Case Report

Toulouse Lautrec syndrome: Report of a rare clinical entity

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ABSTRACT

Pycnodysostosis, first described by Maroteaux and Lamy in the year 1962, is a rare autosomal recessive disorder. It is a lysosomal storage disease of the bone attributed to the mutation of the gene that is responsible for encoding the enzyme cathepsin K, thereby inhibiting the normal osteoclastic function, making the bones abnormally dense and brittle. We report a case of 30-year-old female herewith, who presented with characteristic features such as short stature, acro-osteolysis, open fontanelles, generalized osteosclerosis, and oral manifestations including grooved palate, malpositioned teeth with increased incidence of dental caries. There is an increased risk of mandibular fractures and osteomyelitis following invasive dental treatments. Thus, early diagnosis helps clinicians to manage patients with minimally invasive procedures preventing complications.

Key words: Acro-osteolysis, Cathepsin K, Grooved palate, Obtuse gonial angle, Osteosclerosis

Pycnodysostosis, a rare autosomal recessive sclerosing skeletal dysplasia, was first reported by Montanari in 1923 as atypical achondroplasia [1]. Later, Maroteaux and Lamy in 1962 coined the present term and defined the characteristics of this disorder. It is also called Toulouse Lautrec syndrome, named after the French artist Henri de Toulouse Lautrec, who was affected by this condition [2]. The incidence is estimated to be about 1.7 in 1 million births with equal sex distribution and parental consanguinity in 30% of cases [3]. The word “Pycnodysostosis” is derived from the Greek terminologies (pycnos- dens, dys- defective, exostosis- bone). The defect in the gene located in chromosome 1q21 which encodes for the enzyme Cathepsin K, inhibits normal osteoclastic function causing the bone more dense and brittle [4]. This generalized osteosclerosis is characterized by the thickening of cortices of the long bones, without obliteration of medullary canals. The features include short stature, frontal bossing, proptosis, beaked nose, hypoplastic nails, shortened terminal phalanges, delayed closure of cranial sutures, unossified fontanelles, hypoplastic paranasal sinuses, increased bone density, and fragility. Features such as maxillary hypoplasia, obtuse mandibular gonial angle, grooved palate, malpositioned teeth with increased incidence of dental caries, and compromised periodontal health are often noted. However, lifespan, intellectual ability, and sexual development are normal in affected individuals [5].

The rationale for reporting this case is because of its rarity. Awareness of the key manifestations of this condition facilitates early diagnosis, differentiation from other syndromes, and appropriate treatment planning to prevent complications.

CASE REPORT

A 30-year-old female patient reported a chief complaint of multiple decayed teeth in the upper and lower front tooth region. Her medical history was insignificant with no history of parental consanguinity.

On general examination, the patient was short-statured (Fig. 1a), with a height of 132 cm and weight of 46 kg (BMI - 26.4 kg/m²). Dysmorphic features such as frontal bossing, hypoplastic midface, and depressed nasal bridge were noted (Fig. 1b). The digits were short, broad, and stubby with cutaneous wrinkles and dysplastic nails (Fig. 2a); the toes showed sandal gap deformity (Fig. 2b). Intraoral examination revealed a narrow grooved palate, microdontia, and malpositioned teeth with dental caries in 22, 23, 32, 33, and 34 (Fig. 3). Based on the above findings, a provisional diagnosis of Pycnodysostosis was made. Achondroplasia, Osteopetrosis, Chondroectodermal dysplasia, and Cleidocranial dysostosis were considered in the differential diagnosis.

The patient was subjected to a whole-body skeletal survey which revealed diffuse osteosclerosis with increased bone density. Skull radiographs demonstrated significant suture diastasis with patent fontanelles, wormian bones, and hypoplastic paranasal
sinuses (Fig. 4); Hand-wrist radiograph showed acro-osteolysis of terminal phalanges (Fig. 5a); Long bones showed diffuse osteosclerosis but the medullary cavity is spared (Fig. 5b). Panoramic imaging revealed an obtuse gonial angle, narrowing of the inferior alveolar nerve canal, and elongated condyles (Fig. 6). Blood investigations were normal, including serum calcium, magnesium, and phosphate. No elevation of serum alkaline phosphatase level was found.

Thus, based on the clinical and radiological findings, a final diagnosis of Pycnodysostosis was made. The patient was advised to undergo restoration of decayed teeth and to have regular dental follow-ups.

DISCUSSION

Pycnodysostosis, also known as osteopetrosis acro-osteolytica, is a rare autosomal recessive condition causing systemic osteosclerosis due to decreased bone turnover [4]. It is recognized
at any age from infancy to adulthood, often through incidental radiographic features.

