Case Report **Pathology**

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PYCNODYSOSTOSIS AFFECTING ONLY THE MALE SIBLINGS OF A FAMILY – A RARE CASE REPORT

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ABSTRACT

Pycnodysostosis is a rare genetic disorder with autosomal recesive mode of inheritance. It is characterised by short stature, stubby extremities, facial dysmorphism, frequent pathological fractures of long bones, open anterior fontanelles, blue sclera and absence of mental retardation. Here, we are presenting a rare case report of pycnodysostosis from Tamilnadu, India. In our case, pycnodysostosis is affecting all the male siblings of a family while sparing the female siblings. This rare case portrays non-classic type of inheritance of pycnodysostosis. This is the first case report in medical literature documenting non-classic pattern of inheritance in pycnodysostosis violating the mendelian law of inheritance.

KEYWORDS: Pycnodysostosis, short stature, fractures, male siblings of a family, Non-classic type of inheritance, Tamilnadu.

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INTRODUCTION

Pycnodysostosis is a rare autosomal recessive genetic disorder with skeletal dysplasia. The term 'pycnodysostosis' was first coined and described by Maroteux And Lamy in the year 1962, (Pycno – thick/ dense , dysostosis – defective bone).[1] Pycnodysostosis is a form of short limb dwarfism presenting with fractures but has a good prognosis and normal life span. The clinical and radiological features of this disorder are very distinct. We are presenting a rare case report of pycnodysostosis affecting all the male siblings of a family sparing the female siblings. This case is an example of Non-classic pattern of inheritance violating the mendelian law and it is observed for the first time in pycnodysostosis.

CASE REPORT

A 20 year old boy with short stature came to our hospital with complaints of difficulty in walking and pain in the lowerlimbs during walking. He has a beaked nose, narrow chest, large head, depressed fontanelles, protruded eyes, blue sclera and bowed legs [Figure 1, Figure 2]. He had dental caries and persistent deciduous tooth. He gave a past history of frequent pathological fractures. His mental growth and intelligent quotient was normal.Figure 1, Figure 2

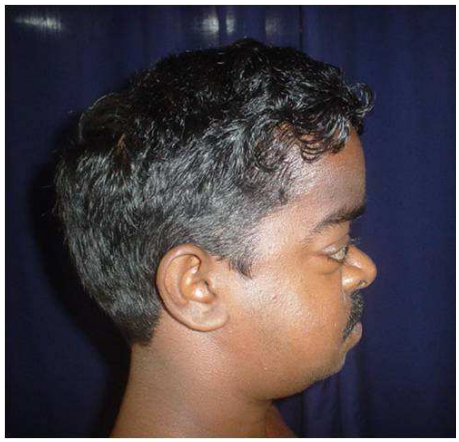

Figure 1
Picture shows the facial dysmorphism with beaked nose.

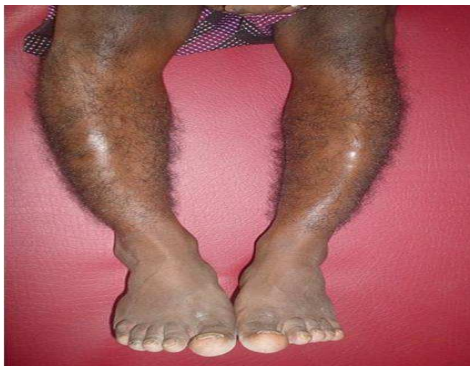

Figure 2
Shows the bilateral bowing of tibia in the lower limbs.

Radiographs revealed bones with high density, intact medullary canal, pathological fracture in the tibia and femur, bilateral bowing of tibia, skull with open fontanelles and sutures, poorly pneumatised para nasal sinuses, increased mandibular angle almost straightened out and persistent deciduous teeth resulting in irregular double row of

teeth. [Figure 3, Figure 4, Figure 5, Figure 6 and Figure 7].

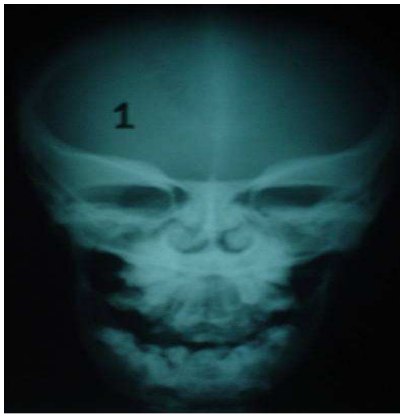

Figure 3

Radiograph shows skull with poorly pneumatised paranasal sinuses, maxillary & mandibular hypoplasia, irregular row of teeth due to persistent deciduous teeth and abnormal eruption.

