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Case Reports

Atypical presentation of the Azerbaijani infant with pycnodysostosis: A case report with a de novo mutation

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ABSTRACT

Pycnodysostosis is a rare, autosomal recessive illness that is generally pathognomonic. It is characterized by the postnatal onset of short limbs, small stature, and global hyperostosis, as well as acro-osteolysis with sclerosis of the terminal phalanges. It has been shown that approximately 30% of patients have parental consanguinity. This condition is brought on by a mutation in the cathepsin K (CTSK) gene. To date, 34 distinct CTSK mutations have been found in patients. This lysosomal enzyme helps break down bone matrix proteins, including some forms of collagen, and is mostly present in osteoclasts. Between 90 and 95 percent of all organic bone matrix is made up of type 1 collagen, which is still uncleaved. Unusual bone and dental development results from the accumulation of undigested collagen fibrils by these patients' fibroblasts. Pycnodysostosis is a clinical characteristic that only occurs when cathepsin K is completely lost. About 10% of patients are found to have mental impairment. We present an infant with pycnodysostosis, undiagnosed before presentation at birth.

Keywords: Cathepsin K, infant, pycnodysostosis

INTRODUCTION

Pycnodysostosis is a rare, autosomal recessive illness that is generally pathognomonic. It is characterized by the postnatal onset of short limbs, small stature, and global hyperostosis, as well as acro-osteolysis with sclerosis of the terminal phalanges. It has been shown that approximately 30% of patients have parental consanguinity. This condition is brought on by a mutation in the cathepsin K (CTSK) gene (1). To date, 34 distinct CTSK mutations have been found in patients. This lysosomal enzyme helps break down bone matrix proteins, including some forms of collagen, and is mostly present in osteoclasts. Between 90 and 95 percent of all organic bone matrix is made up of type 1 collagen, which is still uncleaved. Unusual bone and dental development results from the accumulation of undigested collagen fibrils by these patients' fibroblasts. Pycnodysostosis is a clinical characteristic that only occurs when cathepsin K is completely lost. About 10% of patients are found to have mental impairment (2). We present an infant with pycnodysostosis, undiagnosed before presentation at birth.

CASE REPORTS

A 40-day-old boy was presented to the clinic with concerns regarding inadequate weight gain, respiratory difficulty, and chest deformity. The infant was born at 38 weeks of gestation via cesarean section, following a consanguineous marriage, due to premature rupture of membranes. At birth, the infant's APGAR scores were 7/8 at the 1st and 5th minutes, with a weight of 3070 g, a length of 53 cm, and a head circumference of 35 cm. Immediately after birth, the child exhibited signs of respiratory distress, including chest retraction, tachypnea, and nasal flaring, necessitating intubation due to the severity of the condition. The infant underwent mechanical ventilation for the first 24 hours of life and received a 10-day course of treatment for early-onset gram-negative bacteremia. Neurosonography revealed a grade 2 intraventricular hemorrhage. The infant was discharged home in stable condition on day 10 of life. Upon examination, the child was found to be underweight (3150 gr/5th percentile), exhibited craniofacial abnormalities and snoring. Additional findings included short stature, frontal and parietal bossing, beaked nose, hypoplastic midface,

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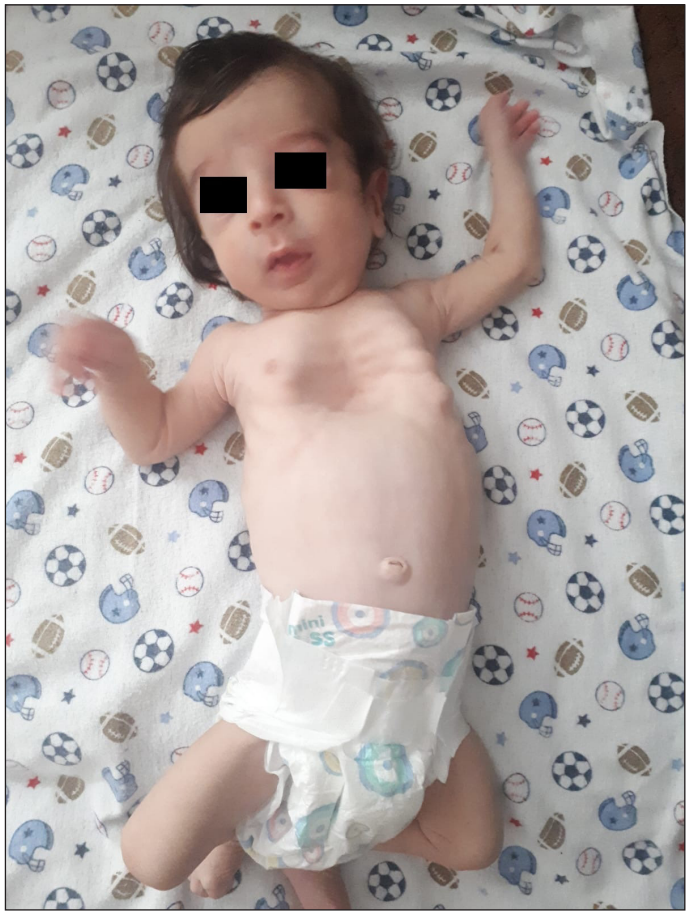

