

could be an alternative in cases where measurement might otherwise be impracticable, although additional studies are needed to verify this.

Conflicts of interest

The authors state that they have no conflicts of interest.

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Kocher-Debré-Semelaigne's syndrome: A case report[☆]

Síndrome de Kocher-Debré-Semelaigne: a propósito de un caso

Kocher-Debré-Semelaigne syndrome is an uncommon condition whose main characteristic is muscle pseudohypertrophy associated with long-standing, untreated severe hypothyroidism.¹ It was first described by Kocher in 1892, and it was not until 1934 that Debré and Semelaigne reported two additional cases. The prevalence of the syndrome is unknown, but identification is vitally important because replacement therapy fully reverses the clinical picture,^{1,2} which is potentially serious.^{3,4}

We report the case of a 9-year-old male who was referred to the endocrinology clinic because he had a very muscular appearance, associated with the occurrence of bilateral supraclavicular and facial oedema, which was most evident in the eyelids. No weight gain, asthenia, growth delay, impaired school performance, behavioural changes, or other associated symptoms were reported. A physical examination showed a significant, generalized increase in musculature both in the trunk and all four limbs, associated with facial and bilateral supraclavicular swelling. The examination was otherwise unremarkable: infantile penis, 3 mL tests, no pubarche or axillary hair, normal cardiac and pulmonary auscultation, a weight of 37.5 kg, a height of 140.9 cm with a

62th percentile (P), a BMI of 18.90 kg/m² (P56), and a bone age of 8 years.

Blood test results included: TSH, 441 mcU/mL; free thyroxine (free T4), 0.1 ng/dL; free triiodothyronine, 0.4 nmol/L; thyroglobulin antibodies, 243 IU/mL; thyroperoxidase antibodies, 1254 IU/mL; creatine phosphokinase (CPK), 983 U/L; glutamic-oxaloacetic transaminase (GOT), 72 U/L; glutamic-pyruvic transaminase (GPT), 44 U/L; total cholesterol (TC), 442 mg/dL; LDL cholesterol, 316 mg/dL; HDL cholesterol, 104 mg/dL; and triglycerides (TG), 469 mg/dL. Because of these findings, thyroid ultrasonography was performed. This showed a thyroid gland of normal size, with an overall decrease in gland echogenicity and a "coarse" echo structure, with millimetric hypoechoic nodules scattered on both sides.

Based on these results, severe hypothyroidism secondary to autoimmune thyroiditis was diagnosed, and treatment was started with levothyroxine 75 µg/day. Laboratory tests performed after six months of treatment showed the following results: TSH, 15 mcU/mL; free T4, 1.4 ng/dL; free T3, 2 nmol/L; CPK, 115 U/L; GOT, 23 U/L; GPT, 15 U/L; TC, 147 mg/dL; LDL, 50 mg/dL; HDL, 87 mg/dL; and TG, 54 mg/dL. An improvement in laboratory test results coincided with phenotype normalization, and muscle pseudohypertrophy and supraclavicular and facial oedema disappeared.

Kocher-Debré-Semelaigne syndrome usually occurs between 18 months and 10 years of age with no sex differences.^{1,2} There is a wide range of clinical symptoms and signs, mainly related to hypothyroidism: lethargy or insomnia, facial myxedema, macroglossia, enlarged fontanelles, mucocutaneous jaundice, constipation, mood changes, thick hair, growth delay, and muscle pseudohypertrophy, preferentially involving the trunk and all four limbs

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and causing a muscular appearance. Despite this muscular appearance, however, patients usually report muscle weakness, which sometimes causes difficulty in sitting and in controlling their head position.^{3,4} The occurrence of disseminated intravascular coagulation syndrome,³ and even arrhythmogenic cardiomyopathies, has been reported in more severe cases.⁴ What makes this case unique and surprising is that the patient only had pseudohypertrophy and facial and supraclavicular oedema, with no bone age impairment, and showed no cretinism or other symptoms characteristic of such severe hypothyroidism.

The pathophysiology of muscle pseudohypertrophy is not known. It is not known either why some patients experience it while others have other initial symptoms, but there is agreement that oxidative glycosaminoglycan abnormalities occur as the result of long-standing hypothyroidism.⁵

Diagnosis is suspected based on the above mentioned clinical symptoms and signs. In blood tests, primary hypothyroidism together with an elevation of CPK or any other muscle enzyme due to pseudohypertrophy is characteristic. Lipid parameters may also be elevated due to hypothyroidism.⁶ Although not required in order for the diagnosis to be made, an electromyogram may be performed, and this may reveal decreased wave amplitude of the motor units of the muscles affected. Impedanciometry to assess subcutaneous adipose tissue and even a muscle biopsy showing an accumulation of glycogen and interstitial tissue and, in very advanced cases, necrosis may also be performed.^{6,7}

A differential diagnosis should be made with other diseases associated with chronic muscle weakness (when this occurs), especially if levothyroxine treatment does not improve the symptoms. Such diseases include polymyositis, myasthenia gravis, congenital muscular dystrophy, myelomeningocele, and amyotrophic lateral sclerosis. On the other hand, Hoffman's syndrome is defined as the occurrence of trunk and limb pseudohypertrophy and other symptoms as the result of severe hypothyroidism in adulthood.⁸

Treatment consists of the administration of levothyroxine, with dose adjustment based on the specific requirements of each case. Hypothyroidism may be transient or permanent, and its treatment and correction usually achieves a reversal of all clinical symptoms and signs, including pseudohypertrophy, within a few weeks.^{9,10} Emphasis should therefore be made on thyroid function assessment in any child seen with any muscle impairment or elevated CPK levels.

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