratio and anisokaryosis. Without any information on histological architecture of the tissue from the lesions, cytological criteria of malignancy are not sufficient to distinguish dysplastic changes from neoplastic proliferation. Detailed knowledge of clinical, radiographic and histological findings is essential for a correct evaluation of fine needle aspirates from these lesions. Fibrous osteodystrophy should be a primary consideration when a mixed population of multinucleated giant cells and mononuclear mesenchymal cells are obtained for cytological evaluation in an animal with a concurrent systemic renal disease (11).

The prognosis for juvenile renal diseases is poor, and in previous reports most patients died or were euthanized because of the severe clinical signs unresponsive to symp-

tomatic therapy associated with chronic renal failure (1,2,8,14). The ages when the patients were first presented ranged from 4 to 11 month (1,5,12,14). Early detection did not appear to influence the survival of the patients, although in one report, an Alaskan Malamute survived exceptionally 19 months after being diagnosed at 6 months of age (12). The patient in this report also followed a similar progression and was euthanized due to its poor condition 3 months after the first diagnosis.

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# 어린 Siberian Husky 견의 섬유성 골형성장애의 세포학적 고찰 증례


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**요 약** : 5개월령의 거세하지 않은 암컷 시베리안 허스키가 상악 병변의 평가를 위해 내원하였다. CBC, 혈청 화학, 요검사 소견에서 염증과 신부전이 지시되었다. 병변의 세포학 검사에서는 거대 다핵 세포들과 원형~방추형의 다향한 모양의 세포들이 개별적으로 탈락되거나 군집을 형성하였다. 두 종류의 세포들 모두 중등도의 핵 대소부동증과 세포부동증을 보였고, 뚜렷한 한 개의 핵소체 또는 여러 개의 작은 핵소체를 갖고 있었으며 성긴 염색질이었다. 조직병리학적 검사 결과, 상악과 비갑개는 전반적으로 확장되어 있었으며 결합조직에 의해 대체되어 있었으며 신장에서는 형성이상이 관찰되었다. 이러한 결과를 바탕으로, 신장형성이상과 섬유화로 인한 섬유성 골형성장애로 진단되었다. 대증적인 처치에도 불구하고 환자의 상태는 악화되어 안락사 되었다.



**주요어** : 골형성 장애, 다핵 세포, Siberian Husky, 개