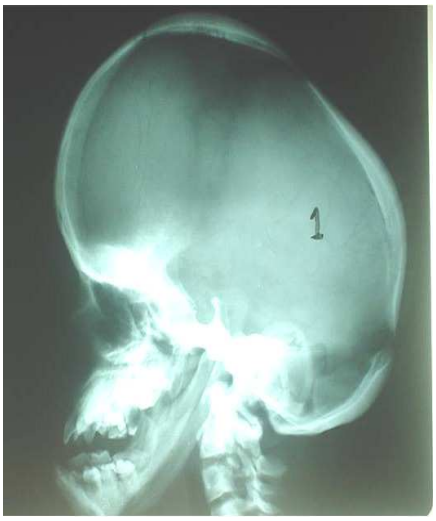

Figure 4

Radiograph shows the open fontenelles and sutures

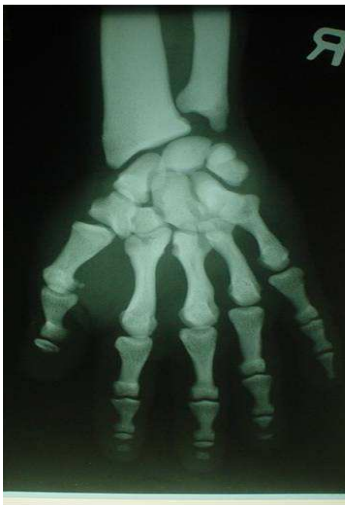

Figure 5

Radiograph shows short and stubby digits with atrophy of terminal phalanges.

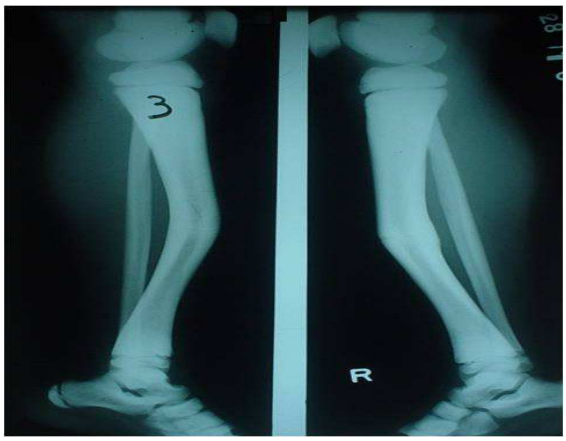

Figure 6
Radiograph shows the bowing of tibia with intact medullary canal

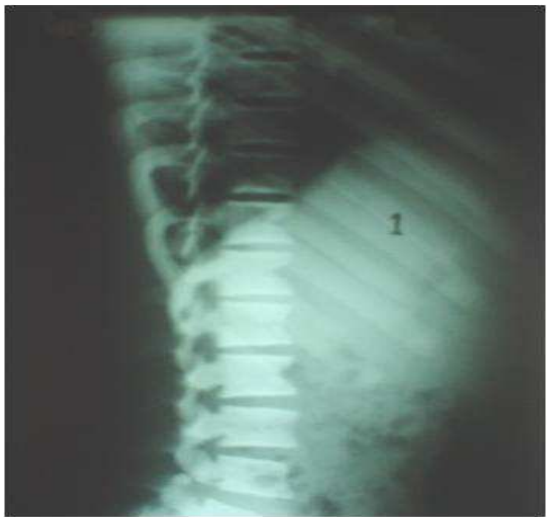

Figure 7
Radiograph shows the notching of the vertebral body giving a fish tail appearance to the anterior end of vertebral bodies.

Histopathological examination of the bone biopsy showed wormian bones with high density. The bone marrow showed normal hematopoiesis. Osteopetrosis, the closest differential diagnosis was ruled out because of the absence of its diagnostic features like anemia, hepatospleenomegaly and cranial nerve palsies.

All the other basic investigations were within normal limits. Serum calcium and serum alkaline phosphatase levels were within normal limits. Based on the clinical, radiological and histopathological features a diagnosis of pcnodysostosis was made. Initially he was treated conservatively with AK cast for his fracture. Then planned for surgical management but nailing/plating could not be carried out due to bowing, very thick bones and a narrow medullary canal. Patient was treated with Ilizarov fixation with posterior hinge at the level of the fracture. Deformity was corrected in three months time. Passing of k-wire was very difficult due to high density, resulting in thermal necrosis of the bone. After removal of external fixator, patient presented with osteomyelitis at the k-wire site. Later his brother was also admitted with similar complaints and fracture femur after a trivial trauma.

