

## Pycnodysostosis- A Review

Ramachandran Sudarshan<sup>1</sup>, G. Sree Vijayabala<sup>2</sup>

### **Abstract:**

Pycnodysostosis was coined by the French physicians Maroteaux and Lamy in 1962. The word "pyknos," in the Greek mean "dense" and word "dysostosis" mean abnormal bone formation. It characterized by osteosclerosis, short stature, wormian bones, last bone of the fingers usually short, open fontanel and several orofacial manifestations. It characterized by spontaneous fracture. This manuscript illustrates this condition with clinical features and management reported in the literature.

**Keywords:** Pycnodysostosis, osteosclerosis, fracture

<sup>1</sup> Senior Lecturer, Department of Oral Medicine and Radiology, Sibar Institute of Dental Sciences, Guntur

<sup>2</sup> Senior Lecturer, Department of Oral Medicine and Radiology, Thai Moogambikai Dental College and Hospital, Chennai

Corresponding Author email: [Sudharshanram@yahoo.co.in](mailto:Sudharshanram@yahoo.co.in)

### **Introduction:**

Pycnodysostosis was first described and its present term coined by Maroteaux and Lamy (1962, 1965, and 1966) under the heading of diastrophic dwarfism. They distinguished the condition from cleidocranial dysostosis and osteopetrosis and claimed that Toulouse-Lautrec had suffered from it.<sup>1</sup>

The disease is characterized by proportionate dwarfism, well developed secondary sex characteristics, peculiar facies, prominent forehead, beaked nose, receding jaw, abnormal dentition with a usually normal palate-although sometimes it

is cleft-and certain skeletal changes with multiple spontaneous fractures; finally there is usually consanguinity in the parents (Maroteaux and Lamy 1966; Dusenberry and Kane 1967). The similarity in appearance of the patients, regardless of sex and race, is striking (Elmore 1967).<sup>1</sup> The aim of this presentation is to describe the etiopathogenesis, clinical features and management of this disorder.

### **Etiopathogenesis**

Pycnodysostosis has an autosomal recessive inheritance, and is characterized by systemic high bone density due to decreased bone turnover. In the 1990s, the

defective gene responsible for pycnodysostosis was located in chromosome 1q21, offering accurate diagnosis, carrier testing and a more thorough understanding of this disorder. Pycnodysostosis represents a lysosomal storage disease of the bone caused by a mutation in the gene that codes the enzyme cathepsin K. This protease plays a major role in osteoclast-driven bone resorption and is responsible for degrading collagen type 1, which constitutes 95% of the organic bone matrix. The bones in individuals afflicted with pycnodysostosis are abnormally dense and brittle as a result of this insufficient reabsorption process.<sup>2</sup>

Clinical features:

***Facies:***

The head appears large because of occipital bulging. A large beaked nose with mild exophthalmos, deep nasolabial skin folds, and micrognathia are characteristic. The micrognathia, together with the relatively long soft palate, can be severe enough to cause chronic respiratory airway obstruction. Several patients have developed sensorineural deafness. Mocan et al described a hemangioma of the skull.<sup>3</sup>

***Eyes:***

The eyes may be somewhat exophthalmic with blue sclera.<sup>3</sup>

***Oral:***

Obtuse mandibular angle is a constant feature. Facial bones are often underdeveloped, with relative mandibular prognathism. Oral and dental anomalies include premature or delayed eruption, ectopic teeth, enamel hypoplasia, malposed

teeth, obliterated pulp chambers and hypercementosis, grooved palate, and sometimes cleft palate. The soft palate tends to be long. Lacey et al described a patient with short and blunted tooth roots and multiple congenitally missing permanent tooth germs. Protrusion of the incisors with anterior open bite may be found, and dental crowding associated with extensive caries and periodontitis is frequent. These conditions cause the premature loss of dentition that may already be complete by the fourth decade of life.<sup>3,4</sup>

Discharging sinuses occur in the jaws because of poor blood supply due to hypercementosis and hyperdense bones. Follicles of impacted teeth may also get infected leading to discharging sinuses or chronic suppurative patient by one hand while being strapped at the back of osteomyelitis.<sup>7</sup>

