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Case Report

Schmid metaphyseal chondrodysplasia: consideration in differential diagnosis of rickets

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ABSTRACT

Schmid metaphyseal chondrodysplasia is a rare inherited cause of skeletal dysplasia caused by COL10A1 gene mutation, characterized by skeletal abnormalities and progressive short stature not usually associated with any other major anomalies or cognitive disability. We report a case of a 3-year-old girl with short stature, genu varum, and motor developmental delay, who was initially misdiagnosed and treated as rickets. Blood investigations and radiographic findings were crucial to guide the diagnosis. Genetic testing allows definitive molecular diagnosis leading to proper treatment and counselling.

Keywords: Schmid metaphyseal chondrodysplasia, Differential diagnosis of rickets, COL10A1 mutation

INTRODUCTION

Metaphyseal chondrodysplasias are skeletal diseases involving the metaphyses of the long bones, resulting in severe disturbance in the longitudinal growth of bones while the development of the epiphyses is preserved. The Schmid type is the most common and least severe type of metaphyseal chondrodysplasias. It is inherited as an autosomal dominant congenital disorder due to heterozygous mutation in gene encoding type X collagen (COL10A1 gene) located on chromosome 6 and is characterized by short stature, waddling gait, coxa vara and bowing of the long bones.[1,2] It is often mistaken for rickets or achondroplasia due to their similar radiological features.[3] Appropriate diagnosis of skeletal dysplasia is essential for genetic counselling and treatment.

CASE REPORT

A 3 year 3 months old girl presented to us with complaints of delayed walking, bowing of legs and short stature. She was the second child of a non-consanguineous marriage. The familial and antenatal history were unremarkable. Child was born at term with a birth weight of 3.1 kg. There was no history of any adverse perinatal events. All the milestones were achieved age appropriate except for the delayed walking. On examination, she had mild frontal bossing, lumbar lordosis with genu varum and a waddling gait. Her height was 76 cm and weight was 8.9 Kg, both below the 3rd percentile for her age, with height being more affected.

The upper segment to lower segment ratio (US: LS) was slightly increased, being 1.4. Her lower limb X rays showed metaphyseal changes in the form of fraying, cupping and splaying. She was on treatment for rickets in the past 18 months from elsewhere with oral vitamin D initially, followed by a total of 36 lakhs of IM vitamin D injections in view of the persistence of radiological features. Her previous (before on initiation of vitamin D) as well as current blood investigations showed normal calcium, phosphorus and alkaline phosphatase levels ruling out the possibility of rickets. Her current serum vitamin D level was in the toxic range (1251 ng/ml) with a suppressed parathormone level (5 pg/ml). Other

relevant blood investigations were also performed including CBC, ABG, TFT, Serum electrolytes and RFT, which were all within the normal range. We went through her previous radiographs which showed distal femoral and proximal tibial metaphyseal irregularities(fraying) along with cupping and splaying. Repeat X-ray lower limbs showed persistence of the metaphyseal changes with similar changes in the X-ray wrist left hand. X-ray spine showed accentuation of the lumbar lordosis.

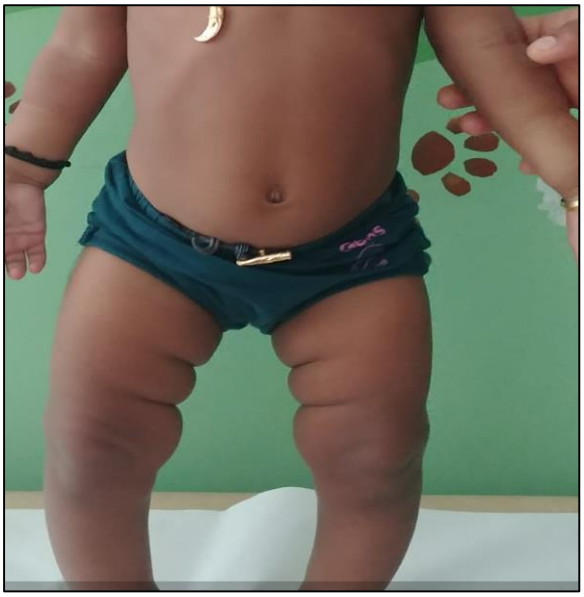

Figure 1: Clinical picture of the child on arrival to OPD.

