Rare disease

Kocher–Debré–Semelaigne syndrome

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Summary

A 4-year-old male child presented with severe growth failure and developmental delay. He had hypertrophy of calf muscles and the thyroid profile showed low levels of T3, T4 and markedly elevated level of thyroid-stimulating hormone thus confirming the presence of hypothyroidism. This combination of hypothyroidism and hypertrophy of muscles is classically described as Kocher–Debré–Semelaigne syndrome. This child was started on 50 µg of levothyroxine.

BACKGROUND

Though it is a rare condition, the combination of features of hypothyroidism and calf muscle hypertrophy make it very easy to pick it up.

Thyroid hormone deficiency is a rare cause of acquired myopathy, comprising only 5% of the total cases.

This hypertrophy is reversible with treatment. Patients usually take months to recover, our patient, on first follow-up at 2 weeks showed clinical reduction in the bulk of muscle which was also observed by the parents.

CASE PRESENTATION

A 4-year-male child, born of non-consanguineous marriage was brought to us with history of growth failure and

developmental delay. The parents took notice of the growth and developmental delay only in last 6 months. They were seeking advice in their village.

There was no history of frequent loose stools, urination or any febrile illness. The antenatal and birth history were unremarkable. There was no history of similar problems in the two siblings. The mother did not have any problem.

This child had coarse features, depressed nose bridge and a large tongue (figure 1).

He weighed 10 kg, his height was 74 cm and head circumference 47 cm (all below third percentile). His height age corresponded to that of an year-old child's. His upper body segment was 44 cm and the lower segment was 30 cm, with an upper and lower segment ratio of almost 1.5 (figure 2).

Figure 1 Coarse facies, large tongue, depressed nose bridge.

Figure 2 Short stature, calf muscle hypertrophy.

His developmental assessment showed normal gross motor milestones. He was able to draw a circle, but could not draw a square, he made a tower of six cubes and he spoke only monosyllables and could not speak sentences.

He showed hypertrophy of both the calf muscles. Gower sign was negative.

Rest of the examination was unremarkable.

INVESTIGATIONS

Complete blood count revealed haemoglobin of 9.0 g/dl, mean corpuscular volume was 90. Electrolytes, creatine phosphokinase (CPK), chest x-ray were normal.

T3<10 ng/dl (60–200), T4 0.7 µg/dl (4.5–12.0), thyroid-stimulating hormone >150 mIU/ml (0.30–5.5). Bone age: 6 months (figure 3).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for a child with the macroglossia, developmental delay and coarse features would include a mucopolysaccharidosis, Beckwith–Wiedemann or Simpson–Golabi–Behmel syndrome. All these could easily be differentiated on clinical grounds.

A combination of macroglossia, developmental delay, stunting and pseudohypertrophy of muscles clinches the diagnosis of Kocher–Debré–Semelaigne syndrome (KDS).

Muscle enlargement, stiffness and cramping are a constellation of findings seen in individuals with hypothyroidism. In adults, these findings are known as Hoffman syndrome. The absence of painful spasms and pseudomyotonia differentiates this syndrome from KDS.

Figure 3 Bone age 6 months.

TREATMENT

This child was started on 50 µg of levothyroxine daily.

OUTCOME AND FOLLOW-UP

The child came for the first follow-up 2 weeks after the start of treatment and his calf hypertrophy had reduced and he was more active and interactive.

DISCUSSION

The KDS is a myopathy of hypothyroidism in infancy or childhood characterised by muscular hypertrophy limited to lower extremity or being generalised, short stature and cretinism. Children with KDS usually present between 18 months and 10 years of age, but reports of cases diagnosed at earlier ages and even in neonates are also available.¹ Kocher–Debré–Semelaigne syndrome comprised 18.7% of cases with a 2:1 female to male ratio.² The patients present with the clinical features of hypothyroidism along with muscle pseudohypertrophy.³ The pseudohypertrophy involves muscles of extremities, limb girdle, trunk, hands and feet but it is more prominent in muscles of limbs; hence the athletic or Herculean look.⁴ Our patient presented with short stature, delayed milestones and the pseudohypertrophy of calf muscle. He did not show any evidence of muscle weakness. His Gower sign was negative and his CPK was normal.

KDS has been found to be associated with all the usual causes of hypothyroidism presenting in childhood, namely, agenesis of thyroid gland, defective synthesis of thyroid hormone or autoimmune causes of hypothyroidism. The long-standing hypothyroidism is presumed to be responsible for the pseudohypertrophy of the muscles.¹ Our patient remained undiagnosed till 4 years of age. Ignorance of the patient and non-availability of medical care in remote villages may be the reason for the hypothyroidism to be missed for so long in this patient.

Stiffness and aching of muscles are common and are worsened by cold temperatures. Delayed muscle contrac-

tion and relaxation cause the slowness of movement and delayed tendon jerks. Muscle mass may be slightly increased, and the muscles tend to be firm. Rarely, a profound increase in muscle mass with slowness of muscular activity may be the predominant manifestation.⁵

Its pathogenesis is unknown; non-specific histochemical and ultrastructural changes seen on muscle biopsy return to normal with treatment. Affected patients have hypothyroidism of longer duration and severity.⁶ The treatment is usually effective in reverting back the muscle changes. This usually takes months. Our patient when he came for the first follow-up after 2 weeks did show clinical reduction in hypertrophy.

Learning points

- ▶ Hypothyroidism is generally associated with hypotonia but rarely may be associated with muscular pseudohypertrophy (KDS).
- ▶ The differential diagnosis for a child with the macroglossia, developmental delay and coarse features would include a mucopolysaccharidosis, Hoffman syndrome, Simpson–Golabi–Behmel syndrome or Beckwith–Wiedemann syndrome.
- ▶ Delay in diagnosis and seeking treatment may be responsible for KDS.
- ▶ Adequate replacement with thyroxine reverses these changes.

Competing interests None.

Patient consent Obtained.

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