

Early diagnosis and treatment reverse clinical features in Hoffmann's syndrome due to hypothyroid myopathy : a case report*

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Abstract

Hypothyroidism is a frequently diagnosed endocrine disorder that has characteristic clinical signs and symptoms. Myopathy is one of the manifestations of hypothyroidism and relatively common. We report a case of Hoffmann's Syndrome due to hypothyroid myopathy documented by clinical features, laboratory findings and positive response to thyroid hormone replacement therapy. A man, age of 22, was diagnosed as having primary hypothyroidism at the age of five, had been describing progressive weakness in his arms and legs for two months and complained about generalized muscle cramps and pain. He was diagnosed with Hoffmann's syndrome with low levels of thyroid hormones and high levels of muscle enzymes. After six months of thyroid hormone replacement therapy, both the clinical picture and laboratory findings were remarkably improved.

Key words : hypothyroid myopathy ; Hoffmann's syndrome.

Introduction

Hypothyroidism is a relatively common endocrine disorder, causing a wide variety of signs and symptoms of neuromuscular dysfunction. Myopathy is a known complication of hypothyroidism and clinical evidence of hypothyroid myopathy occurs in 35-88% of these patients (Torres *et al.*, 1990).

Debre-Kocher-Semelaigne Syndrome in children and Hoffmann's Syndrome in adults are two special patterns of hypothyroid myopathy. The main clinical features are weakness, muscle cramps, delayed relaxation of tendon reflexes, pseudohypertrophy of skeletal muscles, pseudomyothonia and myoedema on percussion (Sidibie *et al.*, 2001). We present a case showing myalgias and cramps during daily activities, high creatine kinase (CK) levels with a well-developed musculature and positive response to thyroid hormone replacement therapy.

Case

A man, age of 22, had been describing progressive weakness in his arms and legs during mild exercise for two months and complained about generalized muscle cramps and pain during daily activities for the last two weeks period. His medical history explains that he was diagnosed with primary hypothyroidism at the age of five and was given thyroid hormone replacement therapy. He gave up the therapy five months ago.

He had a well-developed musculature. Strength was normal in manual muscle testing. His sensation and tendon reflexes were normal. The hypertrophy of trapezoid, deltoid, biceps, gastrocnemius and paravertebral muscles was remarkably noticed bilaterally. Swelling of his face and a hoarse voice was also presented.

Laboratory studies pointed out that serum Thyroid Stimulating Hormone (TSH) level was 170 microIU/ml (normal 0,35-5,5 microIU/ml), Free Tetraiodothyronine (FT4) level was 0,15 ng/dl (normal 0,89-1,76 ng/dl) and Free Triiodothyronine (FT3) level was 0,1 pg/ml (normal 2,3-4,2 pg/ml). In his muscle enzyme study, CK level was 5136 U/L (normal 91-135 U/L) and Lactat Dehydrogenase (LDH) level was 1306 U/L (normal 91-232 U/L). There were no significant changes in other blood biochemistry.

Electromyography (EMG) evaluation showed mild carpal tunnel syndrome (CTS) bilaterally. Needle EMG was normal.

There was no activity observed at the localization of bilateral thyroid gland lobules with the thyroid syntigraphy performed by Tc-99 M.04.

Pathological examination under light microscopy of muscle biopsy specimen of the vastus lateralis muscle was normal before treatment.

He was diagnosed as Hoffmann's Syndrome due to stopping the thyroid hormone replacement therapy prescribed for primary hypothyroidism. He was restarted the thyroid hormone replacement therapy (Levothyroxine, 0,1 mg/day). After two months of period, his complaints were remarkably

decreased except some stiffness in his legs. After six months, his thyroid hormones, serum CK and LDH levels became normal. CTS findings on EMG were greatly improved. His muscle bulk returned to normal appearance.