***Skeletal:***

Pycnodysostosis causes the bones to be abnormally dense (osteosclerosis); the last bones of the fingers (the distal phalanges) to be unusually short; and delays the normal closure of the connections (sutures) of the skull bones in infancy, so that the "soft spot" (the fontanel) on top of the head remains widely open. Pycnodysostosis causes brittle bones which easily break (fracture). The bones in the legs and feet tend to fracture. The jaw and collar bone (clavicles) are also particularly prone to fractures.<sup>5</sup>

There is widening of the anterior fontanelle and skull sutures and there may

also be persistent metopic sutures. The parietal bones frequently show evidence of wormian bone formation. The mastoids may be non-aerated. The paranasal sinuses and maxillary bones are hypoplastic. Some hypoplasia of the mandible is usually seen and a striking feature is the almost total disappearance of the mandibular angle.<sup>6</sup>

There may be S-shaped tibiae or radii, the latter often associated with a Madelung deformity. The vertebrae are dense and of the infantile type. There is frequently lack of closure of the neural arches. There may be spondylolysis, especially of the 5th lumbar component. The pelvis may show shallow acetabula with increase in the angulation of the acetabulum in relation to the perpendicular plane of the body. Coxa valga and coxa vara have both been reported.<sup>6</sup>

#### **Laboratory findings:**

They are usually normal but reduced alkaline phosphatase values and slight hypercalcaemia have been reported. In recent reports cases with anaemia, thrombocytopenia and splenomegaly were described.<sup>6</sup>

#### **Differential diagnosis:**

The differential diagnosis of PKD includes cleidocranial dysostosis and osteopetrosis. Notably, cleidocranial dysostosis presents with a normal height, bone texture, gonial angles and the absence of diffuse oteosclerosis. Osteopetrosis may present with stunted growth, a dense skull base, diffuse oteosclerosis, multiple fractures and malunion. The hands, feet, clavicles, gonial

angles, maxilla and skull vault are normal. Management of PKD is multidisciplinary: supportive treatment includes the management of anaemia, recurrent infections, failure to thrive, hypocalcaemia, fractures of bones and diverse ailments.<sup>7</sup>

#### **Management:**

It is important that the disease be diagnosed and the tendency to fractures be recognized so that

(1) Fractures can be minimized, if not entirely prevented.<sup>5</sup>

(2) The parents and other caregivers are not falsely accused of child abuse! As with any condition causing brittle bones, the infant should be handled with a reasonable degree of care. The older child should be encouraged to engage in safer forms of exercise such as swimming rather than, for example, jumping on a trampoline.<sup>5</sup>

In 1996, Soliman and colleagues reported that there is defective secretion of growth hormone in pycnodysostosis. Replacement treatment with growth hormone was then tested. It was found to increase the growth of the length of bones (linear growth). Since short stature is an important consequence of pycnodysostosis, growth hormone treatment may prove very useful.<sup>5</sup>

Some authors propose early treatment using orthodontic methods, although others argue that the lack of bone remodeling would impede satisfactory results, therefore planned and sequenced extractions would be more recommendable. Tooth extraction in patients who suffer from

pycnodysostosis demands certain special care, such as carrying out the surgery as a traumatically as possible and with proper asepsis, due to the risk of fracture, especially in the mandible. In addition, the greater bone density increases the probability of developing post extraction osteomyelitis.<sup>4</sup>

#### **Future trends:**

Research on specific approaches to correct the abnormal bone metabolism in pycnodysostosis is another hot topic. Due to providing normal osteoclasts and osteoclast-targeted enzymes, bone marrow transplantation is drawing the increasing attention. Gene replacement strategies are other alternative choices. However, considerable research is required in this area. Recently, CTSK (Cathepsin K) was shown to play an important role in autoimmune and inflammatory diseases by animal and in vitro experiments. If the role of CTSK in the human immune system is confirmed, it will be helpful in further understanding of the mechanism of pycnodysostosis and in designing specific treatment strategies.<sup>8</sup>

Pycnodysostosis includes group of disorders that requires a multispecialty approach. Early diagnosis of this disorder is essential as bone deformity and its complications are difficult to manage. Further proper counseling of the patient and their parents are utmost important to avoid osteosclerosis related complications.

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