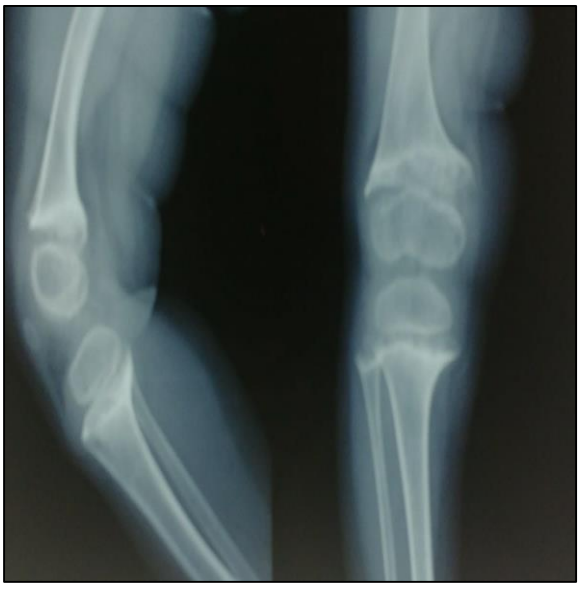

Figure 2: X-ray knee before initiation of vitamin D therapy, showing metaphyseal changes in the form of cupping, splaying and fraying.

Based on the clinical and radiological findings, possibility of metaphyseal chondrodysplasia was considered, and genetic study was sent which came positive for a likely pathogenic mutation involving COL10A1 gene suggestive of Schmid type of metaphyseal chondrodysplasia. Child was then referred to the orthopaedic team for further follow up and surgical correction of the deformity such as valgus osteotomy of the proximal femur.

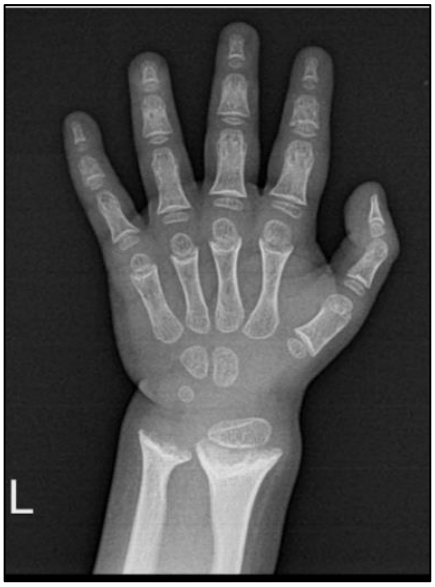

Figure 3: Left wrist X-ray showing the metaphyseal changes with normal epiphysis.

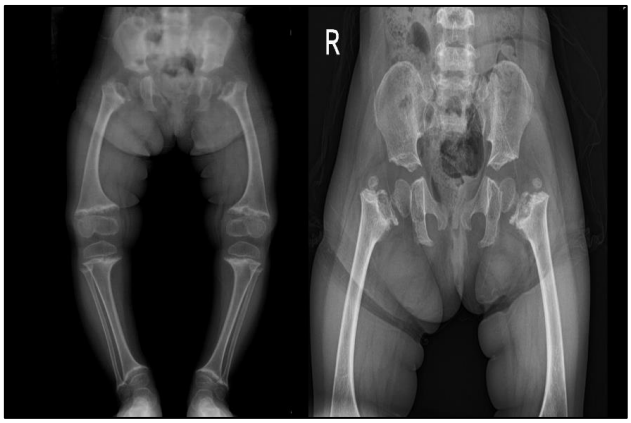

Figure 4: X ray lower limbs with pelvis (on arrival to us/ after vitamin D therapy) showing persistent metaphyseal changes and shortening of the femoral neck and irregular proximal femoral metaphysis with medial beaking.