Figure 1: The patient's physical appearance

micrognathia, brachydactyly with broad thumbs and spoon-shaped fingernails, wrinkled skin over the fingertips and chest deformities in the form of pectus excavatum (Figure 1). Laboratory results indicated HGB-9.7 g/dL, Ca-9.74 mg/dL, P-6.08 mg/dL, and ALP-201 IU/L. The child was referred to pediatric surgery, cardiology, neurology, and genetics due to the presence of dysmorphic facial features. The pediatric surgeon applied vacuum bell therapy, a nonoperative management of pectus excavatum, which led to an improvement in respiratory symptoms. During the neurological examination, the child presented with glossoptosis and micrognathia, suspected Pierre-Robin syndrome, and further diagnostic evaluation was recommended. EEG, neurosonography, echocardiography, abdominal USG, hip joint USG, and metabolic screening test results were all normal. Whole exome sequencing showed that the patient was homozygous for a pathogenic variant in the CTSK gene NM_000396.4 mutation c.830C>T /p. Ala277Val / rs74315304R associated with pycnodysostosis.

DISCUSSION

Pycnodysostosis is a systemic skeletal disorder. Disproportionately small stature, a large cranium, fronto-occipital prominence, proptosis, bluish sclerae, a beaked and pointed nose, a small face and chin, an obtuse mandibular angle, a high-arched palate, and dental malocclusion with primary tooth retention are all characteristics that are seen during infancy and early childhood (3). Cranial sutures remain open. Fingers are short and clubbed from acro-osteolysis or aplasia of the terminal phalanges, and the hands are small and square. Repeated fractures cause knock-knee deformity. Craniosynostosis, low-energy fractures, chronic pain, respiratory problems, and dental complications may cause significant morbidity and reduce quality of life (4).

A review of the literature revealed p.Ala277Val the mutation in our patient had previously been found in a 31-year-old woman with thyroid cancer and in a 1-year-7-month-old girl of Arab origin (5,6). Structural anomalies, including mandibular hypoplasia and a small and narrow palate that contributed to narrowing the airway, were found to be similar to the findings in our patient. Growth and developmental delays were noted, similar to this patient. However, unlike our patient, no fractures developed. We emphasize the importance of early recognition, genetic testing, and multidisciplinary care for effective treatment and support. The most reliable method for diagnosing pycnodysostosis is the detection of mutations in the CTSK gene. Genetic testing for early identification of pycnodysostosis can result in more immediate treatment and therapy (7). Clinicians can monitor patients for complications like fractures, scoliosis, and joint abnormalities and take preventive actions to reduce these risks by knowing the hereditary etiology. Diagnosis of pycnodysostosis is based on the clinical presentation, and medical treatment for the condition is symptomatic. The differential diagnoses of pycnodysostosis include osteopetrosis, acroosteolysis, mandibuloacral dysplasia, cleidocranial dysplasia, and osteogenesis imperfecta. There are no standardized treatment protocols or guidelines for affected individuals (8). Upon reviewing the literature, our case is the earliest diagnosed infant.

Contribution of the authors

Study conception and design: TI, SE; data collection: TI, SE; analysis and interpretation of results: TI, SE; draft manuscript preparation: TI, SE. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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