

Clinical Reports

Myopathy in acute hypothyroidism

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Summary: Hypothyroid myopathy has so far been reported in long standing cases of hypothyroidism. We describe two adult patients with myopathy associated with acute transient hypothyroidism. Both presented with severe muscle aches and cramps, stiffness and spasms. Muscle enzymes were markedly elevated and electromyography in one patient showed myopathic features. Histological changes were absent in muscle biopsy, probably because of the short duration of metabolic disturbance. The myopathy subsided promptly when the hypothyroid state was reversed.

Introduction

Hypothyroid myopathy has been described in patients with long-standing hypothyroidism.^{1,2,3} We report two Chinese patients with muscle involvement in acute transient hypothyroidism, who improved after reversal of the hypothyroid state.

Case reports

Case 1

A 42 year old woman presented at another hospital with a one-month history of heat intolerance, hand tremors, weight loss, palpitations and sweating. The thyroid gland was diffusely enlarged to two times in size. Her serum thyroxine (T_4) level was raised at 237 nmol/l (normal: 58-154). Graves' disease was diagnosed and she was treated with carbimazole 30 mg daily together with propranolol 60 mg daily for 4 weeks. She was seen again 6 weeks later and was noted to be clinically euthyroid. The serum T_4 was 47 nmol/l and the thyroid stimulating hormone (TSH) raised at 12 μ IU/ml (normal up to 7). The dosage of carbimazole was lowered to 20 mg daily and propranolol stopped.

Eight weeks after starting treatment she was referred to our unit because of painful cramps and spasms involving muscles of the shoulder and pelvic girdles. The attacks came on spontaneously or with mild exertion, with severe pain lasting for 10 minutes and gradually wearing off over 2 hours. There was

however no muscle weakness or symptoms of hypothyroidism. She had no preceding viral infection. Examination revealed that the goitre had decreased in size and she was clinically euthyroid. Motor and sensory functions were completely normal.

Investigation showed a T_4 of 44 nmol/l, triiodothyronine (T_3) 1.2 nmol/l (normal 0.77-2.97 nmol/l), and TSH 5.1 μ IU/ml (normal up to 7). The serum creatine kinase level was 11,940 μ mol/min.l (normal 5-165) and the lactic dehydrogenase was 397 μ mol/min.l (normal 130-275), and glutamic-oxalacetic transaminase was 120 μ mol/min.l (normal 28-32). Serum sodium and potassium were normal. The trichinella and cysticercosis antibody titres and serial viral antibody titres for viruses likely to cause myositis were negative, as were anti-nuclear antibody, rheumatoid factor, anti-smooth muscle and anti-striated muscle antibodies. The ischaemic lactate test showed no abnormality. Electromyography (EMG) was performed on the right deltoid, biceps, vastus medialis and iliopsoas. Myopathic changes were found only in the iliopsoas muscle: a full interference pattern with small spiky polyphasic units less than 500 μ V. A needle biopsy performed over the left deltoid muscle was normal under both light and electron microscopy.

With a low T_4 level and the exclusion of other causes of painful myopathy, the diagnosis of hypothyroid myopathy was made. Carbimazole was discontinued and within one week, her symptoms subsided, the muscle enzymes returned to normal and thyroid function also became normal (T_4 of 98 nmol/l and TSH of 1.2 μ IU/ml). Her thyrotoxic symptoms

recurred 2 weeks later and carbimazole at 30 mg/day with thyroxine 50 µg/day and propranolol 30 mg/day daily was restarted. With this regime, there was no recurrence of the painful myopathy over a follow-up period of 4 months.

Case 2

A 38 year old man presented with a weight loss of 13 kg and heat intolerance for 3 months. The thyroid gland was one and a half times enlarged. A diagnosis of Graves' disease was made. Serum T_4 was 287 nmol/l and free thyroxine index (FTI) 284 (normal 76–152). Radioactive iodine 315 MBq was given and he became euthyroid 4 months afterwards. However, T_4 repeated one year later was 208 nmol/l with FTI 236 and so a second dose of 150 MBq radioactive iodine was given.

When seen again 6 weeks later, he complained of tiredness and muscle cramps. T_4 was only 27 nmol/l with TSH of 1.2 µIU/ml. He was admitted 3 days later for severe generalized muscle stiffness and weakness. He was unable to move any of his limbs and the muscle would go into spasm whenever that part was being moved. The spasm was so severe that on one occasion he could not brake his car resulting in a collision. There was clumsiness of movement and weakness of girdle muscles together with myotonic-like reaction. The muscle bulk was increased and all muscles felt stiff and firm. There was delay in relaxation of the bicep and ankle reflexes.

