CASE REPORT

PYCNODYSOSTOSIS; A RARE DISEASE CASE REPORT

Farida Aziz[1], Fatima Farida[2], Neelam Bashir[1]
[1]Frontier Medical College, Abbottabad, [2]Ayub Medical College, Abbottabad-Pakistan

Pycnodysostosis is a rare disease with very few reported cased all over the world. It was first described in 1963 by Maroteaux and Lamy. It is also known as Toulouse-Lautrec syndrome, after a French artist, Henri de Toulouse Lautrec. The affected gene, CTSK, was first isolated in 1996. It is an autosomal recessive osteochondrodysplasia, characterized by disrupted function of osteoclasts. Incidence of this disease is 1.7 per 1 million births with a male to female ratio of 1:1 30% cases arise from consanguineous marriages.

Keywords: Pycnodysostosis; Toulouse-Lautrec syndrome; Osteochondrodysplasia

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INTRODUCTION

Pycnodysostosis is a rare disease with very few reported cased all over the world. It was first described in 1963 by Maroteaux and Lamy.[1] It is also known as Toulouse-Lautrec syndrome, after a French artist, Henri de Toulouse Lautrec. The affected gene, CTSK, was first isolated in 1996. It is an autosomal recessive osteochondrodysplasia, characterized by disrupted function of osteoclasts. Incidence of this disease is 1.7 per 1 million births with a male to female ratio of 1:1 30% cases arise from consanguineous marriages.[2]

CASE

Our patient S, 8years old, from Khyber Pakhtunkhwa, Abbottabad, was an incidental diagnosis as he presented with noisy breathing, especially during sleep and was thought to have adenoid problem.

On examination, patient had short stature, large head with frontal and parietal bossing. Anterior and posterior fontanelles and cranial sutures were widely open. Jaw was hypoplastic with a beak shaped nose. Eyes were prominent. He had a high arched palate with deep grooves and there was overriding of supernumerary teeth.

Fingers were short with dysplastic nails and short distal phalanges. Feet had sandal gap deformity. The child was a school going student, was good in studies and had good behaviour.

Parents were first cousins. His older sister was married to her first cousin, with a similarly affected male child. There was another affected female cousin, 13 years old from a consanguineous marriage. She was in 7th grade and was doing well in school. She also had a large head with wide open sutures. Xray showed increased density and skull x rays showed Wormian bones. Audiometry report was misplaced but showed some degree of conduction defect. Repeat audiometry will be done on follow up.

Other investigations like serum calcium, phosphate, alkaline phosphatase and LFTs were all normal.

Figure-1: standing, two sisters, younger sister 14 years old (S) affected. The little boy (A) son of the older sister out of cousin marriage also affected

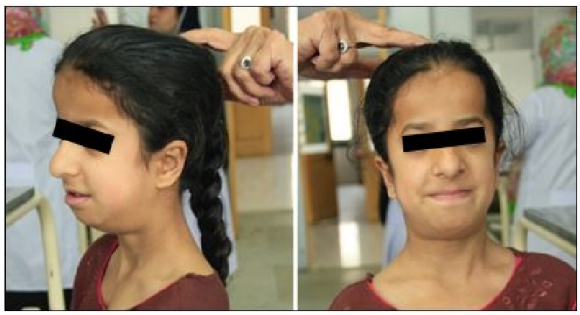

Figure-2: Open fontanelle, wide sutures, beak shaped nose, obtuse angle of jaw, short stature

