Imperial Journal of Interdisciplinary Research (IJIR)
Vol-2, Issue-9, 2016
ISSN: 2454-1362, http://www.onlinejournal.in

Adult Pycnodysostosis With Unusual Presentation

Dr. Neela J. Sinduja[1], Dr. K. Kanakaraj[2] & Dr. Ramachandra Prasad[3]
Sree Balaji Medical College, India

Abstract: *Pycnodysostosis is one of the rare groups of congenital osteosclerotic skeletal dysplasias. It is an autosomal recessive disorder that manifests as generalized osteosclerosis of the skeleton as a result of decreased osteoclastic activity . Patients classically present with short stature, fractures, large head with frontal and parietal bossing, open anterior fontanelle and cranial sutures, obtuse mandibular angle, prominent eyes with bluish sclera , underdeveloped facial bones, dental anomalies, short ,broad hands and feet with dystrophic nails and trunk deformities such as kyphosis or scoliosis. However bilateral basal ganglia has not yet been reported in patients with pycnodysostosis. Here we describe the hitherto unreported association of basal ganglia calcification with pycnodysostosis in two siblings in a family and describe the radiological features of pycnodysostosis and its differentials.*

1. Introduction

Pycnodysostosis is a rare genetic osteosclerotic disorder first described by Maroteaux and Lamy in 1962. The disease has also been named Toulouse-Lautrec syndrome, after the French artist Henri de Toulouse-Lautrec, who (it has been surmised) suffered from the disease. It is an autosomal recessive osteochondrodysplasia. Pycnodysostosis is a lysosomal storage disease of the bone caused by a mutation in the gene that codes the enzyme cathepsin K, usually diagnosed at an early age with incidence estimated to be 1.7 per 1 million births. Pycnodysostosis has a number of characteristic radiographic signs that differentiate it from other osteosclerotic conditions. Recognition of these radiological signs is important though the lysosomal enzyme is identified in order to make the diagnosis and prevent possible complications.

2. Case Report

We present two cases who presented clinical and radio-graphic characteristic typical of Pycnodysostosis.

3.1. CASE 1

23 years male came with complaints of nasal block and discharge on and off for several months. On general physical examination, demonstrated short stature, frontal and parietal bossing, depressed nasal bridge, beaked nose, hypoplastic midface, malocclusion of dentition and wrinkled skin over the finger tips. H / O tibial fracture (Figure 1C) 10 years back managed conservatively and again fractures were preceded by only trivial traumatic events and had been surgically managed with open reduction and internal fixation. Dental examination (Figure 1 B) revealed a narrow palate, crooked teeth with overcrowding. X-rays . Skull (Figure 2 A) showed widely separated cranial sutures and widely open anterior and posterior fontanelle. The paranasal sinuses were hypoplastic with angle of the mandible being obtuse. Acro-osteolysis was also increased in one density and incomplete fracture of the mid-shaft of the left tibia with callous formation. Skiagrams of the hands (Figure 2 D) showed trident aplastic terminal phalanges in keeping with acro-osteolysis. CT brain (Figure 2 B) showed widened sutures and both fontanelles and normal cortical grey and white matter differentiation. Bilateral dense basal ganglia calcification was the only intra-cranial positive finding peculiar to sclerotic skeletal dysplasias.

The patient has a sibling having similar features.CT PNS showed obtuse angle of the mandible and hypoplasia of sinuses (Figure 2 C).

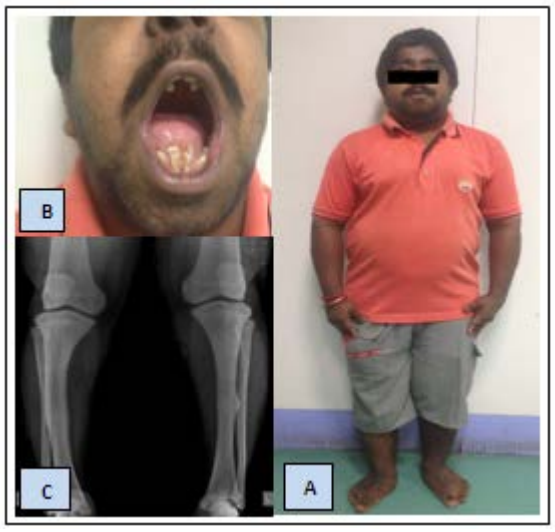

Figure 1(A-C)

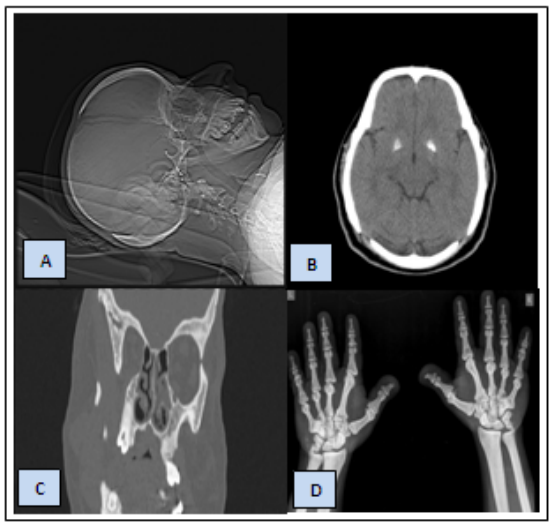

Figure 2(A-D)

3. 2. CASE 2

A 30 year old female (member of the same family) sustained a fall back at home, following which she was brought to the hospital. She was diagnosed with fracture of the right femur (Figure 3 D)and was surgically managed with open reduction and internal fixation. The patient has now come for follow-up and if possible, removal of the plate and screws.

