

A Rare Case of SCHMID Metaphyseal Chondrodysplasia Associated with Hypothyroidism, Growth Hormone Deficiency and Celiac Disease: Case Report

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1. Abstract

1.1. Introduction and Importance: SCHMID metaphyseal chondrodysplasia is a rare cause of short stature with a good prognosis regarding other types of chondrodysplasia in reason of the normal integrity of the growth plate.

1.2. Case Presentation: The authors present a rare case of 4-year-2-month-old boy referred to our Unit for harmonious short stature, he had a waddling gait, subtle micromelia, and hyperlordosis, no special facies.

1.3. Clinical Discussion: The skeletal scan made the diagnosis of SCHMID metaphyseal chondrodysplasia. The first laboratory workup showed elevated thyroid stimulating hormone and anti-tissue transglutaminase immunoglobulin A. The duodenal biopsies confirmed the diagnosis of coeliac disease. Treatment of levothyroxine was initiated with a gluten-free diet .6 years later, his re-evaluation showed a low insulin-like growth factor 1 and low growth hormone peaks confirming the diagnosis of growth hormone deficiency, Growth hormone therapy was initiated with an adjusted dose of levothyroxine.

1.4. Conclusion: Other causes of short stature should not be missed when diagnosing chondrodysplasia, and further investigations should be carried out to detect other concomitant disorders since metaphyseal chondrodysplasia is a rare cause for short stature while hypothyroidism and coeliac disease are relatively common.

2. Highlights

- Metaphyseal chondrodysplasia, schmid type, is a very rare inherited disorder characterized by short stature with abnormally short arms and legs (short-limbed dwarfism) and bowed legs (genu varum).
- Hypothyroidism is where your thyroid gland does not produce enough hormones.
- Coeliac disease) is a systemic autoimmune disease caused by a lifelong intolerance to gluten. Growth hormone deficiency, also known as dwarfism or pituitary dwarfism, is a condition caused by insufficient amounts of growth hormone in the body.
- Short stature is a general term used to describe a condition in which a child or a teen's height is well below the average height of his or her peers.

3. Introduction

Short stature is a common cause for paediatric endocrinologist consultation, it is a general term for children whose height is two SDs or more below the mean height for children of the same sex and age, short stature may indicate pathologic causes like systemic disorders, endocrine conditions and genetic disease [1].

Chondrodysplasias are a heterogeneous group of skeletal disorders characterized by short stature and other skeletal malformation [2,3]. The incidence as a group is 1 per 4000 birth [3]. SCHMID metaphyseal chondrodysplasia) SMCD) is a mild type of chondro-

dysplasia with a better prognosis [3,4].

SMCD is a rare autosomal dominant disorder caused by heterozygous mutations in the gene encoding type X collagen with unknown incidence.[5] The main manifestation is short stature, genu varum, and waddling gait during the first years of life. Radiologic findings are enlarged capital femoral epiphyses, metaphyseal abnormalities of the long bones, anterior cupping, sclerosis, and splaying of the ribs, mild hand involvement. No extraskeletal anomalies were reported. Intelligence and life expectancy are preserved [6].

Subclinical hypothyroidism (SCH) is a biochemical condition characterized by increased thyroid stimulating hormone with normal levels of thyroid hormone. It is typically asymptomatic. The most common cause of SCH is chronic autoimmune thyroiditis. SCH is a common disorder with an incidence of 2% in children [7].

Coeliac disease (CD) is a common systemic autoimmune disease that primarily affects the small intestine caused by gluten intolerance, which causes immunologically mediated inflammatory destruction. There is a remarkable association with the human leucocyte antigen DR3-DQ2 and/or DR4-DQ8. The Clinical presentation is variable and ranges from gastrointestinal symptoms to non-gastrointestinal manifestation with increased risk for some malignancies. The pooled global prevalence is 1.4% but can vary considerably by region [8].

