PIKNODİZOSTOZİS’İN KRANİOFASİYAL VE AĞIZ İÇİ DEĞERLENDİRİLMESİ:
(BİR VAKA RAPORU)

CRANIOFACIAL AND INTRAORAL EVALUATION PYCNODYSOSTOSIS:
(A CASE REPORT)

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Makale Kodu/Article code: 534
Makale Gönderilme tarihi: 06.04.2011
Kabul Tarihi: 05.09.2011

ÖZET


Anahtar Kelimeler: Piknodizostozis, Hipoplastik Orta Yüz, Multidisipliner Tedavi

INTRODUCTION

Pycnodysostosis (PKND) is a rare autosomal recessive inherited disease belonging to a group of craniotubular bone dyplasias. The syndrome is characterized by a variety of craniofacial anomalies, including a dolichocephalic skull with persistent fontanels, a hypoplastic middle face, exophthalmus, delayed exfoliation of deciduous teeth, a beaked nose and a bluish sclera in some cases. A lateral cephalogram, panoramic radiograph, computer tomography and hand radiographs were taken to assess craniofacial, dental and skeletal features. Flow cytometry immunophenotypic was used to evaluate the immune system. Our case presented with craniofacial anomalies characteristic of PKND, including delayed closure of fontanelles, a hypoplastic middle face, exophthalmus, a beaked nose, congenitally missing teeth, a grooved palate and dental malalignment. The making of differential diagnosis of pycnodysostosis is important in the prognosis of disease and determining of treatment. Risk factors should be carefully addressed in treatment planning. Ideally, a multi-disciplinary approach should be taken that involves the orthodontist and oral and maxillofacial surgeon in the management of dental and craniofacial problems.

Key-Words: Pycnodysostosis, Hypoplastic Middle Face, Multidisciplinary Treatment

ABSTRACT

Pycnodysostosis (PKND) is a rare autosomal recessive inherited disease belonging to a group of craniofacial bone dysplasias. The syndrome is characterized by a variety of craniofacial anomalies, including a dolichocephalic skull with persistent fontanels, a hypoplastic middle face, exophthalmus, delayed exfoliation of deciduous teeth, a beaked nose and a bluish sclera in some cases. A lateral cephalogram, panoramic radiograph, computer tomography and hand radiographs were taken to assess craniofacial, dental and skeletal features. Flow cytometry immunophenotypic was used to evaluate the immune system. Our case presented with craniofacial anomalies characteristic of PKND, including delayed closure of fontanelles, a hypoplastic middle face, exophthalmus, a beaked nose, congenitally missing teeth, a grooved palate and dental malalignment. The making of differential diagnosis of pycnodysostosis is important in the prognosis of disease and determining of treatment. Risk factors should be carefully addressed in treatment planning. Ideally, a multi-disciplinary approach should be taken that involves the orthodontist and oral and maxillofacial surgeon in the management of dental and craniofacial problems.

Key-Words: Pycnodysostosis, Hypoplastic Middle Face, Multidisciplinary Treatment

First described by Maroteaux and Lamy in 1962, the syndrome derives its name from the Greek word “pyknos”, meaning dense, in reference to the increased bone density of PKND subjects. PKND maps to the human chromosome 1q21 and is caused by a mutation in the gene that codes the enzyme cathepsin K (CTSK). CTSK is normally secreted into the

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subosteoclastic space where the bone matrix is degraded and possesses substantial collagenase activity that is critical for bone remodeling. As a result of CTSK deficiency, most individuals affected by PKND have a history of recurrent fractures of the long bones.

PKND has an estimated incidence of 1.7 per 1 million births, and it affects men and women equally, with parental consanguinity found in about 30% of reported cases. The syndrome is usually diagnosed at an early age on the basis of clinical features and radiographs, with a CTSK gene mutation analysis as the confirmatory test. In their review of the literature, Bathi & Masur identified more than 100 cases of PKND from different parts of the world. The following report presents a case of pycnodysostosis, with emphasis on the intraoral, craniofacial, immunological and biochemical characteristics of this rare syndrome.

