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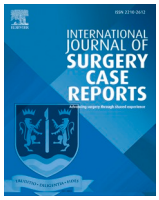

Case report

Pyknodysostosis: A case report of an 8-year-old male with a rare genetic disorder

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ABSTRACT

Introduction and importance: Pyknodysostosis is a rare genetic disorder characterized by skeletal and craniofacial abnormalities. It is an autosomal recessive disorder caused by mutations in the gene encoding cathepsin K. Pyknodysostosis is associated with short stature, brittle bones, and distinctive facial features.

Case presentation: This case report presents the clinical manifestations, diagnostic challenges, and management strategies of an 8-year-old male with pyknodysostosis, an extremely rare genetic disorder characterized by skeletal and craniofacial abnormalities. The patient's clinical presentation, radiographic findings, genetic testing results, and treatment approach are discussed. Additionally, the importance of genetic counseling and multidisciplinary care in managing this condition is emphasized.

Clinical discussion: A multidisciplinary approach involving orthopedics, genetics, dentistry, and psychological support is crucial for managing patients with pyknodysostosis. Regular follow-up visits, careful monitoring of fractures, and appropriate interventions can improve the patient's quality of life and reduce complications.

Conclusion: The importance of early recognition, genetic testing, and multidisciplinary care is emphasized for effective treatment and support. Further research is needed to enhance our understanding of this rare genetic disorder and develop targeted therapies.

1. Introduction

Pycnodysostosis, also known as Toulouse-Lautrec Syndrome, is an exceedingly rare genetic disorder characterized by a range of skeletal abnormalities and potential associated complications [1]. First described by Maroteaux and Lamy in 1962, this autosomal recessive disorder is caused by mutations in the gene encoding cathepsin K, a lysosomal cysteine protease. The resulting dysfunctional cathepsin K impairs the normal remodeling and resorption of bone, leading to the progressive thickening of the skeletal tissue [2].

Clinically, individuals affected by pycnodysostosis present with a distinct set of physical features, including short stature, abnormally shaped skull, delayed closure of fontanelles, a prominent forehead, and an underdeveloped mid-face with a beaked nose [3]. Moreover, these individuals may have dental anomalies, such as delayed eruption and retention of primary teeth, hypoplastic enamel, and increased susceptibility to caries. Additionally, their bones are particularly fragile and prone to fractures, partly due to reduced mineralization and increased bone density [4].

Beyond the characteristic physical manifestations, individuals with pycnodysostosis commonly experience a range of functional impairments. These often include a restricted range of joint mobility, skeletal deformities such as genu valgum (knock-knees) and genu varum (bow-legs), and abnormal curvature of the spine [5]. These issues can significantly impact the quality of life of affected individuals, as they may face challenges in mobility, physical activity, and general self-care [6].

Due to its rarity, pycnodysostosis remains a relatively understudied condition, with limited understanding of its pathophysiology, natural history, and optimal management strategies. This academic introduction aims to provide an overview of pycnodysostosis, an uncommon genetic

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disorder characterized by skeletal abnormalities and associated complications. Through further research and investigation, a deeper understanding of the underlying molecular mechanisms and effective interventions can contribute to improved management and support for individuals living with this challenging condition. The work has been reported in line with the SCARE 2020 Criteria [7].

2. Presentation of case

An 8-year-old male from a Kurdish community in a rural village presented with concerns of delayed growth which failed to reach normal height milestones, recurrent fractures, and distinct facial features. He had a small, rounded skull (microcephaly), a small and underdeveloped midface, delayed closure of the fontanelles, and a prominent forehead. Dental manifestations was another symptom, represented overcrowding of teeth, multiple missing or malformed teeth, and a high arched palate. Due to the remoteness of the village and limited resources, the family had limited access to healthcare services. The family sought medical assistance after witnessing multiple fractures and noticeable bone deformities in the child.

Clinical examination revealed short stature (height: <3rd percentile for age and gender), craniofacial dysmorphism including a small nose, and dental abnormalities with delayed tooth eruption (Fig. 1). The musculoskeletal examination demonstrated stubby fingers (Fig. 2), shortened metacarpals and phalanges, and restricted joint movements (Fig. 1).

2.1. Diagnostic assessment

In the village where healthcare resources were limited, a visiting healthcare team took on the responsibility of conducting the initial diagnostic assessments. Despite the limitations, the team had access to basic imaging facilities, which proved to be invaluable in the diagnostic process. Using these facilities, the clinician was able to perform X-rays on the patient. The X-rays revealed significant findings that provided crucial insights into the patient's condition. Specifically, the radiographs displayed widened metaphyses, which is a characteristic feature associated with an Erlenmeyer flask deformity. This deformity is a distinct abnormality in the shape of the long bones, resembling the shape of a flask. Additionally, the X-rays showed that the clavicles, which are the collarbones, were hypoplastic, meaning they were underdeveloped, and exhibited incomplete ossification, indicating that the process of bone formation was not fully completed.

Fig. 1. Stubby fingers.