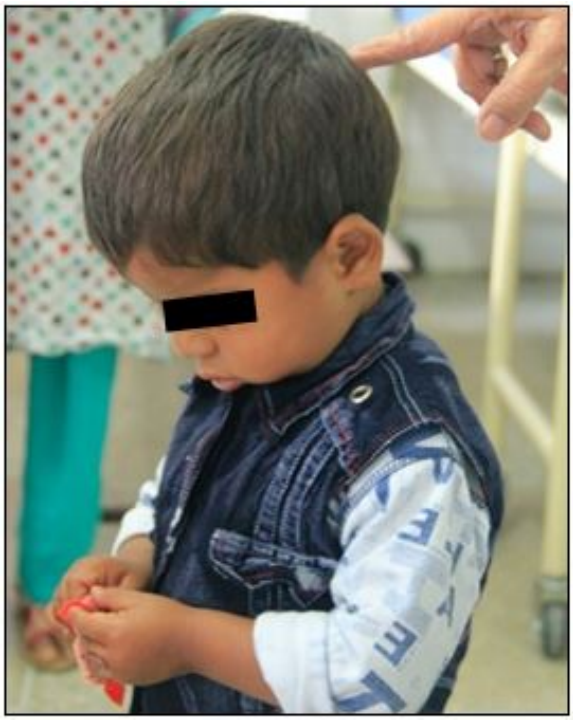

Figure-3: Affected child (A) has open anterior and posterior fontanelle

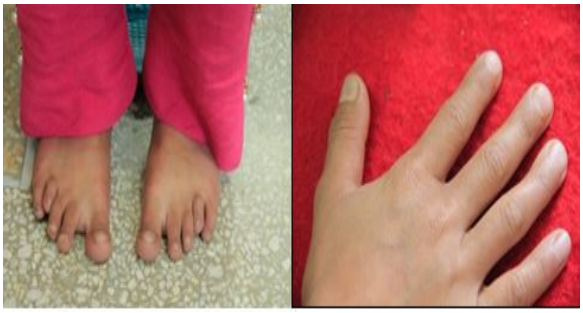

Figure-3: Short distal phalanges, dystrophic nails. Sandal gap in toes

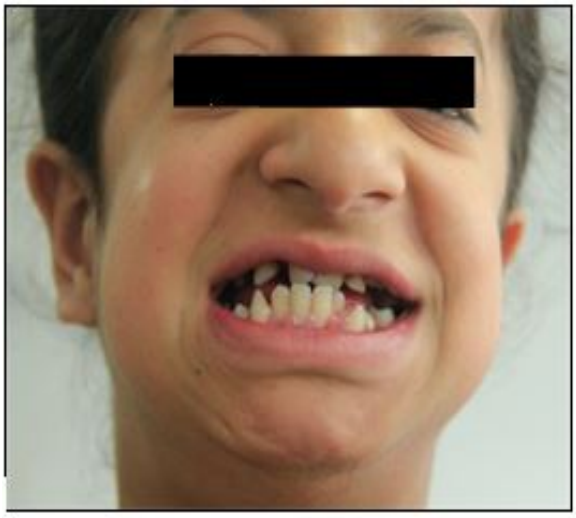

Figure-4: Supernumerary teeth

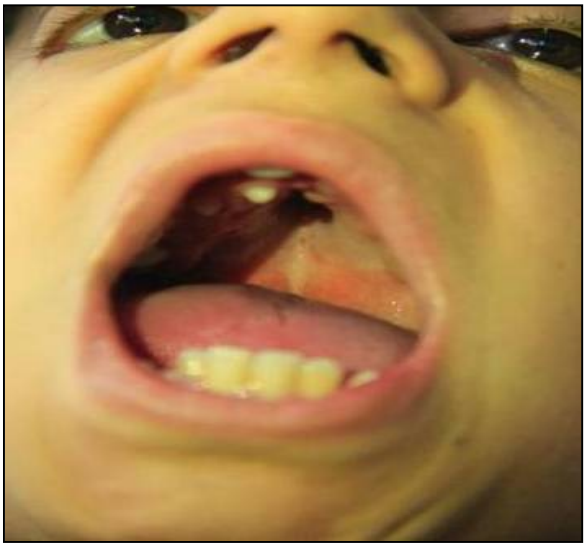

Figure-5: High arched palate with deep grooves

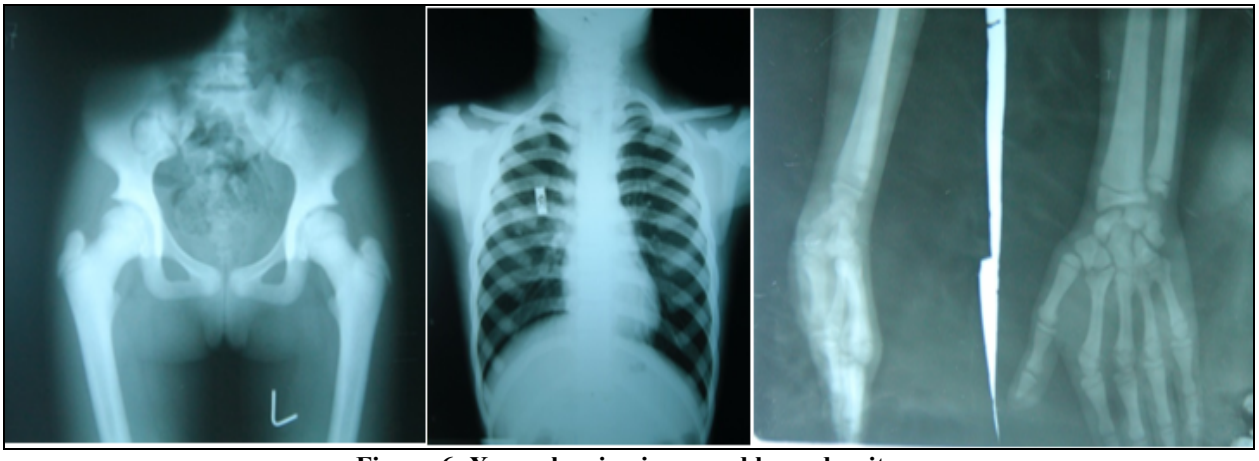

Figure-6: X ray showing increased bone density

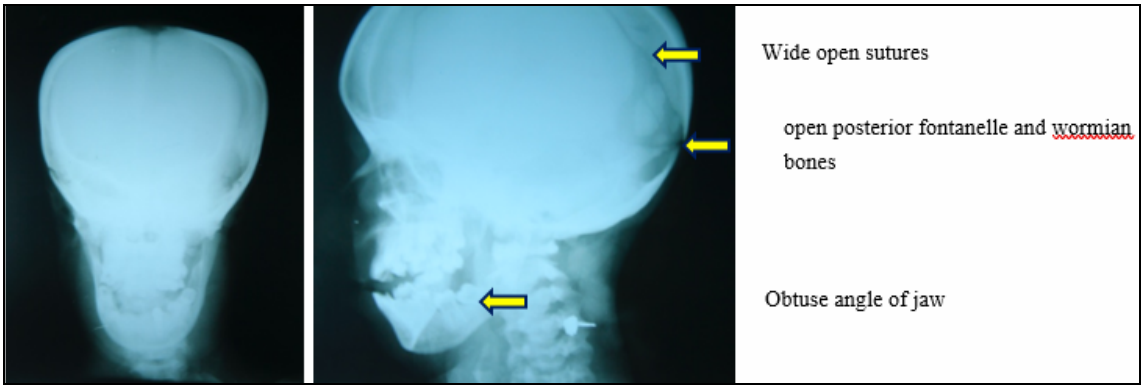

Figure-7: X ray skull of child (A) showing increased density, open sutures, open fontanelle and Wormian bones

DISCUSSION

Pycnodysostosis in an autosomal recessive disorder classified as a low bone remodelling osteochondrodysplasia.[3] It is a lysosomal storage disease of bones due to mutations in the gene that codes the enzyme Cathepsin K, which disrupts the normal function of osteoclasts.

The chromosome involved is 1q21.[4] There are mutational changes in lysosomal cystine protease, cathepsin K and reduced expressions of these in osteoclasts. The protease is responsible for degrading type 1 collagen in 95% of the organic bone matrix, along with type 2 collagen, osteopontin and osteonectin, resulting in thick, fragile and brittle bones. There is systemic osteosclerosis leading to decreased bone turnover, impaired resorption and remodeling.[5]

Clinical features of Pycnodysostosis are short stature, large head with open fontanelles and cranial sutures, hypoplastic/obtuse mandibular angle, prominent eyes, underdeveloped facial bones, dental anomalies such as dental crowding, retained/impacted teeth, enamel hypoplasia.[6] They have a narrow, deep palate. The person has short, broad hands and feet with partial agenesis of distal phalanges. There is presence of trunk deformities such as kyphosis, scoliosis, increased lumbar lordosis. There may be a history of recurrent chest infections, stridorous breathing, snoring and sleep apnea. Life expectancy is normal. There is no cognitive impairment.[7]