CASE REPORT

A 33-year-old female with pycnodysostosis was referred to the Department of Orthodontics because of an inability to chew tough or hard food. The patient was the youngest of three siblings born of a second-degree consanguineous marriage. The patient’s siblings and parents were normal, and the patient herself did not appear to have any mental retardation.

On clinical examination, the patient presented a height of 134.7 cm and a weight of 30.2 kg, brachydactyly, dystrophic fingernails, a slightly retrognathic, convex profile and mid-facial hypoplasia with proptosed eyes. Intra-oral examination revealed a hypoplastic maxilla; a narrow, high-arched, grooved palate; and enamel hypoplasia (Fig.1a-d). With the exception of the mandibular right second molar, all teeth showed normal morphology. However, the mandibular first molars were tipped mesially due to the absence of the mandibular premolars, and there was a slight misalignment of teeth. In addition, an anterior crossbite of the upper and lower central incisors had caused a posterior open bite that resulted in difficulties in chewing (Figure 1e). The right posterior open-bite was 11mm and the left one was 8mm.

Craniofacial and intraoral characteristics were evaluated from panoramic radiograph, lateral cephalogram and computed tomography (Figure 2a-f) of the maxillofacial region.

Panoramic radiographs revealed the developmental absence of the mandibular third molars, two mandibular premolars and two maxillary premolars and an impacted maxillary left third molar. Reductions in both height and width of the ramus and the body of the mandible were observed. Moreover, due to the narrow body of the mandible, the mandibular canals were positioned close to the lower border (Fig.2a).

Computed tomography of the maxillofacial region showed delayed closure of the cranial sutures, particularly the lambdoid suture (Fig.2d-f). Hand radiographs showed acro-osteolysis of the terminal phalanges, with metatarsal fractures on both sides (Fig. 2g).

Liver-function, creatinine, fasting plasma glucose, serum electrolytes, acid and alkaline phosphatases, creatine phosphokinase, blood cell counts, hormonal values were all within normal limits, and T- and B-lymphocyte function and proportions were also normal. However, phagocytic and oxidative mechanisms of monocytes and granulocytes were lower than normal (Table-I).
**Table 1: Phagocytic and oxidative functions of monocytes and granulocytes**

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Normal Range</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD 14 (Monocytes)</td>
<td>2-8</td>
<td>0.81</td>
</tr>
<tr>
<td>Monocytes (% Phagocytizing cells)</td>
<td>65-95</td>
<td>34.29</td>
</tr>
<tr>
<td>Granulocytes (% Phagocytizing cells)</td>
<td>95-99</td>
<td>44.74</td>
</tr>
<tr>
<td>Monocytes (% Oxidizing cells)</td>
<td>70-100</td>
<td>67.92</td>
</tr>
<tr>
<td>Granulocytes (% Oxidizing cells)</td>
<td>95-100</td>
<td>34.30</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Since Maroteaux and Lamy first provided a thorough description of the common clinical manifestations of PKND in 1962, the literature has referred to very specific craniofacial features of PKND. These include a hypoplastic maxilla and mandible, a highly retrognathic profile, an obtuse gonial angle, hypoplastic paranasal sinuses, a grooved palate, dental crowding, overly retained deciduous teeth and delayed eruption of permanent dentition. A tendency towards the development of severe dental caries and periodontal disease have also been described.8-10

The differential diagnosis of pycnodysostosis includes various bone diseases such as cleidocranial dysostosis, acroosteolysis, osteogenesis imperfecta and osteopetrosis.11 Both pycnodysostosis and cleidocranial dysostosis present with multiple wormian bones and delayed closure of the cranial sutures, particularly the lambdoid and sagittal sutures. Both cleidocranial dysostosis and pycnodysostosis open fontanels and cranial sutures are also observed at an advanced age, although in this case the clavicle was also involved, a bone rarely affected by pycnodysostosis. Whereas pycnodysostosis is autosomally recessive, cleidocranial dysostosis is transmitted by autosomal dominant inheritance.12 The fractures in pycnodysostosis are much more severe with other associated features like choanal atresia and blue sclera, while bone fragility and a history of frequent fractures may suggest osteogenesis imperfecta.

