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Case Report

Pycnodysostosis: A rare cause of short stature

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Introduction

Pycnodysostosis is a rare bone disease. It is inherited as an autosomal recessive trait and is characterized by short stature, diffuse osteosclerosis, acro-osteolysis along with finger and nail abnormalities. Other features include open fontanelles and sutures, relative proptosis and obtuse mandibular gonial angle with relative mandibular prognathism. Pycnodysostosis was first described and its present term coined by Maroteaux and Lamy in 1962, under the heading of diastrophic dwarfism. They distinguished the condition from cleidocranial dysostosis and osteopetrosis.¹

We report a case of Pycnodysostosis in a 12 year old female patient, born to unrelated parents who presented with short stature.

Case report

A 12 year old female patient was brought by her parents for evaluation of short stature. She was the product of a non-consanguineous marriage, delivered at term after an uneventful antenatal period, through lower segment cesarean section. She had one elder sibling who was normal. She was fully vaccinated for age and was attending school with normal scholastic performance. On examination her height was 119 cm (below 5th percentile for her age), weight 29 kg, and head circumference was 52 cm. The upper-lower segment ratio 1:1.1 and her arm span was 112 cm. The head was brachycephalic with frontal and parietal bossing (Fig. 1A). She had ocular proptosis and a beaked nose. The anterior fontanelle was open. The face was small and narrow. The oral cavity showed double row of teeth, high arched palate. The chest was barrel shaped with a prominent sternum and the spine showed lumbar lordosis. The hands and feet had short terminal phalanges and koilonychia (Fig. 1B). The joint mobility was normal. Her SMR staging was II (Tanner's) and she had not attained menarche. Examination of the cardiovascular and respiratory systems was normal. Her neurological evaluation was also normal. Per abdomen examination did not show any hepatomegaly and spleen was not palpable.

All the hematological parameters were normal. Serum alkaline phosphatase values and serum calcium were within normal limit. Her growth hormone levels were also normal.

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Fig. 1 – (A) Photograph showing characteristic craniofacial features – Head appears large because of occipital bulging. A large beaked nose, deep nasolabial skin folds, and micrognathia. (B) Photographs of both hands showing short fingers.

(both baseline and after clonidine stimulation) Skeletal survey showed a generalized increase in bone density especially in the calvarium, long bones and phalanges with preservation of medullary cavity. Her bone age was about 12 yrs as evidenced by appearance of ossification centre of pisiform bone on roentgenogram of wrist joints. The roentgenogram of skull showed a) Increased density of the skull base, b) Wide coronal suture c) Hypoplastic facial bones, d) Wide angle of the mandible (Fig. 2A). Radiograph of the hands showed sclerotic bones, absent ungual tufts and terminal osteoacrolsis (Fig. 2B). The roentgenogram of the chest revealed osteosclerotic ribs, normal clavicles, and normal cardiac outline (Fig. 2C). The roentgenogram of the dorsolumbar spine showed spool shaped vertebral bodies with prominent anterior aspect (Fig. 2D). The roentgenogram of the pelvis showed increase in bone density with scalloped outline of the acetabulum

(Fig. 2E). On the basis of clinical and radiological features a diagnosis of Pycnodysostosis was made.

Discussion

Pycnodysostosis is an autosomal recessive osteosclerosing bone disorder characterized by increased bone density, dwarfism and skeletal fragility. It was described first by Maroteaux and Lamy in 1962.¹ Pycnodysostosis is a rare bone disease with an incidence of 1.7 per million births.²

20% of children are born from consanguinous marriages with male: female ratio of 2:1. It is characterized by proportionate short stature, wide open sutures and fontanelles, short stubby fingers, hypoplastic/dysplastic distal phalanges, retrograde mandible, multiple fractures and

Fig. 2 – Imaging findings (A) Radiograph skull shows a) Increased density of the skull base, b) Wide coronal suture c) Hypoplastic facial bones, d) Wide angle of the mandible. (B) Radiograph of the both hands showing acro-osteolysis (arrow). (C) & (D) Radiograph of dorsolumbar spine (Lateral and antero-posterior view) showing the spool shaped vertebral bodies (arrow) with prominent anterior defects. (E) Radiograph of the pelvis antero-posterior view – showing increased bone density with scalloped outline of acetabulum.

osteosclerosis. It is caused by mutations in the CTSK (Cathepsin K) gene at 1q21 which codes the lysosomal cysteine protease – cathepsin K. These mutations affect the metabolism of bones causing bone resorption and remodeling.³

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.²

In these patients, the head appears large because of occipital bulging. A large beaked nose with mild exophthalmos, deep nasolabial skin folds, and micrognathia are characteristic. 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. 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.⁴

The differential diagnosis of Pycnodysostosis includes cleidocranial dysostosis and osteopetrosis. Notably, cleidocranial dysostosis presents with a normal height, bone texture, gonial angles and the absence of diffuse osteosclerosis. Osteopetrosis may present with stunted growth, a dense skull base, diffuse osteosclerosis, multiple fractures and malunion. The hands, feet, clavicles, gonial angles, maxilla and skull vault are usually not involved.

Among the laboratory findings, reduced alkaline phosphatase values and slight hypercalcaemia have been reported. In few published case reports of pycnodysostosis, patients had anaemia, thrombocytopenia and splenomegaly.⁴ However in our patient we did not find these findings. In our patient, diagnosis of Pycnodysostosis was made based on clinical and radiological features. We found characteristic radiological findings in form of:

- Diffuse increase in bone density
- Spool shaped vertebrae

- Hypoplasia of mandible with obtuse mandibular angle
- Widely open cranial sutures and absence of frontal sinuses

It is important that the disease be diagnosed and the tendency to fractures be recognized so that fractures can be minimized, if not entirely prevented.⁵

To conclude, we have presented a rare case of Pycnodysostosis in a 12 year old female patient, born to unrelated parents and presented with short stature. 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. Research on specific approaches to correct the abnormal bone metabolism in pycnodysostosis is going on. CTSK (Cathepsin K) was shown to play an important role in autoimmune and inflammatory diseases by animal and in vitro experiments. If the exact 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.⁶

Conflicts of interest

All authors have none to declare.

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