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Case Report

Kniest dysplasia in girl aged 4 years: a case report

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Kniest dysplasia is a rare chondrodysplasia characterized by distinct musculoskeletal and craniofacial abnormalities. Additional features like hearing loss and some ocular abnormalities can also be present. We report a case of Kniest dysplasia from eastern India with a rare mutation confirmed by genetic testing. A 4-year-old girl presented with skeletal deformities with normal intelligence. On examination, she had dysmorphism, short stature, barrel-shaped chest, scoliosis, short limbs with enlarged joints, and dental problems. The skeletal survey showed platyspondyly, epiphyseal enlargement, and a hypoplastic femoral head with cloud-like calcification. Clinical suspicion of Kniest dysplasia was kept based on characteristic skeletal abnormalities and radiological findings. The diagnosis was confirmed by genetic analysis, which revealed a mutation in the COL2A1 gene (c.905C>T) on chromosome 12 exon 14. **[Paediatr Indones. 2024;64:559-62; DOI: https://doi.org/10.14238/pi64.3.2024.559-62**].

Keywords: *Kniest dysplasia; short limbs; epiphyseal enlargement*

Kniest syndrome was first described by Wilhelm Kniest in the year 19521. Kniest syndrome is a rare autosomal dominant disorder resulting from the dysfunction of collagen II, encoded by the COL2A1 gene mapped on chromosome 12q13.112. Type II collagen is mostly present in cartilage and vitreous tissues, and its abnormalities result in skeletal dysplasia and retinal detachment. Differential diagnoses are spondyloepiphyseal dysplasia, Morquio's disease, and metatropic dysplasias.[1]

The case

Our patient is a 4-year-old girl who presented with complaints of difficulty in walking noted after ten months of age, followed by painful restriction of movements with enlargement of knee and elbow joints. The child was born out of non-consanguineous marriage with a birth weight of 2.6 kg, delivered by vaginal delivery. There is no history of stunting or skeletal deformities on either of the parental sides. Intelligence and cognitive milestones were normal, but there was a speech delay. She could stand with support by the age of ten months and moved support of hands and trunk support by one year. She had no corneal opacity or cataract, and vision was normal. She had moderate hearing loss and speech delay, but intelligence was normal.

On examination, there was a disproportionate short stature with normal head circumference. There were flat facies, depressed nasal bridge, hypertelorism,

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small jaw, dental anomalies, scoliosis, enlarged elbows and knee joints, painful restriction of movement around the hip and knee, and flexion contractures in the elbow joints (**Figure 1**). Neurological examination was normal. There was no hepatosplenomegaly or corneal clouding. Skeletal survey showed irregular platyspondyly, hypoplastic femoral head, epiphyseal enlargement, and cloud-like calcification.

Genetic testing revealed presence of a single nucleotide variant seen at position g.48387611 (G>A substitution) of COL2A1 gene (NM_001844.5) on both forward as well as reverse reads, visualized on integrative genomics viewer (IGV) (**Figure 2**).

Discussion

Kniest dysplasia is a rare inherited disease manifested due to collagen dysfunction. A short trunk with kyphosis, short extremities with prominent joints, and restricted mobility are distinctive features that are present in the first few years of life.[3] Other abnormalities like cleft palate, dental anomalies, and hearing loss may be present. Morquio's syndrome was unlikely as consanguinity, corneal clouding, cardiac valvular defects, and hepatosplenomegaly were absent. Moreover, flaring of ribs, flared iliac