Detailed history taken revealed that he was born from a second degree consangunious marriage and has two brothers with the similar features [Figure 8]. His two sisters and parents were normal. This report was so unique that only all the male siblings of a family were affected while the female siblings

were unaffected. This interesting feature made us to think of a non-classic pattern of inheritance in pycnodysostosis , which is a very rare entity.

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Figure 8
Picture shows all the three male siblings of a family affected by pycnodysostosis.

We suggested gene mapping studies for the family members to find the mutation and for confirming our diagnosis but it could not be done due to financial constraints.

DISCUSSION

Pycnodysostosis is an autosomal recessive disorder with estimated incidence of 1.7 per 1 million births. It is due to the genetic defect located in chromosome 1q21 causing a mutational change in the cystine protease cathepsin K. The expression of which is reduced in the osteoclasts of these patients. This protease is responsible for degrading collagen type I , that constitutes 95% of organic bone matrix.[3]

Pycnodysostosis is usually diagnosed at an early age by the presence of short stature and facial abnormalities. If undiagnosed in infancy, it is recognised in the adulthood due to frequent pathological fractures. The pathological fractures are due to highly dense brittle bones . The other clinical signs and symptoms are large head, frontal and parietal bossing, short stature, blue sclera, short stubby hands, dental caries, respiratory tract infections, beaked nose and persistent deciduous teeth.[4] Trunk deformities like kyphosis, scoliosis and narrow chest can also be present.

In our case the eyes were proptosed resembling exopthalmos and sclera was bluish in colour. The face was small, triangular due to hypoplastic maxilla and mandible. The angle of the mandible was flattened and eruption of the teeth was disorganized with persistent deciduous teeth resulting in double row of deformed teeth. [5]

The characteristic radiological features were facial dysmorphism due to maxillary and mandibular abnormalities, non pneumatised paranasal sinuses, open anterior fontanelles, open cranial sutures, dense bones with intact medullary canal, atrophy of the terminal phalanges, obtuse mandibular angle, bilateral anterior bowing of tibia and pathological fractures. [6] Most of these findings were present in our case and his siblings.

Rarely it is reported in literature that pycnodysostosis can be associated with

conductive hearing loss due to otosclerosis, sandal gap deformity and unusual ophthalmological findings. [7]

The differential diagnosis for this disorder are osteopetrosis, cleidocranial dysplalsia and idiopathic acro osteolysis. In our case entire skeleton shows increased density with narrow medullary canal and there is preservation of the bone marrow with normal haematopoiesis and this is the major differentiating feature from osteopetrosis. In osteopetrosis, there is generalised increase in bone density with absent medullary canal resulting in aplastic anaemia, hepato splenomegaly with multiple cranial nerve palsies. Generalised osteosclerosis with recurrent pathological fracture are quite common in osteopetrosis. Cleido cranial dysostosis is another differential diagnosis characterized by the total or partial absence of clavicle with normal dense bones. Beaked nose and small face is also seen in Apert syndrome but it is characterized by craniosynostosis, syndactyly and mild mental retardation.[8]

There is no known treatment for pycnodysostosis. Ilizarov technique is the better treatment modality for the pathological fracture with deformity in pyknodysostosis.

Otherwise conservative treatment including supportive measures to prevent fractures and regular dental check up for dental caries is advised.

CTSK gene mutation testing is the confirmatory test. Life expectancy is normal with good prognosis.

As the disorder is autosomal recessive in inheritance there is 25% chance of either male or female child being affected, but in our case all male children are affected and all female children are spared . Therefore this is not a classical mendelian inheritance. Our case follows a single gene defect with a Non - classic pattern of inheritance most probably a gonadal mosaicism or germline mutation like osteogenesis imperfecta. In that case a phenotypically normal parent who has a germ line mutation can transmit the disease causing mutation to the offspring through the mutant gamete. Because the progenitor cells of the gamete carry the mutation , there is a definite possibility that more than one child of such parents would be affected.[9]

CONCLUSION

Pycnodysostosis, an autosomal recessive disorder can involve any sex but we observed in our case that pycnodysostosis was affecting only the male siblings of a family while sparing the females. It is a very rare occurrence. We suggest that the possible mode of inheritance is a single gene defect with Non-classic pattern of inheritance like gonadal mosaicism or a germline mutation. This is the first case report of its kind in literature.

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