# Can Cathepsin K be related to periodontal status in Pycnodysostosis patients? A Case Report

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**ABSTRACT:**

**Purpose:** The objective of this case was to determine the absence of cathepsin K can be the reason of severe periodontitis in patients with pycnodysostosis

**Material and methods:** Two brothers with pycnodysostosis were enrolled. A complete family history, genetic analysis, detailed medical history were collected. Findings of clinical examination and radiological investigations were thoroughly studied.

**Results:** All two patients had disclosed pectus excavatum, thick-short and stubby fingers, small feet and short toes. Craniofacial features included patent anterior and posterior fontanelles, prominent forehead, proptosis, baked nose, high palatal arch, double row of the teeth, microretrognathia and severe periodontitis.

**Conclusion:** Although further studies are needed to prove these assumptions absence of cathepsin K can be the reason of severe periodontitis in pycnodysostosis patients.

**Keywords:** Cathepsin k, Periodontitis, Pycnodysostosis.

## INTRODUCTION

Pycnodysostosis is an extremely rare autosomal recessive skeletal dysplasia caused by defects of metabolic pathways which are responsible for degradation of organic matrix from mineralized bone. This bone disorder is phenotypically uniform and recognizable by osteosclerosis of the skeleton, proportionate short stature, recurrent bone fractures caused by bone fragility, acroosteolysis of the distal phalanges, spondylolysis of the lumbar spine, skull deformities with delayed suture closure and typical facial dysmorphism including frontal bossing, hypoplasia of the midface, beaked nose and micrognathia. Furthermore, it is also reported that patients with pycnodysostosis have a tendency to develop mandibular osteomyelitis (Kato et al., 2005) and chronic alveolitis (Nakase et al., 2007). The patients are normal of intelligence.

The disease was linked to the 1q21 region by homozygosity mapping (Gelb et al., 1995) and identification of the responsible gene cathepsin K (CTSK) gene, followed (Gelb et al., 1996). The gene product; cathepsin K is a lysosomal cysteine protease highly expressed in osteoclasts and crucial for the degredation of collagen and other organic matrix proteins from mineralized bone. Mutations of CTSK gene result in osteoclastic dysfunction and decreased bone turnover. Based on this, bone mass increases, but bone quality deteriorates with respect to trabecular architecture and lamellar arrangement (Fratzl-Zelman et al., 2004)

## CLINICAL-GENETIC FINDINGS

Two affected brothers aged 18 and 16 were referred to Istanbul University Department of Periodontology due to bleeding, gingival hyperplasia and positioning anomalies of the teeth from Istanbul University Department of Genetics which analysed the dysplasia of the patients with radiographic evaluation and clinical findings (Figure1-3). The parents are first degree cousins. Family history was uneventful. The pregnancies were not followed-up and both children were born at

home. The parents noticed no postnatal adaptation problems. The older brother walked at the age of 18 months and was able to make two-word sentences at the age of 2, whereas the younger brother walked at the age of 24 months and made his first sentence at the age of 2.