Further investigations were conducted using cranial imaging techniques. The results of the cranial imaging revealed two important findings. Firstly, there was evidence of skull thickening, indicating an abnormal increase in the thickness of the skull bones. Secondly, a widened diploic space was observed. The diploic space refers to the spongy layer of bone found between the inner and outer layers of the skull. The widening of this space can be indicative of certain pathological conditions.

To confirm the diagnosis and gain a deeper understanding of the underlying cause, the healthcare team decided to proceed with genetic testing. Blood samples were collected from the patient and carefully transported to a nearby laboratory that possessed the necessary capabilities to perform genetic analysis.

After a waiting period of several weeks, the results of the genetic testing finally arrived. The findings from the analysis confirmed the presence of a homozygous mutation in the cathepsin K (CTSK) gene. This specific gene mutation played a crucial role in establishing the diagnosis of pyknodysostosis, a rare genetic disorder characterized by abnormal bone development and skeletal abnormalities.

The detailed sequence of diagnostic tests, including initial assessments, X-rays, cranial imaging, and genetic testing, along with the subsequent confirmation of a homozygous mutation in the CTSK gene, provided the healthcare team with a comprehensive understanding of the patient's condition, ultimately leading to the diagnosis of pyknodysostosis.

2.2. Management and outcome

Given the limited access to specialized healthcare services, management strategies were adapted to the available resources. The healthcare team educated the family on fracture prevention techniques and provided splints to minimize the risk of further fractures. Rehabilitation exercises and physical therapy sessions were demonstrated to improve joint mobility and muscle strength.

Local oral health workers were engaged to provide basic dental care, emphasizing the importance of oral hygiene and referring the patient to a nearby dental clinic for proper evaluation and treatment of dental abnormalities.

Additionally, the healthcare team organized group sessions to educate the community, emphasizing the genetic nature of the disorder, and fostering a supportive environment for affected families. The visiting clinicians collaborated with local healthcare workers to establish regular follow-up visits to monitor the patient's progress and address any emerging concerns.

3. Discussion

Pyknodysostosis is an extremely rare genetic disorder characterized by a variety of skeletal abnormalities and potential associated complications. Affected individuals exhibit a unique set of physical characteristics, including short stature, an atypical skull shape, delayed closure of fontanelles, a prominent forehead, and an underdeveloped mid-face with a beaked nose [8]. Dental anomalies are also frequently observed, such as delayed eruption and retention of primary teeth, hypoplastic enamel, and an increased susceptibility to caries. Moreover, individuals with pyknodysostosis have bones that are particularly fragile and prone to fractures, which can be attributed, in part, to reduced