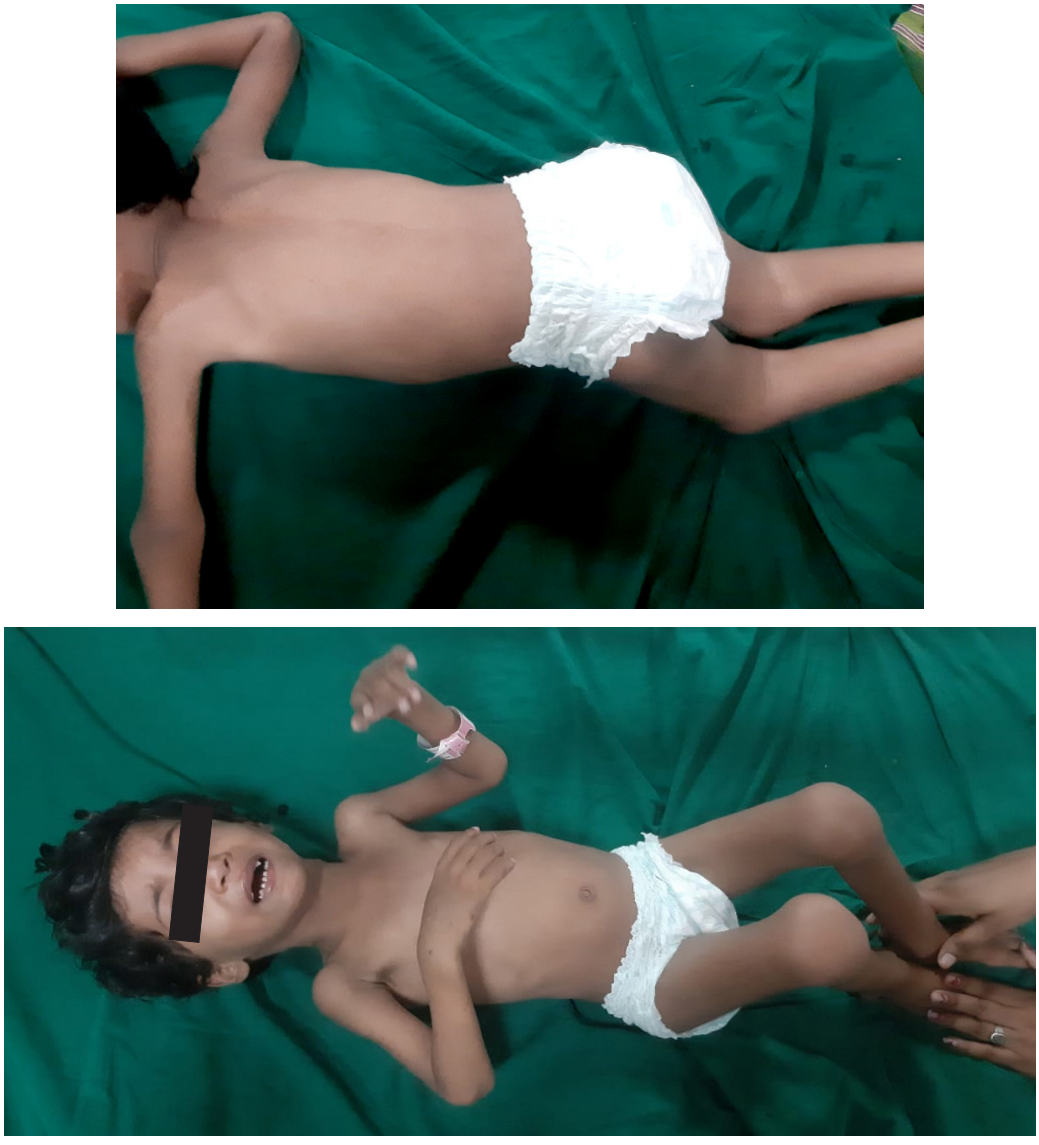

Figure 1. Clinical picture of patient

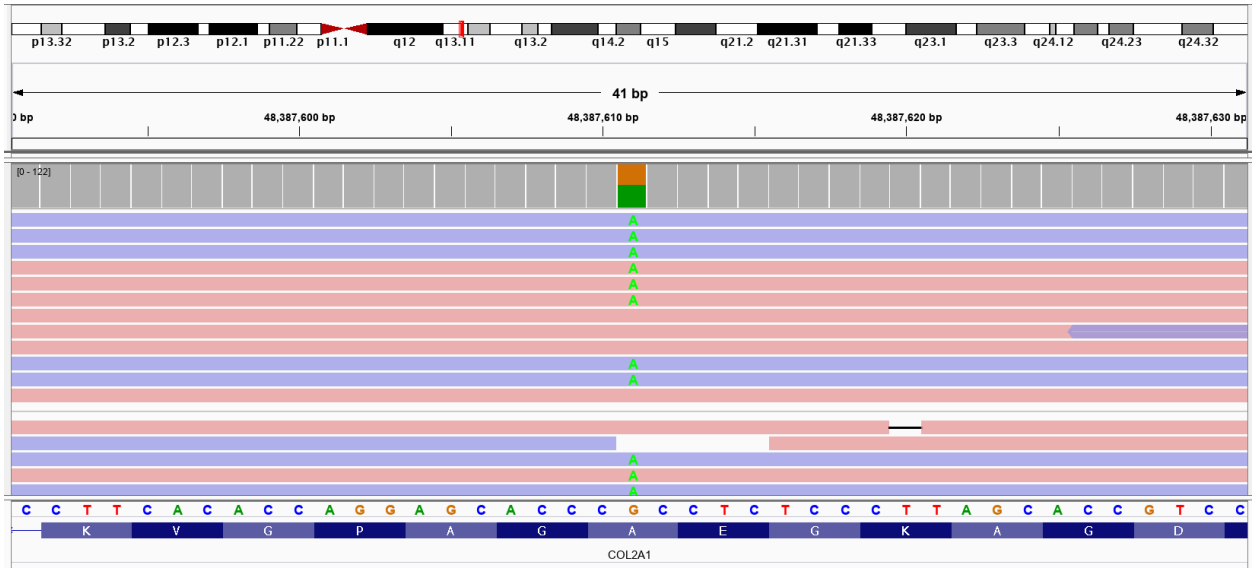

Figure 2. Genetic analysis

bones, and proximal pointing of metacarpal bones were not present in our girl. Both spondyloepiphyseal dysplasia and Kniest syndrome have platyspondyly and hypoplastic femoral heads, but epiphyseal enlargement with cloud-like calcification points towards Kniest syndrome. Speech delay may be a result of moderate hearing loss because of recurrent ear infections. Clinical and radiographical suspicion was confirmed by genetic analysis, which showed a pathogenic variant (p.Ala302Val) in the COL2A1 gene in chromosome 12q13 (**Figure 2**).

Kniest syndrome is inherited as autosomal dominant, but most cases are sporadic. Common phenotypic manifestations of Kniest syndrome are high myopia, sensorineural hearing loss, cleft palate, and short-trunked dwarfism. Skeletal abnormalities include flat rounded facies, flat nasal bridge, short or barrel-shaped thorax, platyspondyly, small iliac bones, dumbbell-shaped femoral bones, and enlarged epiphyses with cloud-like calcification.[4] Routine flexion/extension radiographs of the cervical spine in all patients with or without symptoms in severe phenotypes of Kniest is recommended.[5] If there is instability, stabilization may be required. Treatment of kyphoscoliosis typically consists of a brace for mild curves, and if progressive, serial spine casting can be considered. Regular ophthalmologic check-ups must be conducted for myopia and retinal detachment. Hearing evaluation should be done to assess chronic hearing loss.

Kniest dysplasia is a rare inherited syndrome with typical facial dysmorphism and skeletal abnormalities. Permanent deformities occur from progressive joint enlargement and contracture in most joints, including small metacarpophalangeal and interphalangeal joints. Treatment must be multi-disciplinary as the condition affects several systems. Among non-surgical methods, bracing and physiotherapy are important. On the other hand, as the child grows and develops debilitating deformities, surgeries like spinal fusion or implantation of growing rods to stabilize the child's spine may be necessary. In some cases, careful monitoring may be all that is required.

Conflict of interest

None declared.

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