Laboratory investigation revealed elevated muscle enzymes (creatine kinase 7290 µmol/min.1). Serum T_4 was undetectable on two occasions and TSH was 36 µIU/ml. EMG of the right deltoid, biceps, vastus medialis and iliopsoas did not reveal myotonia or myopathic changes. The patient refused a muscle biopsy. The clinical picture was compatible with Hoffman's syndrome. Thyroxine was started at 50 µg/day together with triiodothyronine 60 µg/day. His muscle power showed marked improvement and his muscle cramps and stiffness gradually subsided over one month. The muscle bulk also reverted to normal. Triiodothyronine was stopped 3 months later and the thyroxine dosage was gradually increased to 150 µg/day. His thyroid function returned to normal 4 months after the onset of muscle stiffness.

Discussion

Myopathy is a known complication of long-standing hypothyroidism and the incidence of musculoskeletal symptoms varies from 30–80% in different series.^{4,5,6} Kocher¹ and Debre & Semelaigne² described a syndrome of muscular hypertrophy associated with delayed muscle relaxation in two athyreotic cretins. Hoffman³ in 1897 reported an adult who developed

stiffness and difficulty in relaxation of muscles with typical myotonic response to contraction, percussion, and electrical stimulation after thyroidectomy. In Hoffman's syndrome, the patients typically complain of cramps, ache and pain in muscles of the shoulder and pelvic girdles. They have enlarged muscles, weakness, slow movements and delayed relaxation of tendon reflexes. Although the Kocher-Debre-Semelaigne syndrome and Hoffman's syndrome were initially described in different age groups, some authors regard them as variants of the same disease process.^{7,8}

Elevation of the serum creatine kinase in hypothyroidism is common, and the level is proportional to the degree of the hypothyroid state.⁹ Electromyographic abnormalities are also common with an overall incidence of 61%.¹⁰ These usually take the form of myopathic changes with frequent small-amplitude and short-duration polyphasic motor units on moderate volition. A myotonic-like reaction or pseudomyotonia has rarely been described, being differentiated from true myotonia by the absence of the classical waxing and waning characters seen in the latter.^{7,11} The mounding phenomenon of myxoedema on percussion of the exposed muscles is electrically silent on EMG.¹² Histologically, muscle fibre enlargement, focal myofibrillar degeneration, increases in central nuclei, glycogen and mitochondrial aggregates, subsarcolemmal accumulations of lipofuscin are present.^{13,14} There is also dilatation of the sarcoplasmic reticulum and proliferation of the T-system. Some authors described an increase in Type I fibre area and selective atrophy of Type II fibres, together with low mitochondrial enzyme activities. The mitochondrial abnormalities are postulated to be due to metabolic disturbances in oxidative phosphorylation.^{15,16} Upon treatment with thyroxine, the symptomatology, creatine phosphokinase, the EMG changes and the muscle morphology all revert back to normal.^{16,17,18}

Myopathy may occur in patients with hypothyroidism of idiopathic,¹⁹ or familial cases,²⁰ post-thyroid irradiation,²¹ post-Hashimoto's thyroiditis,²² post-thyroidectomy,³ and post-radioactive iodine therapy hypothyroidism.²³ All the cases reported so far had long duration of hypothyroidism with florid features of myxoedema and a very low T_4 level. Our two patients had only a short period of biochemical hypothyroidism – 2 weeks in the first and 6 weeks in the second. Moreover, the degree of hypothyroidism was very mild in the first patient. Thus, while there was marked elevation of muscle enzymes, EMG only showed mild myopathic changes, and the muscle biopsy was normal. The explanation may be that morphological changes in the muscles have not taken place within the short duration of mild hypothyroidism. In a study with rabbit, histological changes cannot be detected till 4 to 8 weeks after thyroidec-

tomy.²⁴ In the second case, although the duration of hypothyroidism was also relatively short, the degree of hypothyroidism was profound and hence the full picture of Hoffman's syndrome was produced. In both patients, the muscle enzymes were markedly elevated when the T₄ levels were low, but returned to normal upon being rendered euthyroid.

Acute transient hypothyroidism is encountered frequently in acute thyroiditis due to lymphocytic thyroiditis or de Quervain's thyroiditis and over-treatment in Graves' disease and Hashimoto thyrotoxicosis. It may also occur immediately after thyroidec-

tomy, or a few months after radioactive iodine therapy for Graves' disease. The majority of these patients tend to be clinically euthyroid, and their thyroid function usually normalises once the thyroid gland has recovered from the insult or when the anti-thyroid drug is withdrawn. We suggest that myopathy in acute transient hypothyroidism is not rare and should be considered as a differential diagnosis of painful myopathy in the appropriate clinical setting. Our patients, particularly the first one, illustrate that the dramatic symptoms of myopathy may be the initial presentation in acute hypothyroidism.

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