Unusual case report: Pycnodysostosis with typical radiological findings

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ABSTRACT
Pycnodysostosis is an inherited disorder of the bone caused by a mutation in the gene that codes the enzyme cathepsin K located on chromosome 1q21. The bones are abnormally dense and brittle as a result of this insufficient reabsorption process. Clinical features are short stature, large head with frontal and parietal bossing and open anterior fontanelle. On X-ray open anterior fontanelle and sutures with small facial bones, nonpneumatised paranasal sinuses, flattened mandibular angle, acroosteolysis and acromial ends of the clavicles may be aplastic. Differential are cleidocranial dysostosis, osteogenesis imperfecta, and osteopetrosis. The diagnosis of pycnodysostosis is primarily based on clinical features and Radiographs; however a CTSK gene mutation analysis is the confirmatory test.

Keywords: Paediatrics, Musculoskeletal, Skeletal Dysplasia.

INTRODUCTION
Pycnodysostosis is a rare genetic osteosclerotic disorder first described by Maroteaux and Lamy in 1962¹. It is an autosomal recessive illness¹ that manifests as generalised osteosclerosis of the skeleton as a result of decreased bone turnover.

CASE REPORT
History: A 13-year-old Indian female from Panchmahal district of Gujarat State, India was referred to the paediatric unit of the Baroda Medical College, S.S.G. Hospital with history of short stature, dysmorphic facies and failure to thrive for evaluation. Patient’s weight was in the normal range and had normal full term delivery at home. Immunization was adequate with normal developmental milestones and intelligence. Parents denied any history of trauma or fractures. There was no history of frequent respiratory tract infections, snoring or tuberculosis contact. She was the elder of three siblings born of non-consanguineous marriage.

Examination: child’s weight was 35 kg. Her standing height was 120 cm. Head circumference was 53.5 cm. She had mid facial hypoplasia with proptosed eyes. She had frontal, and bilateral parietal bossing. The sagittal, coronal and lambdoid sutures were separated and anterior and posterior fontanel were widely open on palpation. Examination of the mouth revealed a narrow high arched grooved palate. The teeth were hypoplastic with lateral open bite and multiple missing teeth. Bilaterally temporomandibular joints were retracted. Her digits were short, spoon shaped, stubby with joint laxity. Metaphyseal widening and dystrophic nails were noted. There was no significant pallor, hepatomegaly or lymphadenopathy. Sexual maturity rating showed pre-adolescent stage.

Investigations: Laboratory investigations such as complete blood count, serum calcium, serum inorganic phosphate and alkaline phosphatase were normal. The radiological findings were significant showing diffuse skeletal hyperostosis with sparing of medullary cavity. Skull X-rays showed widely separated cranial sutures and widely open anterior and posterior fontanel. The parasanal sinuses were...
non-pneumatised with angle of the mandible being obtuse. [Figure-1] Acro-osteolysis was seen. The bone age was equal to her chronological age. [Figure-2] Right clavicle appears hypoplastic. [Figure-3] Patient is diagnosed as Pycnodysostosis based on characteristic clinical and radiological findings. The parents of the child were offered an option for CTSK gene mutation testing for confirmation of diagnosis of pycnodysostosis, however they refused for same in view of financial constraints as the same testing is not available currently in our country (India).

DISCUSSION

Pycnodysostosis is an inherited disorder of the bone caused by a mutation in the gene that codes the enzyme cathepsin K. This enzyme is important for normal bone cells called osteoclasts, to reabsorb into the bone and build new bone. The normal functioning of osteoclasts in individuals with pycnodysostosis is disrupted by a lack of cathepsin K, rendering individuals afflicted with this disorder to be unable to adequately reabsorb the component of bone called the organic matrix. This process, also called remodelling, is vital for normal bone maintenance. The bones in individuals afflicted with pycnodysostosis are abnormally dense and brittle as a result of this insufficient reabsorption process. The sclerosing activity of pycnodysostosis is due to a genetic defect located on chromosome 1q21. This anomaly consists of mutations that produce mutational changes in a lysosomal cystine protease, cathepsin K, the expression of which is reduced in the osteoclasts of these patients. This protease is responsible for degrading collagen type 1 that constitutes 95% of the organic bone matrix. A recent study classified the various metabolic bone diseases according to the component of the affected bone matrix. Pycnodysostosis is included in those caused by low bone remodelling. Radiological findings may show some degree of widening of the distal femur. The skull shows open anterior fontanelle and sutures with small facial bones, nonpneumatised paranasal sinuses and flattened mandibular angle. Terminal phalanges in the hand are partially or totally aplastic with loss of ungual tufts. The acromial ends of the clavicles may be aplastic. Other abnormalities include failure of complete segmentation of the atlas, axis, and the lower lumbar spine, coxa valga and abnormal radioulnar articulation. Various bone diseases should be considered in the differential diagnosis of pycnodysostosis, particularly cleidocranial dysostosis, osteogenesis imperfecta, and osteopetrosis. In cleidocranial dysostosis open fontanelles and cranial sutures are also observed at an advanced age, although in this case the clavicle is also involved, a bone rarely affected in pycnodysostosis. Cleidocranial dysostosis is transmitted by autosomal dominant inheritance whereas Pycnodysostosis is autosomal recessive. Bone fragility and a history of frequent fractures may suggest the possibility of diagnosing osteogenesis imperfecta, although the fractures are much more severe with other associated features like chonual atresia and blue sclera. Clinical features of pycnodysostosis are short stature, fractures, large head with frontal and parietal bossing, open anterior fontanelle and cranial sutures, obtuse mandibular angle, prominent eyes with bluish sclerae, underdeveloped facial bones, dental anomalies, short, broad hands and feet with dystrophic nails and trunk deformities such as kyphosis, scoliosis, increased lumbar lordosis, recurrent chest infections, stridorous breathing, snoring and narrow chest. Laboratory investigations usually give results within normal limits. Life expectancy for a Pycnodysostosis patient is normal. Histologically, the appearance is similar to that of osteopetrosis but the medullary canals are present and microscopic evidence of attenuated haversian canal system is seen. The diagnosis of pycnodysostosis is primarily based on clinical features and Radiographs; however a CTSK gene mutation analysis is the confirmatory test. Various novel mutations of cathepsin K gene in patients with pycnodysostosis have been reported in literature. There is no specific treatment as of date for this disorder and treatment is supportive. Since bone fractures are a primary threat to those affected by Pycnodysostosis, it is important that care is taken to prevent or minimize tendencies for a fracture to occur. Such precautions include careful handling of an affected child, along with exercise and activities that are safe and do not require too much impact. Dental hygiene and regular dental checkups are especially helpful for affected individuals due to various dental anomalies.

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REFERENCES