In differentiating pycnodysostosis from osteopetrosis, the presence/absence of severe anemia and hepatosplenomegaly should be taken into consideration.13 Osteopetrosis is known to result in constriction of the cranial foramina, with subsequent loss of hearing, optic nerve atrophy, facial nerve palsy, hydrocephalus and mental retardation. Histologically, the appearance of pycnodysostosis is similar to that of osteopetrosis but the medullary canals are present and microscopic evidence of attenuated haversian canal system is seen.12,13

In fact, in pycnodysostosis, the number of osteoclasts is normal but the region of demineralized bone surrounding them is larger than normal. In the case presented here, ultrastructural examination showed large, abnormal cytoplasmic vacuoles containing bone collagen fibrils, suggesting that although pycnodysostosis osteoclasts function normally in demineralizing bone, they are unable to adequately degrade the organic matrix.

Neither anemia nor hepatosplenomegaly were present in our patient. Cephalometric radiography and tomography revealed open fontanels, which is a common finding of PKND.13 A diagnosis of pycnodysostosis was also supported by hormonal levels and clinical findings.

In a review of 54 cases of pycnodysostosis, Muto et al.14 reported common oral findings to include an obtuse gonial angle (n=53), grooved palate (n=38), maxillary hypoplasia (n=40), malpositioned teeth (n=33), maxillary sinus hypoplasia (n=24), mandibular fracture (n=6), osteomyelitis (n=9), cross
bite (n=11) and hypercementosis (n=4). In our patient, maxillary hypoplasia, an obtuse gonial angle and grooved palatal mucosa were evident.

The literature mentions both Class II and Class III malocclusions in association with PKND. Our patient had a skeletal Class II and Dental Class III malocclusion.

Hormonal levels were within normal limits in our patient, which is in line with reports by Karkabi et al and Ilankovan and Moos. Karkabi et al reported a case of PKND in which monocytes possessed normal phagocytic capacity, but impaired killing activity. Another study has indicated that PKND may face the enhanced possibility of infection, impaired wound healing, osteomyelitis and pathological fracture in connection with surgical procedures.

PKND patients usually have a normal life span, making early diagnosis of utmost importance in terms of fracture prevention and quality of life, which require proper attention to risk factors during treatment planning. Currently, no recommendation or information is available in the literature regarding the efficacy and safety of orthodontics in children or even young adults with PKND. Orthodontic and orthopedic movements are fully dependent on osteoclastic activity and bone resorption and remodeling capacities. A deficient activity of the lysosomal cysteine protease cathepsin K has been identified as the cause of this osteopetrotic disease, now classified as a lysosomal disorder.

Highly expressed in osteoclasts and a key enzyme in the process of bone matrix protein degradation, deficiency in this enzyme generates osteoclastic dysfunction and reduced bone resorption and remodeling, rendering a net increase in bone mass with a resultant increased generalized osteosclerosis, directly responsible for many of the observed clinical features, probably rendering an orthodontic approach as a nonpromising treatment strategy.

Surgery and comprehensive oral rehabilitation are a challenge, since osteomyelitis has been described as a common occurrence in adults with PKND, therefore surgical intervention should preferably be done earlier in life when risk factors for osteomyelitis development are reduced. Unfortunately, orthognathic surgery has not been previously described in the literature for these patients, aside from a recent report where distraction osteogenesis technique was used.

Unfortunately, these patients searched for care later in life, having missed early childhood prevention of oral disease. Early intervention to relieve dental crowding has been recommended to the pediatric patient to allow better dental alignment and oral hygiene of the primary and erupting permanent dentition reducing chances of dental impaction, periodontal disease, and dental caries. Because of serious limitations imposed by dentofacial discrepancies, it would be advisable for these patients to be treated as high-risk patients with frequent recall visits in order to prevent dental caries and periodontal disease, providing early intervention if restorative procedures become needed.

In conclusion, the ideal approach to the management of gingival, dental and craniofacial problems associated with PKND should be multidisciplinary, involving the orthodontist and oral and maxillofacial surgeon. Any correction of the severe dentofacial deformities described in this report by routine orthognathic surgery would require osteosynthesis and bone grafting. Risk of infection and/or nonunion after such a surgical procedure was considered too great, and therefore the possibility of treatment by distraction osteogenesis of the maxilla may be evaluated.

**KAYNAKLAR**