Laboratory investigations are normal, including serum Ca+ and Alkaline phosphatase. Radiological findings are important and are an essential part to making a diagnosis. There will be some degree of widening of distal femur, open anterior and posterior fontanelles and open cranial sutures. Small facial bones, non-pneumatised sinuses, flattened mandibular angle. Terminal phalanges may be partially or completely aplastic with loss of ungual tufts. If clavicle is involved, which is rare, the acromial end will be aplastic. There is failure of complete segmentation of atlas, axis and lower lumbar spine, coxa valga. There is also abnormal radioulnar articulation.[8]

Histologically the appearance is similar to osteopetrosis but unlike it, there is presence of medullary canals and microscopic evidence of attenuated Haversian canal system.[9]

Differentials for Pycnodysostosis could be

- Cleidocranial dysostosis
- Osteogenesis imperfecta
- Osteopetrosis

Cleidocranial dysostosis has features similar to Pycnodysostosis, like open fontanelles and sutures but the clavicle is affected which is rare in Pycnodysostosis. It is also an autosomal dominant disease

In history of frequent fractures and finding fragile bones, we can think of osteogenesis imperfecta, if there is presence of blue sclerae and choanal atresia. Diagnosis is primarily on clinical and radiological features. Confirmatory test is gene analysis of CTSK, which is gold standard.

There is no specific treatment. It is a multidisciplinary approach to provide supportive treatment. It includes dental hygiene and regular dental checkups. Minimizing the chances for a fracture to occur. Providing hearing aid to correct any hearing loss.

There should be gene screening in families with history of Pycnodysostosis.

CONCLUSION

This patient's diagnosis could have been missed if complete and detailed examination including examination of skull for sutures and fontanel was note done. Therefore, complete examination with

open mind for rare disorders must be performed on every child. Advice about dental hygiene and dental checkups and risk for fractures must be highlighted to the patients and their caretakers.

Consent: Verbal and written consent about publication has been given by the patient's parents.

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Address for Correspondence:

Farida Aziz, Frontier Medical College, Abbottabad-Pakistan
Email: fazizabd@gmail.com