This patient is the elder sister of the patient discussed under case 1, and during general physical examination, she exhibited features similar to her sibling. Consequently x-rays were taken which showed similar findings too, as in the skull (Figure 3 B)showing widely separated cranial sutures and widely open anterior and posterior fontanelle, the paranasal sinuses being hypoplastic with an obtuse mandibular angle, acro-osteolysis and the hands showing trident aplastic terminal phalanges. Similarly CT brain showed widening of the sutures and both the fontanelles with bilateral dense basal ganglia calcification.

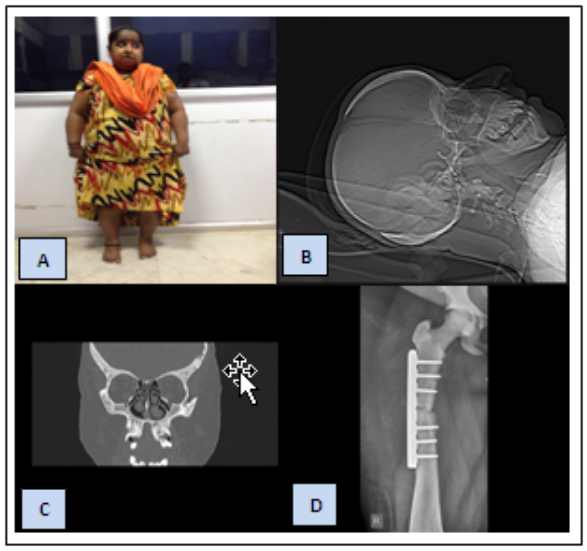

Figure 3 (A-D)

An association of the clinical and radiographic data suggested pycnodysostosis as the most likely diagnosis.The written informed consent of patients has been obtained for their photograph publication

3. 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 remodeling, is vital for normal bone maintenance. The bones in individuals afflicted with Pycnodysostosis are abnormally dense and brittle as a result of this insufficient re-absorption process [1] with the persistance of cartilaginous matrix.

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 [2]. 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 remodeling [3].

Various bone diseases should be considered in the differential diagnosis of Pycnodysostosis. In cleidocranial dysostosis open fontanels 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 [5].

Ribbing's disease is a rare form of sclerosing dysplasia characterized by painful but benign overgrowth of both endosteal and periosteal bone in the dysphyses of the long bone. Onset is usually after puberty.

In Vonbucem disease rare hereditary sclerosing bone dysplasia. This is characterised most notably by mandibular enlargement and thickening of the skull

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 choanal 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 sclera , 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.

Radiological findings may show some degree of widening of the distal femur. The skull shows open anterior frontanelle and sutures with small facial bones, non-pneumatised paranasal sinuses and flattened mandibular angle [6,7]. Terminal phalanges in the hand are partially or totally aplastic with loss of ungula 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.

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 [8,9].

There is no specific treatment as on 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 not requiring too much impact. Dental hygiene and regular dental checkups are especially helpful for affected individuals due to various dental anomalies [10].

3. Conclusion

Bilateral symmetrical basal ganglia calcification could be a new associated feature in pycnodysostosis as its not due to metabolic cause since patient had normal PTH level and serum calcium.

4. Reference

1. Elmore SM: Pycnodysostosis: a review.J Bone Joint Surg [Am]1967,49:153-161.

2. Motyckova G, Fisher DE:Pycnodysostosis: Role and Regulation of Cathepsin K in Osteoclast Function and Human Disease.Curr Mol Med 2002,2:407-421.

3. Chavassieux P, Seeman E, Delmas PD:Insights into material and structural basis of bone fragility from diseases associated with fractures: how determinants of the bio-mechanical properties of bone are compromised by disease.Endocrine Rev2007,28:151-164.

4. ormans J and Flynn J:Pathological Fractures associated withTumours and Unique Conditions of Musculoskeleteal Sys-tem.InRockwood and Wilkin's Fractures in Children 6th edition. Edited by Beaty JH, Kasser JR. Philadelphia: Lippincott Williams & Wilkins;2005:195

5. ratzl-Zelman N, Valenta A, Roschger P, Nader A, Gelb BD, Fratzl P,Klaushofer K:Decreased bone turnover and deterioration of bone structure in two cases of pycnodysostosis.J Clin EndocrinolMetab2004,89:1538-1547

6. Maroteaux P, Lamy M:Pyknodysostosis.Presse Med1962,70:999-1002.

7. olpowitz A, Matisonn AA comparative study of pycnodysostosis, cleidocranial dysostosis, osteopetrosis and acro-osteolysis.S Afr Med J1974,48:1011-1018.

8. onnarumma M, Regis S, Tappino B, Rosano C, Assereto S,Corsolini F, Di Rocco M, Filocamo M:Molecular analysis and characterization of nine novel CTSK mutations in twelve patients affected by pycnodysostosis Mutation in brief #961.Online. Hum Mutat2007,28:524

9. ujita Y, Nakata K, Yasui N, Matsui Y, Kataoka E, Hiroshima K,Shiba RI, Ochi T:Novel mutations of the cathepsin K gene inpatients with pycnodysostosis and their characterization.J Clin Endocrinol Metab 2000,85:425-431.

10. Hide and Seek Foundation for Lysosomal Disease.[http://www.hideandseek.org/index.php?option=com_content&task=view&id=158