DISCUSSION

Diagnosing metaphyseal chondrodysplasia, particularly Schmid-type (SMCD), presents significant clinical challenges due to its overlap in clinical and radiological features with rickets.[4,5] Distinguishing between these conditions based solely on these findings can be complex. Therefore, genetic analysis becomes essential to establish an accurate differential diagnosis between SMCD and

rickets. Specifically, identifying mutations such as those in the COL10A1 gene through genetic testing is crucial. This molecular approach provides definitive confirmation when clinical and radiological features are ambiguous or similar to rickets.[6,3]

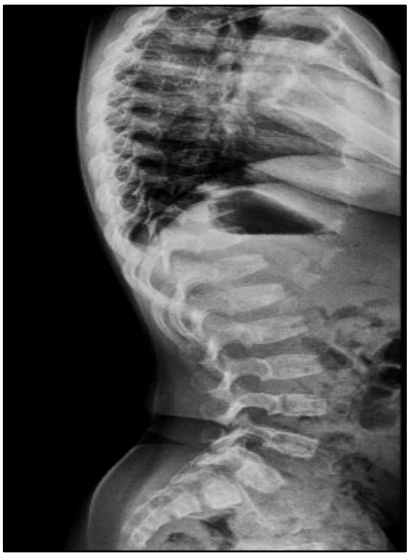

Figure 5: X ray spine showing accentuation of the lumbar lordosis.

LIKELY PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

Gene (Transcript) #	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
COL10A1 **(-)** (ENST00000327673.4)	Exon 1	c.53G>T **(p.Gly18Val)**	Heterozygous	Schmid-type metaphyseal chondrodysplasia	Autosomal dominant	Likely Pathogenic

Figure 6: Genetic study revealed COL10A1 gene heterozygous mutation, which is likely pathogenic, thus confirming the molecular diagnosis.

The clinical features of Schmid metaphyseal chondrodysplasia typically emerge during the first 2-3 years of life and include notable characteristics such as short stature and waddling gait.[7] This specific type of metaphyseal chondrodysplasia is attributed to a deficiency in type X collagen, which is normally localized in the hypertrophic zone of growth plate cartilage.[7–9]

According to Lachman et al., key imaging findings in Schmid metaphyseal chondrodysplasia include mild hypoplasia and/or irregularity of the acetabular roof, coxa vara (reduced femoral neck angle), femoral bowing, enlarged capital femoral epiphyses, and abnormalities in the proximal and distal femoral metaphyses.[10] These radiographic features are pivotal for the diagnostic evaluation and characterization of this form of metaphyseal chondrodysplasia. Follow-up care for patients diagnosed with Schmid metaphyseal chondrodysplasia (SMCD) is of utmost importance. Currently, no curative treatment exists, but surgical intervention (osteotomy) may be considered if there is progressive or symptomatic deformity to maintain function and alleviate discomfort.[1] Genetic counselling is vital for family planning, as each affected individual has a 50% chance of passing on the condition to their next child also. It's important to note that within the same family, there can be variations in the severity of symptoms due to variable expressivity. Therefore, careful evaluation of the patient's parents is essential.[1]

Skeletal dysplasia encompass a diverse range of disorders, and radiological findings play a pivotal role in guiding accurate diagnosis.[6,8] Our case underscores the importance of clinical observations complemented by radiography and confirming the molecular diagnosis promptly thus avoiding unnecessary investigations and mismanagement.

CONCLUSION

This study enhances knowledge and understanding in the field by underscoring the clinical and diagnostic challenges of distinguishing Schmid metaphyseal chondrodysplasia from conditions like rickets. It highlights the pivotal role of genetic testing in identifying COL10A1 mutations, which provides a definitive diagnosis and prevents mismanagement. By emphasizing

the importance of integrating clinical observations, radiological findings, and molecular diagnostics, this case underscores the need for a multidisciplinary approach to improve patient outcomes and guide genetic counselling.

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