Cathepsin K encodes a lysosomal cysteine protease enzyme which is predominantly found in osteoclasts aiding in their normal functioning by degrading Type 1 collagen. Any genetic defect to this enzyme, as in Pycnodysostosis, impairs the osteoclastic remodeling of the bone making them dense and brittle, and highly susceptible to fractures.

The clinical features would include short stature, larger head with frontal and parietal bossing, prominent eyes with a bluish sclera, underdeveloped facial bones, short and broad extremities with dystrophic nails along with trunk deformities including kyphosis, scoliosis, lumbar lordosis, narrow chest with difficulty in breathing, sleep apnea, and increased susceptibility to fractures [6]. The increased bone density of sella turcica compresses the pituitary gland, causing hypoplasia and deficient production of growth hormone, resulting in short stature [7].

Dental anomalies such as malpositioned teeth, narrow and grooved palate, retained deciduous dentition, delayed eruption of permanent dentition, anterior cross-bite, lateral open-bite, hypodontia, abnormal tooth morphology, multiple carious, and impacted supernumerary teeth with poor oral hygiene are often encountered.

Radiographic investigations would reveal unossified fontanelles, obtuse mandibular angle, hypercementosis of teeth, accentuated sigmoid notch, non-pneumatized paranasal sinuses, acro-osteolysis with sclerosis of the terminal phalanges, osteosclerosis with narrowed medullary cavities, aplasia of acromial ends of clavicle, increased opacity of base of skull, long bones, and spine with hypoplasia of facial bones [8]. Other abnormalities include failure of complete segmentation of the atlas and axis with abnormal radioulnar articulation [9]. Sparing of the medullary cavity within the long bones is characteristic of this disorder, resulting in normal hematopoietic function [5].

Pycnodysostosis has to be differentiated from Achondroplasia, Osteopetrosis, Chondroectodermal dysplasia, and Cleidocranial dysostosis. Achondroplasia is due to the mutation in the FGFR3 gene leading to impaired endochondral ossification, often presenting with features like short stature, macrocephaly, frontal bossing, midfacial hypoplasia, relative mandibular prognathism, flat nasal bridge, Trident hand configuration, and bowing of legs. However, features such as a grooved palate, obtuse mandibular gonial angle, and acro-osteolysis of terminal phalanges are absent. Osteopetrosis, also known as marble bone disease or Albergs-Schonberg disease, is due to the impaired osteoclastic function resulting in marked increased density of bone causing diffuse osteosclerosis. Dense skull bones cause frontal bossing and narrowing of cranial nerve foramina causing compression effects on the nerves leading to nerve palsy, deafness, and visual disturbances. Obliteration of medullary canals in long bones causes impaired bone marrow function leading to anemia [10]. However, there will be normal cranial sutures and gonial angle with elevation in serum alkaline phosphatase level. Chondroectodermal dysplasia or Ellis-van Creveld syndrome is due to the mutation in the EVC gene located in chromosome 4. It often presents with disproportionate dwarfism, bilateral postaxial polydactyly of the hands, congenital cardiac malformations, sparse hair, dystrophic nails, hypodontia, malformed teeth, and labiogingival adhesions. In Cleidocranial dysostosis, the mutation in chromosome 6p21 affects intramembranous ossification resulting in features like frontal and parietal bossing with metopic depression, open fontanelles and skull sutures, presence of multiple wormian bones, and multiple supernumerary teeth. However, unlike pycnodysostosis, the affected individual presents with normal stature and bone texture.

Although the diagnosis is purely based on clinical and radiological findings, CTSK gene mutation analysis is confirmatory [2]. The management is mainly supportive, also aiming at the primary prevention of fractures [4]. The complications in patients with pycnodysostosis would include multiple fractures, respiratory insufficiency due to a decrease in upper airway space and osteomyelitis of the jaw due to defective osteoclastic activity with a resultant increase in bone formation that gradually jeopardizes the vascular supply by eliminating the medullary spaces. This disorder is often diagnosed at a younger age by the typical dysmorphic facies. However, in some cases, the condition is diagnosed later as a result of complications such as fractures or osteomyelitis following tooth extractions.

As bone fractures are a primary concern in those affected by pycnodysostosis, any therapeutic approach should be as atraumatic as possible following proper asepsis. Maintaining good oral hygiene with regular dental follow-ups is helpful for the affected individuals.

**CONCLUSION**

Despite various advanced diagnostic innovations, the diagnosis of pycnodysostosis continues to be based on clinical and radiographic features. The importance of early recognition of this condition allows an atraumatic treatment approach to reduce the complications, thereby ensuring a better quality of life for the patient.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Najmutheen BB, Manoharan MG, Karthikeyan B. Toulouse Lautrec syndrome: Report of a rare clinical entity. Indian J Case Reports. 2023; July 29 [Epub ahead of print].