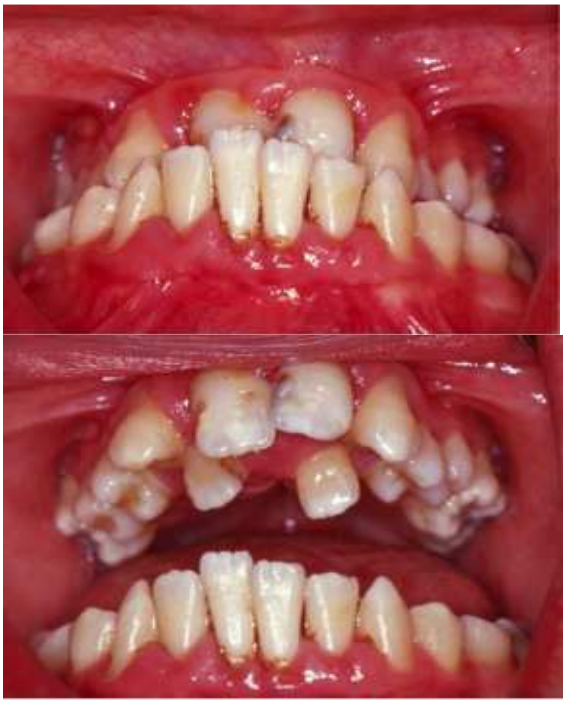

Figure 1 & 2: Analysis of dysplasia of the patient with clinical findings

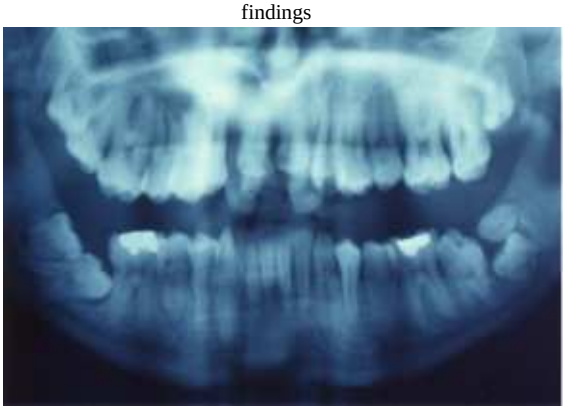

Figure 3: Analysis of dysplasia of the patient with radiographic finding

The older brother had graduated from high school with mediocre grades and younger brother was attending high school. The older brother had recurrent femur fractures at he ages of 3 and 17, while his younger brother did not. At examination, height of the older brother was 150 cm (3$^{rd}$ centile), weight 63 kg (between 25$^{th}$ and 50$^{th}$ centile), head circumference 55 cm (between 50$^{th}$ and 75$^{th}$ centile). Physical examination of the older brother showed disclosed pectus excavatum, thick-short and stubby fingers, small feet and short toes. Craniofacial features included patent anterior and posterior fontanelles, prominent forehead, proptosis, baked nose, high palatal arch, double row of the teeth and microretrognathia (Figure 4).

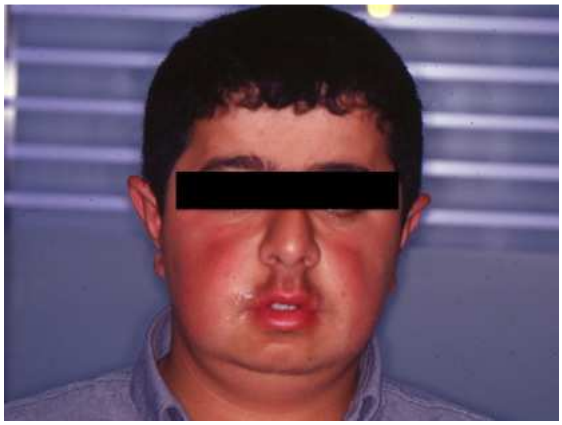

Figure 4: Physical Examination

His similarly affected brother's height at the time of examination was 141 cm (3$^{rd}$ centile), weight 47.5 kg (between 3$^{rd}$ and 10$^{th}$ centile), head circumference 51 cm (3$^{rd}$ centile). Physical examination revealed similar findings, except the younger brother had distal hypoplasia of the 1$^{st}$ and 2$^{nd}$ fingers bilaterally and did not have double row of teeth. According to the Tanner staging they have achieved full-blown puberty. X-ray imaging of the whole skeleton was performed; both brothers demonstrated diffuse osteosclerosis and generalized cortical thickening of the whole skeleton, open cranial sutures, dolichocephaly, absence of frontal sinuses, hypoplasia of the maxillary sinuses. The younger brother had additionally acroosteolysis of the distal phalanges of the first and second digits of the hand bilaterally.

In oral examination and radiological assessments abnormal teeth positioning and deep palatal arch was observed. There were gingival edema, gingival bleeding and halitosis. PI score was %26 an GI was %30. Periodontal probing depth level were at 12 sites with 4-6 mm, at 9 sites 6mm and at one site 10 mm. The elder brother's periodontal status was also diagnosed as chronic severe

periodontitis but he refused to be taken photograps and radiographs.

## DISCUSSION

Periodontitis is defined as the destruction of periodontal tissues such as the alveolar bone due to microbial, genetic and environmental factors. Microbial dental plaque is the main cause for severe periodontitis. Periodontopathogens which are seen in microbial dental plaque are not only the trigger factors for periodontitis they also indirectly influence proteolytic host enzymes such as MMPs which cause connective tissue degradation and bone extracellular matrix degradation.

Garlet et al. (2006) investigated the expression of several matrix metalloproteinases (MMPs), osteoclastogenic factors and cathepsin K in response to periodontopathogens that trigger periodontic tissue destruction in mice. They demonstrated that high expression of cathepsin K and MMPs was associated with high experimental disease activity, while lower cathepsin K and MMP levels were detected in the lower disease activity period. It is also stated that there is a non-osteoclastic biochemical pathway available for degradation of bone matrix (Sassi et al., 2000) and when cathepsin K activity is absent, bone lining cells that have MMP activity enter into the resorption lacunae and degrade demineralized collagen left over from osteoclasts (Everts et al 2002).

In our case, due to patients age, PI and GI levels and 7mm clinical attachment loss is not predictable. Considering the unexpected level of periodontitis observed in our patients, there should have been another factor which accelerates bone destruction. Evaluation of the literature suggests that in the absence of cathepsin K the balance between various enzymes, inhibitors and regulatory factors may have shifted in favor of MMPs and other factors that trigger resorption and the profoundly deteriorated bone ultrastructure might also have contributed to this process, although further studies are needed to prove these assumptions.

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