Report of Two Cases of Kocher-Debre Semelaigne Syndrome

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SUMMARY
Myopathy associated with hypothyroidism classically presents with proximal weakness, fatigue, exertional pain, slowed movement, myoedema, diminished deep tendon reflexes, stiffness, myalgia, less commonly cramps and rarely muscle enlargement. Muscle enlargement and hypothroidism is known as Kocher-Debre Semelaigne syndrome (KDS). We report ed here two brothers at the ages of 11 and 7 year-old diagnosed as KDS syndrome. We aimed to emphasize the effects of hypothyroidism on muscle tissue.

Key Words: hypothyroidism, myopathy, child

Kocher-Debre Semelaigne Sendromlu İki Olgu Sunumu

ÖZET
Hipotroidi ile ilişkili miyopati klasik olarak, proksimal kas güçsüzlüğü, yorgunluk, egzersiz ağrısı, hareketlerde yavaşlama, kas ödemi, derin tendon reflekslerinde azalma, kaslarda sertleşme, ağrı daha nadir olarakta kramp ve kasın büyümesi şeklinde kendini gösterir. Kasın büyümesi Kocher-Debre Semelaigne sendromu (KDS) olarak bilinir. Biz burada 11 ve 7 yaşlarında KDS sendromlu iki erkek kardeş olguyu sunarak hipotroidinin kas dokusu üzerindeki etkilerini vurgulamayı amaçladık.

Anahtar Sözcükler: Hipotiroidi, miyopati, çocuk

INTRODUCTION

Hypothyroid myopathy has been reported in 30-80% of the hypothyroidism (1,2) Myopathy associated with proximal weakness, fatigue, exertional pain, slowed movement, myoedema, diminished deep reflexes, stiffness, myalgia, and less commonly cramps. Muscular hypertrophy is reported in less than 10 % of hypothyroid myopathy (3,4). Severity of myopathy generally correlates with the duration and the degree of thyroid hormone deficiency (5).

Kocher-Debre Semelaigne (KDS) syndrome occurs in children with cretinism and is characterized by an increase in muscle mass (3,6). Thyroid hormone replacement therapy reveals complete recovery of muscular symptoms (3,5,6).

We presented two brother diagnosed as KDS syndrome. It is aimed to emphasize the effects of hypothyroidism on muscular tissues.

CASE REPORTS

An 11-year-old boy was referred to our Hospital because of growth failure, mental retardation and muscular weakness. He was the second child of healthy consanguineous parents (first- degree relatives). There was an 8-year-old brother who had similar complaints.

On physical examination he had coarse facies, macroglossia, and hypertrophy of the muscles of gastrocnemius were noticed. Deep tendon reflexes were lost. He weighed 23 kg and he was 111 cm in height. Proximal muscles were weak. He had positive Gowers sign (Figure 1).

Laboratory data revealed the following: Serum thyroid stimulating hormone (TSH) 0.1 mIU/L (N:0.7-6.4 mIU/L), serum total triiodothyronine (T3) 0.3ng/dl (N:90-240 ng/dl), serum total thyroxine (T4) 1.3 µg/dl (N:5.5-12.8 µg/dl) and creatine phosphokinase(CPK) 502 IU/L (N:25-140). His IQ test was assessed as 60. Electromyography (EMG) revealed low-amplitude and short motor units potentials (MUAPs) in the quadriceps and gastrocnemius muscles. Radiograph of the wrist indicated a bone age of 3 years.

His brother was 8 years old and he had similar manifestations. On examination he had coarse facies, macroglossia, weight 22 kg, height 107 cm , deep tendon reflexes were normoactive

bilaterally and gastrocnemius, quadriceps muscles were hypertrophied and proximal muscles were weak (Figure 2).

His TSH, total T3, T4, and CPK levels were 0.2 mIU/L (N:0.7-6.4 mIU/L), 5 ng/dl (N:90-240 ng/dl), 0.7µg/dl (N:5.5-12.8 µg/dl) , and 370 iU/L (N:25-140); respectively. EMG was normal. A radiograph of the wrist showed a bone age of 2 years.

The patients were treated with appropriate thyroid hormone replacement therapy and were followed up at monthly intervals. Seven months after the treatment, serum levels of enzymes returned to normal. Proximal weakness was diminished and enlarged muscles normalized.