Discussion

Hoffmann's Syndrome was first described by Hoffmann in 1897 in an adult who developed muscle stiffness and difficulty in relaxation of muscles after thyroidectomy (Kung *et al.*, 1987). Post-thyroid irradiation, post Hashimoto's thyroiditis, primary hypothyroidism, stopping the treatment of thyroid hormone replacement therapy can also be the reasons of Hoffmann's Syndrome. The most common findings are enlarged muscles, slow movements, delayed relaxation of tendon reflexes, muscle cramps, proximal muscle weakness, pseudomyothonia, myoedema on percussion.

Although the muscle enzymes CK and LDH are markedly increased, the exact pathophysiological mechanism of this condition is incompletely understood. However, inadequate production of thyroid hormones is associated with a decrease in the myosin content of muscles. This effect is ascribable to a decrease in RNA content. Thus, T3 acts not only in the nucleus but also on the mitochondria; truncated forms of the T3 receptor, C-erb-A-alpha I, have been identified within mitochondria. The mitochondrial protein p43 may be a T3 dependent transcription factor (Sidibie *et al.*, 2001).

Despite the high incidence of hypothyroid myopathy, few pathologic studies of muscle have been described. Many biopsies are normal and most of the abnormalities that have been noted are mild and nonspecific. The reported histological changes include Type I Fiber predominance, Type II Fiber atrophy and increased numbers of internal nuclei. Ultrastructural changes include excessive amounts of glycogen, lipid accumulations, abnormal mitochondria, dilated sarcoplasmic reticulum, proliferation of T-tubules and focal myofibrillar degeneration (Evans *et al.*, 1990).

Lochmüller reported a case with hypothyroidism and high levels of CK (Lochmuller *et al.*, 1993). Muscles biopsy of that patient showed signs of rhabdomyolysis. Although our patient's CK levels were

higher, we could not see any fiber degeneration indicating rhabdomyolysis. The patient reported by Scott (Scott *et al.*, 2002) showed a well-developed musculature and marked elevations of CK levels with degenerative changes in muscle biopsy. Central changes were reported by Evans (Evans *et al.*, 1990) in hypothyroid myopathy but Ono (Ono *et al.*, 1987) pointed out that there was no correlation between the presence or absence of "core-like" structures and clinical characteristics. Most of the cases presented in the literature (Sidibie *et al.*, 2001, Evans *et al.*, 1990, Lochmuller *et al.*, 1993, Scott *et al.*, 2002) with or without muscle biopsy changes responded well to thyroid hormone replacement therapy as in our case.

Our case suggests to study the muscle enzymes and thyroid hormones of the patients who are suspected of myopathy so that early diagnosis and treatment of hypothyroid myopathy may help patients recover completely.

REFERENCES

1. TORRES C. F., MOXLEY R. T. Hypothyroid neuropathy and myopathy : clinical and electrodiagnostic longitudinal findings. *J Neurol*, 1990 ; **237** : 271-274.
2. SIDIBIE E. H., DIOP A. N., THIAM A., DIAGNE P. M., SARR A., TOURE M., DIOP M. Hoffmann's syndrome in hypothyroid myopathy. Report of a case in an African. *Joint Bone Spine*, 2001 ; **68** : 84-6.
3. KUNG A. W., MA J. T., YU Y. L., WANG C. C., WOO E. K., LAM K. S., HUANG C. Y., YEUNG R. T. Myopathy in acute hypothyroidism. *Postgrad Med J*, 1987 ; **63** : 661-663.
4. EVANS R. M., WATANABE I., SINGER P.A. Central changes in hypothyroid myopathy : a case report. *Muscle Nerve*, 1990 ; **13** : 952-6.
5. LOCHMULLER H., REIMERS C. D., FISCHER P., HEUSS D., MULLER-JOCKER J., PONGRATZ D. E. Exercise-induced myalgia in hypothyroidism. *Clin Investig*, 1993 ; **71** : 999-1001.
6. SCOTT K. R., SIMMONS Z., BOYER P. J. Hypothyroid myopathy with a strikingly elevated serum creatine kinase level. *Muscle Nerve*, 2002 ; **26** : 141-144.

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