Growth hormone deficiency (GHD) is defined as impaired secretion of growth hormone (GH) by the pituitary gland that results in growth failure, this could be congenital or acquired, isolated or combined with other pituitary hormonal deficits [9]. The incidence of GHD in children is ~1:4000 [9].

We report a case of a 4-year-2-month-old male with severe short stature caused by SMCD associated with subclinical hypothyroidism, GHD, and CD.

This case report has been reported in line with the SCARE criteria 2020.[10]

4. Case Presentation

A 4-year-2-month-old boy (Figure 1) was referred to our Endocrinology Clinic to evaluate for Severe Short Stature. He was the offspring of consanguineous parents, born at term by normal vaginal delivery. The family medical history was only positive for a familial short stature.

His weight was 13 kg (1.74th) percentile his height was 85 cm (0.1) percentile and his head circumference was 47 cm (-3.3 SD) on CDC growth charts. The blood pressure was 100/60 mmHg, the heart rate of 85 bpm, and the respiratory rate of 20 bpm.

On physical Examination, he was conscious, and oriented, with no facial dysmorphism, subtle short upper and lower limbs, bowing of the lower limbs, waddling gait, and hyperlordosis.

The urogenital examination showed micropenis. The rest of his physical examination was normal.

The initial biochemical workup is shown in Table 1. The results were unremarkable.

Hormonal workup is shown in Table 2:

Table 2 showed an elevated thyroid stimulating hormone and positive anti-tissue transglutaminase immunoglobulin A.

The child had Duodenal Biopsies confirming CD (Marsh type 3b).

Due to the presence of mild microcephaly, he had a computed tomography-SCAN of the brain which was normal.

A complete skeletal scan showed changes in the bone structure at the terminal parts of the femoral bones and no changes in the pelvis (Figure 2). there were no remarkable changes in the bone structure of the vertebrae (Figure 3) which lead to the diagnosis of Metaphyseal chondrodysplasia type SCHMID.

A treatment with levothyroxine 25 mcg per day was initiated, with a gluten-free diet.

Lost to follow up. At the age of 10 years and 4 months, his height was 117 cm (0.1 percentile), and his weight was 26 kg (0.4 percentile) rising concerns about the integrity of his pituitary gland.

His hormonal workup is shown in Table 3.

The dose of levothyroxine was adjusted to 50 mcg/kg per day. A GH provocation test (Table 4) with insulin (0.01 unit/kg) showed low peaks.

To exclude any possibility of an autoimmune polyendocrine syndrome, parathyroid hormone and glycated haemoglobin were within normal limits (Table 5).

MRI of the brain and pituitary gland was normal (Figure 4).

The estimation of his bone age based on the Greulich and Pyle atlas was 6 years.

A GH therapy with a dose of 0.24 mg/kg per week was initiated associated with free gluten diet.



Figure 1: A 4-year-2-month-old boy with short stature, bowing lower limbs, and micromelia.



Figure 2: Pelvis and lower limbs radiograph show bowing femurs, large capital epiphyses, and short femoral necks. Wide growth plate of tubular bones.



Figure 3: Normal spinal column.



Figure 4: Showed a normal MRI of the brain and the pituitary gland.

Table 1: The results of biochemical workup.

Test	Result	Normal values	Test	Result	Normal values
HGB	11	11–14 g/dl	Urea	17	5–18 Mg/dl
MCV	72	75–86 fl	Creatinine	0.4	0.2–0.5 Mg/dl
Calcium	9.4	8.8–10.8 mg/dl	AST	64	15–50 U/l
Phosphorous	3.8	4–7 mg/dl	ALT	25	4–36 U/l
ALP	163	65–210 U/L	Glucose	84	70–110 Mg/dl

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; HGB, haemoglobin; MCV, mean corpuscular volume

Table 2: The results of hormonal findings.

Test	Result	Normal values	Test	Result	Normal values
TSH	7.8	0.3–5 mIU/ul	Anti-TTG-IgA	145	0–3 U/ml
FT4	1.13	0.8–2 ng/dl	IGF1	55	5–128 ng/dl

Anti-TTG-IgA, anti-tissue transglutaminase immunoglobulin A; FT4, free thyroxine 4; IGF1, insulin-like growth factor 1; TSH, thyroid stimulator hormone.