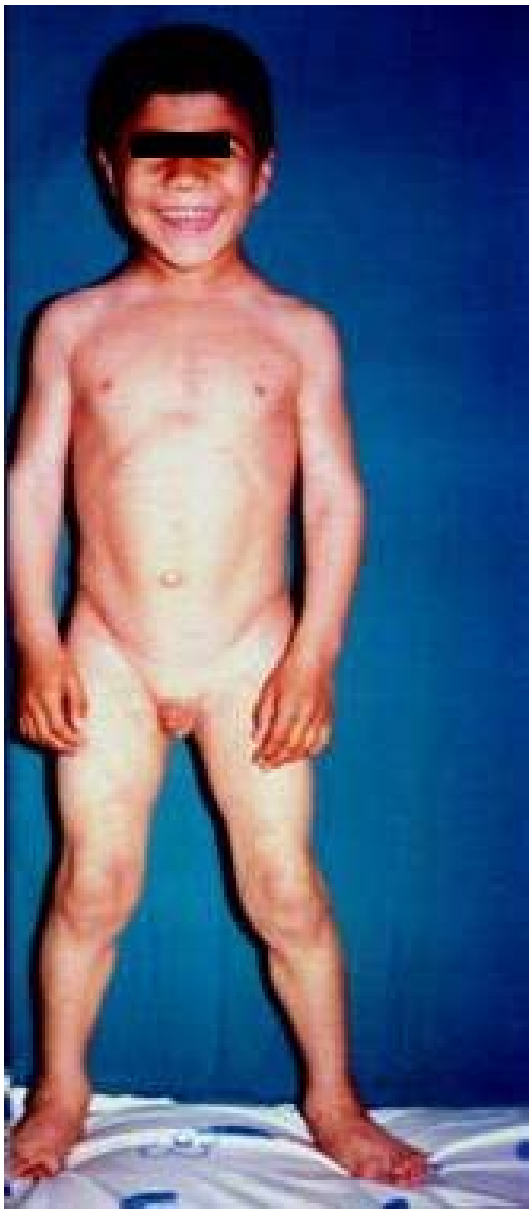

Figure 1. The appearance of the first case with KDS

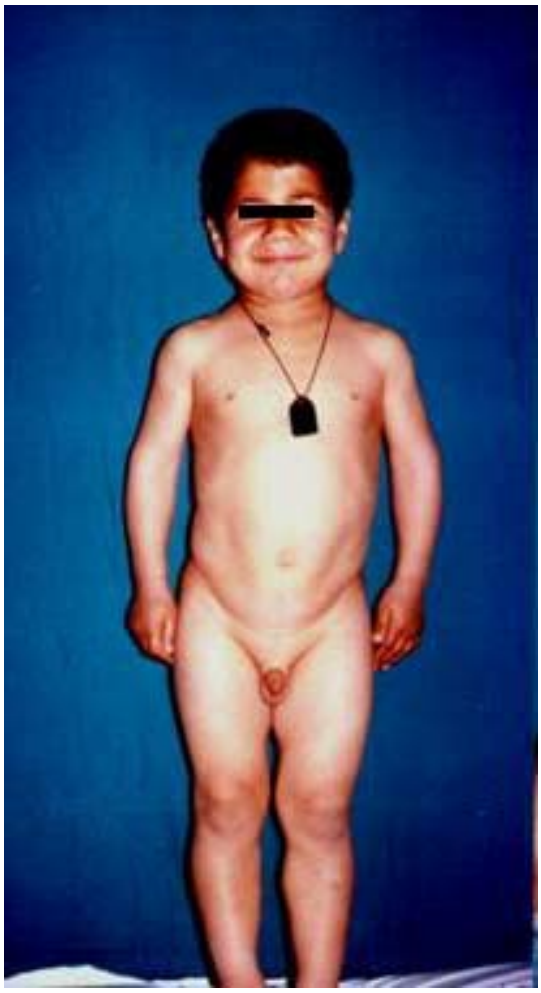

Figure 2. The appearance of the second case with KDS

DISCUSSION

There are several mechanisms whereby thyroid hormone deficiency may interfere with the normal structure and function of skeletal muscles leading to a myopathy. The lack of thyroid hormone results in slowed or reduced metabolic function such as decreased protein turnover and impaired carbohydrate metabolism. These metabolic changes occur in many organ systems, including muscles. Glycogen accumulation and decreased activity of enzymes involved in energy production have been described in hypothyroid myopathy. The presence of T3 receptors on the mitochondria membrane of skeletal muscle suggests a direct impact of thyroid hormones on oxidative metabolism. Among the molecular mechanisms by which thyroid hormones regulate expression of nuclear genes encoding for regulatory proteins of mitochondrial respiratory function, the mitochondrial transcription factor A (h-mt TFA) has been proposed to be a target of thyroid hormone action. Thyroid hormone is also necessary for the expression of fast myofibrillar

