Pyknodysostosis: A Case Report

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Abstract:
Pyknodysostosis is a rare bone disease that has autosomal dominant trait. It is characterized by short stature, diffuse osteosclerosis, acro-osteolysis, finger, and nail abnormalities. Other features include open fontanelles and sutures, relative proptosis and obtuse mandibular gonial angle with relative mandibular prognathism. Intraoral features such as dental abnormalities also have been reported.

In this report, a case of pyknodysostosis in a 9-year-old boy is presented. Most of the observed features were comparable to the other case reports but some findings such as repeated chest infection, sleep apnea, kyphosis, scoliosis, root shortness, pulp narrowing, supernumerary and hypodontia could not be observed in this case.

Instead, in this patient features such as anterior open bite and decreased anterior tooth display, not reported in other cases, was evident.

Key Words: Bone Diseases, Developmental; Craniofacial Abnormalities; Open Bite

INTRODUCTION
Pyknodysostosis, first described in 1962 by Maroteaux and Lamy [1], is a rare autosomal-recessive disorder of osteoclast dysfunction causing osteosclerosis. The name derives from the Greek "Pyknos" meaning "dens". The disease show equal sex distribution with high consanguinity among parents of the patient.

Pyknodysostosis overlaps the more common osteopetrosis and cleidocranial dysostosis [2]. The syndrome was considered a type of osteopetrosis or cleidocranial dysostosis before 1962 [3].

General features include short stature (<150 cm) that is mainly due to shortness of the extremities and not the trunk [4], generalized diffuse osteosclerosis with a tendency for fracture after minimal trauma [5], hypoplastic clavicles as well as acro-osteolysis with sclerosis of the terminal phalanges –a feature that is considered essentially pathognomonic [2]. Other features include wrinkled skin, finger and nail abnormalities [6], kyphosis and scoliosis [7]. The intellectual and sexual development is usually normal in these patients. In some patients a history of repeated chest infection and sleep apnea due to upper respiratory obstruction has been reported [8].

Fronto-parietal bossing, thick calvaria, open fontanelles and sutures, hypoplastic paranasal sinuses, wormian bones in the lambdoidal region, relative proptosis, beaked nose, blue sclerae and obtuse mandibular gonial angle often with relative prognathism [2,9] and hypoplastic midface [10] are among cranial and maxillofacial features of this disorder.

According to some studies, intraoral features such as persistence of deciduous teeth with premature or delayed eruption of permanent teeth leading to crowding [2], enamel hypopla-
ria, extensive dental caries [3,10], narrowing of pulp cavities, shortness of tooth root, hypodontia [11] or supernumerary [7] and hypercementosis [12] are specific to pyknodysostosis. Other abnormalities reported in literature are midline antero-posterior ridge of the palate [10], macroglossia [7], and infection of unerupted permanent teeth follicules, leading to abscess formation [2].

A greater tendency for fractures, especially of the long bone is a common finding in this disorder. Spontaneous fractures of the mandible during mastication are uncommon and are usually due to trauma, exodontia and postosteomyelitis [12].

Based on a case report, osteomyelitis of the mandible after dental extraction has rarely been reported in the literature [10].

As it has been reported by Fleming et al [2], some of the cranial and radiological features of pyknodysostosis are similar to cleidocranial dysostosis and osteopetrosis. These diseases share certain common features that are shown in Table 1 [5].

**CASE REPORT**

A 9-year-old boy was referred to Orthodontic Department, Shiraz University of Medical Sciences, Dental School for orthodontic consultation and treatment. Upon physical examination, a short stature was evident with no abnormality in mental capacity. The anterior and posterior fontanelles were wide open and boggy to touch, and the face was small and narrow with a poorly developed maxilla and zygomatic arch. In full smile there was no incisor display probably due to the vertical maxillary deficiency. The patient had significant