Table 3: The results of hormonal workup.

Test	Result	Normal values	Test	Result	Normal values
TSH	6.8	0.3–5 mIU/ul	Cortisol 8 AM	18.67	3–21 mcg/dl
FT4	1.88	0.8–2 ng/dl	IGF1	39.1	5–128 ng/dl

Table 3 showed a high level of TSH and a low IGF1.

FT4, free thyroxine 4; IGF1, insulin-like growth factor 1; TSH, thyroid stimulator hormone.

Table 4: Parathyroid hormone and glycated haemoglobin results.

Test	Result
GH fasting at rest	0.78 ng/ml
GH after ½ h	1.46 ng/ml
GH after 1 h	0.37 ng/ml
GH after 1 + 1/2 h	0.02 ng/ml

GH, growth hormone.

Table 5: Parathyroid hormone and glycated haemoglobin results.

Test	Result	Normal values	Test	Result	Normal values
PTH	40	15–65 Pg/ml	Calcium	9	8.8–10.8 mg/dl
Glycated haemoglobin	5	4–6.8%	Phosphorous	4.3	4–7 mg/dl

PTH, parathyroid hormone.

5. Discussion

Chondrodysplasia is a rare cause of short stature which might be easily diagnosed by clinical aspects and skeletal scan. However, SMCD is a subtle type of chondrodysplasia with mild manifestations [1-6].

In the present case, the suspicion of SMCD was made by a clinical examination which showed short stature, waddling gait, microcephaly, and subtle micromelia. A skeletal survey showed signs suggesting SMCD, and more investigations showed hypo- thyroidism and CD. 6 years later, his degraded measurements raise concerns about GHD.

SMCD is rarely associated with other hormonal deficiencies. To the best of our knowledge, this is the first description of an association between SMCD, hypothyroidism, GHD, and CD which might be just an accidental event.

Alenazi et al [11]. described a case of a Saudi female with GHD and Achondroplasia.

The gold standard for the diagnosis of SMCD is based on genetic testing [6], which is not available in our case.

In our case, GH therapy could have double benefits due to the presence of GH deficiency and the normality of the growth plate which is not affected in SMCD, this theory is confirmed by Knawaza et al [12]. who studied 85 Japanese children- with different types of

skeletal dysplasia—treated with GH therapy for 1 year. The trial concluded that GH therapy was effective for height gain.

GH therapy is considered an indication of short stature in Turner syndrome patients even in the absence of GHD with promising results due to the integrity of the growth plate, early initiation of GH therapy is important to achieve a reasonable final height in these girls [13].

SMCD is a rare cause of short stature but CD and acquired hypothyroidism are relatively common [9,11–14] in our region whose early diagnosis and management might improve the height expectancy.

CD is a chronic autoimmune disease caused by gluten ingestion, the clinical manifestations may vary from asymptomatic to severe malabsorption with extraintestinal symptoms such as growth failure, learning disorders, iron deficiency, and high risk of autoimmune diseases.[8] In our case, the patient had no specific symptoms and the diagnosis was made accidentally in the context of first-line investigations for short stature.

There is an association between CD and autoimmune hypothyroidism three times higher than the general population [15], thus, at the time of diagnosis one of them, it is important to investigate the other for appropriate management.

At the supposed age of puberty, other investigations regarding the

pituitary-gonadal axis should be performed to determine delayed puberty in the context of another hormonal deficiency.

After puberty, another possibility of management as surgical correction and limb lengthening could be helpful for SMCD patients [16,17].

6. Conclusion

SMCD is a mild type of chondrodysplasias characterized by short stature and other subtle skeletal malformation and requires the patient's growth chart monitoring. In case the growth chart started to deteriorate over time, the possibility of other associated disorders should be considered that could be treatable so the final height expectancy may improve.

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