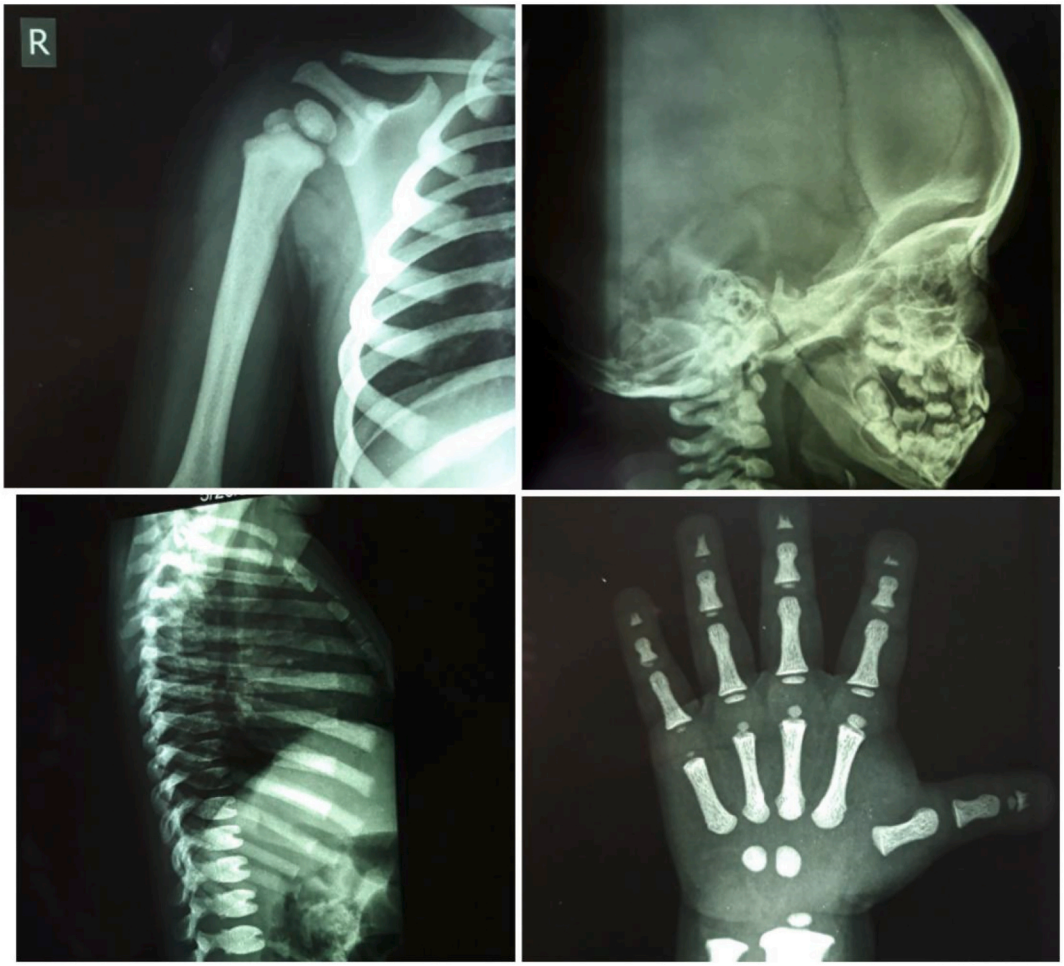

Fig. 2. Radiography manifestations in different views.

mineralization and increased bone density. Additional skeletal deformities, including genu valgum and genu varum, as well as abnormal spinal curvature, further contribute to functional impairments [9].

Pyknodysostosis is caused by mutations in the CTSK gene, which encodes for cathepsin K, a lysosomal enzyme responsible for bone remodeling [10]. The loss of function mutations in CTSK lead to impaired bone resorption, resulting in increased bone density and reduced skeletal growth. Clinical features of pyknodysostosis include short stature, craniofacial abnormalities, dental anomalies, acroosteolysis, and susceptibility to fractures [11].

The rarity of pycnodysostosis poses significant challenges for diagnosis, as limited awareness among healthcare professionals often results in delayed or missed diagnoses. Clinical evaluation, radiographic findings, and genetic testing are key components of the diagnostic process [12]. Genetic analysis plays a crucial role in confirming the diagnosis by identifying pathogenic mutations in the cathepsin K gene. Genetic counseling is an essential aspect of diagnostic evaluation, enabling affected individuals and their families to understand inheritance patterns and make informed reproductive decisions [13].

Given the complex nature of pycnodysostosis and its wide-ranging effects on various systems, a multidisciplinary approach is imperative for the comprehensive management of affected individuals. Orthopedic interventions are crucial in addressing the increased susceptibility to fractures, skeletal deformities, and limitations in joint mobility that are commonly observed in individuals with pycnodysostosis. These interventions may include the use of orthopedic devices, such as braces or splints, to provide support and stability to fragile bones [14].

Dental care plays a critical role in managing the oral health issues associated with pycnodysostosis and promoting proper tooth development. Dentists specializing in the treatment of individuals with rare genetic disorders are well-equipped to address the unique dental anomalies exhibited by individuals with pycnodysostosis. They may employ strategies such as early orthodontic interventions, regular dental check-ups, and preventive measures to manage dental caries and malocclusion effectively [14].

Physiotherapy and rehabilitation programs are invaluable components of the management plan for individuals with pycnodysostosis. These programs aim to improve mobility, joint function, and overall quality of life by implementing targeted exercises, stretching routines, and assistive devices. Physical therapists work closely with affected individuals to develop personalized rehabilitation plans that address their specific needs and limitations [15].

Managing fractures and complications in pycnodysostosis requires a multidisciplinary approach. Conservative measures such as splinting and casting are used to immobilize and protect fractures, while surgical intervention may be necessary for severe cases. Dental care, regular monitoring of bone density, and comprehensive medical management are also crucial. A multidisciplinary team collaborates to provide appropriate interventions and support, aiming to improve the overall well-being and quality of life for individuals with rare disease [16].

Genetic counseling remains an integral part of the management of pycnodysostosis. Genetic counselors play a vital role in assisting families in understanding the genetic implications of the disorder, including inheritance patterns and potential risks of recurrence. They provide emotional support and help families navigate through the challenges associated with living with a rare genetic disorder. Genetic counseling

also facilitates informed decision-making regarding family planning options and prenatal testing [17–19].

The global worry surrounding the novel coronavirus stems from its sudden appearance, unfamiliarity, and high fatality rate [20–24]. Given this scenario, medical professionals bear the primary responsibility of devising coping mechanisms to deal with these challenging circumstances [25–27]. Nurses play a crucial and significant part in enhancing both the mental and physical well-being of patients, thereby alleviating their anxiety and distress [28,29].

4. Conclusion

Pycnodysostosis is a rare genetic disorder with skeletal abnormalities and associated complications. Clinicians can suspect it based on clinical features like short stature, skeletal deformities, dental anomalies, and recurrent fractures. A definitive diagnosis requires radiographic evaluation and genetic testing. Ongoing research is crucial for understanding the molecular mechanisms and improving clinical management to enhance the quality of life for those affected.

Consent

Written informed consent was obtained from the parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

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Author contribution

Rasoul Goli, Amireh Hassanpour and Navid Faraji: Study concept, data collection, writing the paper and making the revision of the manuscript following the reviewer's instructions. Fatemeh Nikkhah and Fatemeh Imanzadeh: Study concept, reviewing and validating the manuscript's credibility.

Guarantor

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Research registration number

1. Name of the registry: not applicable
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Conflict of interest statement

None.

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