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**Table 1.** Salient features of cleidocranial dysostosis, osteopetrosis and pyknodysostosis.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cleidocranial dysostosis</th>
<th>Osteopetrosis</th>
<th>Pyknodysostosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inheritance pattern</strong></td>
<td>Autosomal dominant</td>
<td>Autosomal dominant (benign)</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td></td>
<td>Autosomal recessive</td>
<td>Autosomal recessive (malignant)</td>
<td>Decreased osteoclastic activity</td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td>Hypoplastic/normal bones</td>
<td>Diffuse osteosclerosis involving medullary bone.</td>
<td>Medullary bone not involved</td>
</tr>
<tr>
<td><strong>Clinical features:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>Normal</td>
<td>Stunted growth</td>
<td>Dwarf (Height below 150 cm)</td>
</tr>
<tr>
<td>Skull vault</td>
<td>Bigger (brachycephalic)</td>
<td>Normal</td>
<td>Bigger (brachycephalic)</td>
</tr>
<tr>
<td>Skull base</td>
<td>Normal</td>
<td>Dense</td>
<td>Dense</td>
</tr>
<tr>
<td>Diffuse sclerosis</td>
<td>Absent</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Cranial sutures</td>
<td>Open</td>
<td>Normal</td>
<td>Open</td>
</tr>
<tr>
<td>Wormian bones</td>
<td>Present</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Maxilla</td>
<td>Hypoplastic</td>
<td>Normal</td>
<td>Hyoplastic</td>
</tr>
<tr>
<td>Maxillary sinus</td>
<td>Under-pneumatized</td>
<td>Not altered</td>
<td>Under-Pneumatized</td>
</tr>
<tr>
<td>Gonial angle</td>
<td>Normal</td>
<td>Normal</td>
<td>Obtuse</td>
</tr>
<tr>
<td>Clavicle</td>
<td>Aplastic/hypoplastic</td>
<td>Normal</td>
<td>Normal/hypoplastic</td>
</tr>
<tr>
<td>Hands and feet</td>
<td>Normal</td>
<td>Normal</td>
<td>Short stubby fingers and aplasia/ hypoplasia of terminal phalanges</td>
</tr>
<tr>
<td>Fracture tendency</td>
<td>Normal</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Long bones</td>
<td>Normal</td>
<td>Deformity: multiple fractures &amp; malunion</td>
<td>Deformity: multiple fractures &amp; malunion</td>
</tr>
<tr>
<td>Bone texture</td>
<td>Normal</td>
<td>Dense with obliteration of intramedullary canals</td>
<td>Dense, without obliteration of intramedullary canals</td>
</tr>
<tr>
<td>Cranial nerves</td>
<td>Not involved</td>
<td>Involved: deafness, blindness &amp; facial paralysis observed</td>
<td>Not involved</td>
</tr>
<tr>
<td>Extra-medullary hemopoiesis</td>
<td>Absent</td>
<td>Present</td>
<td>Absent</td>
</tr>
</tbody>
</table>
frontal and parietal bossing, exophthalmos, mild ocular proptosis, double chin and beaked nose (Fig 1A). Lateral cephalometric view of the skull and facial bone demonstrated marked sclerosis of skull base, patent fronto-temporal and parieto-occipital sutures along with wormian bone (Fig 1B). Cephalometric analysis confirmed the gross skeletal class III relationship with steep mandibular plane surprisingly in contrast to the patient's profile showing a convex pattern that was not in accordance with his skeletal pattern. The upper incisors were proclined whereas the lower incisors had normal inclination (Fig 1B).

The radiographic findings showed the presence of dense and sclerotic mandibular cortex with a very obtuse gonial angle, which is a prominent characteristic of this syndrome. The mandibular rami were reduced in vertical as well as antero-posterior dimension with inferior dental canal placed in a posterior position. Also, deep sigmoid notches as a result of presence of long condylar and coronoid processes were evident (Fig 1C).

In intraoral examination, a characteristic groove along the midline of the hard palate was evident (Fig 2A). The teeth with normal morphology were malaligned and had multiple caries. The upper arch was V-shaped form and the sagittal, vertical, and transverse relationship showed a 3mm reverse overjet, anterior open bite and bilateral crossbite respectively (Fig 2B). A proper occlusion and teeth interdigitation was not possible due to the dental class III relationship. The dentition showed evidence of enamel hypoplasia and slight marginal gingivitis (Fig 2C).