proteins in muscles. In hypothyroidism, where the expression of these proteins is deficient there is an increased accumulation of slow myofibrillar proteins. Hypertrophy of muscle due to increased amounts of connective tissue and mucopolysaccharide deposits (6-9). All these factors may contribute to muscle weakness, slowed muscle contraction, diminished deep tendon reflexes, fatigue and exertional pain.

Myopathy is a known complication of hypothyroidism with an incidence of musculoskeletal symptoms varying from 30-80% in different series. Although muscular symptoms may occur in many patients with hypothyroidism, muscular hypertrophy is reported in less than 10% of the patients (1,2,4). The muscular hypertrophy (gastrochnemius, quadriceps) and muscles weakness were observed on physical examination in our patients.

The elevation of serum creatine kinase was reported in 80% of the hypothyroidism even with the absence of muscle involvement. The mechanism of the release of these enzymes is attributed to the changes in cell membrane permeability (6,10). Elevation of CPK levels were detected in patients as well.

Electromyogram is usually normal or may shows myopathic MUAPs with reduced duration and amplitude (11). Low-amplitude and short MUAPs in the quadriceps and gastrocnemius muscles were shown on the EMG of one of our patients. The most involving muscle in KDS is gastrocnemius (12). The bone age was considerably delayed in both children.

With the appropriate thyroid hormone replacement therapy, serum levels of enzymes, enlargement of the muscles and proximal weakness returned to normal in 7 months.

Kocher-Debre Semelaigne syndrome is a specific, rare form of hypothyroid myopathy, which causes hypertrophy of muscles. In this report, we aimed to emphasize the effects of hypothyroidism on muscular tissues.

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REREERENCES

1. Kung AWC, Ma JTC, Yu YL: Myopathy in acute hypothyroidism. Post Med j 63:661-663,1987.
2. Lochmüller H, Reimers CD, Fischer P: Exercise induced myalgia in hypothyroidism. Clin Invest. 17: 1697-1700,1993.
3. Mehrtra P, Chandra M, Mitra MK: Kocher Debre Semelaigne syndrome: regression of pseudohypertrophy of muscles on thyroxine. Arch Dis Child. 86: 224,2002.
4. Klein I, Levey G: Unusual manifestations of hypothyroidism. Arch Intern Med. 144:123-128,1984.
5. Klein I, Mantell P, Parker M, Levey GS: Resolution of abnormal muscle enzyme studies in hypothroidism. Am J Med Sci. 279:159-162,1980.
6. Thasko V, Davachi F, Baboci R, Drishti G, Hoxha P: Kocher-Debre Semelaigne syndrome. Clin Pediatr (Phila). 38:113-115,1999.
7. Monzani F, Caraccio N, Siciliano G, Manca L, Murri L, Ferrannini E. Clinical and biochemical features of muscle dysfunction in subclinical hypothyroidism. J Clin Endocrinol Metab. 82: 3315-3318,1997.
8. Siciliano G, Monzani F, Manca ML, Tessa A, Caraccio N, Tozzi G, Piemonte F, Mancuso M, Santorelli FM, Ferrannini E, Murri L: Human mitochondrial transcription factor A reduction and mitochondrial dysfunction in Hashimoto's hypothyroid myopathy. Mol Med 8: 326-333,2002.
9. Ghilardi G, Gonvers JJ, So A: Hypothyroid myopathy as a complication of interferon alpha therapy for chronic hepatitis C virus infection. Br J Rheumatol. 37:1349-1351,1998.
10. Mastropasqua M, Spagna G, Baldini V, Tudesco I, Paggi A: Hoffman's syndrome: muscle stiffness, pseudohypertrophy and hypothyroidism. Horm Res. 59:105-108,2003.
11. Ruurd FD, Bosch J, Laman DM: Neuromuscular findings in thyroid dysfunction aprospective clinical andelectrodiagnostic study. J Neurol Neurosurg Psychiatry. 68:750-755,2000.
12. Najjar SS: Muscular hypertrophy in hypothyroid children: The Kocher-Debre-Semelaigne Syndrome. J Ped 85:236-239,1974.