His hand and wrist radiograph showed aplasia of the distal phalange (Fig 3A). His extremities were short, the hand phalanges were small, and club shaped with malformed nails and wrinkled skin (Fig 3B). The patient had a history of right leg fracture due to external trauma. His family history revealed that his female cousin is also affected by the same disorder. The clinical, as well as radiographic findings with the genetic background, established a diagnosis of pyknodysostosis.

**DISCUSSION**

In this report some of the general features such as short stature, history of long bone fracture, acro-osteolysis, wrinkled skin, finger and nail abnormalities was comparable to the other reports [2,5,6], but no history of repeated chest infection, sleep apnea, kyphosis and scoliosis – as reported by other researches [7,8] – was found in this study. Considering the cranium, maxillofacial symptoms reported by other studies [2,9,10] – such as beaked nose, exophthalmos, proptosis, mandibular prognathism, dense mandibular cortical bone, obtuse gonial...
Fig 2. Intraoral features of the patient: Upper V-shaped arch with midline groove (A) Reverse overjet, anterior openbite and posterior crossbite (B) Enamel hypoplasia and marginal gingivitis in lower arch (C).

angle, patent cranial sutures, wormian bone, hypoplasia of paranasal sinuses –were evident in this patient. Profile view did not show any concavity despite 3 mm reverse overjet due to the soft tissue compensation. Intraoral examination revealed that the observed symptoms such as antero-posterior palatal fissure, delayed eruption of permanent teeth, multiple caries and enamel hypoplasia were comparable to other studies [2,3,10]; but there was no sign of root shortness, pulp narrowing, supernumerary or hypodontia, contrary to some studies [7,11]. On the other hand, anterior open bite and decreased anterior tooth display –not reported by other studies –were observed in this patient. No environmental etiologic factor such as thumb sucking could be found for the anterior open bite.

Comparable to the present report many studies has shown the familial background and the role of autosomal dominant gene in this disease [3,4,11]. Usually active endosteal bone formation can produce a reduction in bone marrow volume, but despite the presence of this feature in pyknodysostosis, there is not sever anemia in this disease that suggest active medullary hematopoiesis [7]. The MRI studies in pyknodysostosis patients show the cortex has normal thickness and the increase in trabecular bone is limited to the space with in the medullary canal [13].

Hunt has shown that the pyknodysostotic osteoclasts have normal appearance and attachment to the bone surface with abnormal ruffled border and adjacent clear zone. Large vacuoles –that contain collagen fibrils within the cytoplasm– indicate a defect in the lysosomal degradation of the bone organic matrix [3]. Mutation in the cathepsin –k gene that encodes cathepsin k can cause this problem. This gene has type I collagenolytic, gelatinolytic and elastinolytic activity. Impairment of cathepsin k secretion makes this disease a lysosomal disorder [3].

Gelb et al [14] have shown this defect to be localized to chromosome 1 q 21. This implies that the bone response to orthodontic force would appear to be greatly impaired if gene replacement therapy or bone marrow transplants to provide normal osteoclasts has not been used properly [3].

For treatment, unlike osteopetrosis, bone surgery is possible in pyknodysostosis with slow but satisfactory bone healing. With the help of advances in understanding of osteoclast cell biology we can separate pyknodysostosis from the complex of osteopetrotic state and can develop a therapeutic innovation that would normalize dentoskeletal development to facilitate orthodontic tooth movement [3].

As a real complication, mandibular fracture and subsequent osteomyelitis should be considered when seemingly minor surgery such as tooth extraction or dental implants are indicated in these cases. In pyknodysostosis, fracture and osteomyelitis of the jaws are more popular in adulthood [7]. In several studies the success or failure of
mandibular reconstruction after osteomyelitis in this syndrome has been cited [7,12]. According to Schmitz et al [7], since the mandible is loaded multicentrically, cyclic loading could result in fatigue fracture of bone plates after mandibular reconstruction. A bone graft could protect the plate from fatigue failure, because it resists bending forces and alters modulus of elasticity adjunct to the plate [7]. In the case of pseudoarthrosis, chronic osteomyelitis, or atrophic mandibular fracture in pyknodysostotic patients, mandibular reconstruction using reconstruction plate associated with anterior iliac crest graft could be a good option of treatment [12].

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