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Hoffmann's Syndrome As Manifestation of Hypothyroidism : A Rare Presentation

Medical Science

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ABSTRACT

Hypothyroidism is a common disorder and its manifestations are associated with several systemic disease like cardiovascular, neurological and musculoskeletal system and in the musculoskeletal system the involvement is unclear, although cross reactivity of anti-thyroid auto-antibodies or auto-reactive T cells with other organs may play a significant role in the proccess. Presenting as myopathy and muscular hypertrophy of calf muscles a very rare presentation.[1] Hoffmann's syndrome is a specific form of hypothyroid myopathy , which causes proximal muscle weakness and pseudo hypertrophy of calf muscles due to connective tissue deposition. [2] Similar presentation of calf muscle hypertrophy with weakness is also seen in Duchenne and Becker muscle dystrophy, focal myositis, sarcoid granulomas, and due to amyloid deposits in muscles. Thyroid myopathy is reversible with treatment.

INTRODUCTION

Hoffmann's syndrome was first described in 1897 in an adult who developed muscle stiffness and difficulty in relaxation of muscles after thyroidectomy.[3] Similar presentation in children with cretinism is referred as Kocher-Debré-Sémélaige syndrome. Hypothyroid myopathy being responsible for 5% of acquired myopathies.[4] The hypothyroid myopathy could be divided into four subtypes hoffmann's syndrome, kocher-debre-semelaigne syndrome ,atrophic form and myasthenic syndrome. Severity of myopathy depends on duration and degree of thyroid hormone deficiency. Although it is a rare condition , the myopathy may be the first presentation of hyothyroidism.

CASE REPORT

A 20-year-old male presented with complaint of weakness in lower limbs and easy fatigability for last 6 months. He had difficulty in getting up from squatting position and climbing stairs. He also had complain of frequent muscular cramps, stiffness and pain in muscles.The patient had no significant past history in terms of diabetes mellitus, hypertension, any prolonged drug intake or any chronic disease as well as no significant family history



Figure 1: Coarse facial features and tongue hypertrophy in hoffmann's and improvement after thyroxine replacement

On examination, he was found to have coarse facial features including periorbital puffiness, dry skin with large tongue [Figure1] and hoarseness of voice as well as mild pedal edema. He had a pulse rate of 62/min and blood pressure was 110/90 mm Hg. Evaluation of cardiovascular and respiratory systems did not reveal any significant abnormality. On neurological examination upper limbs were normal in terms of mid-arm circumference and in lower limbs hypertrophy of bilateral calf muscles [Figure2] was present, with normal tone and Grade 3 power in bilateral proximal group of muscles and Grade 4 power in distal groups of muscles. On examination of deep tendon reflexes there was a classical prolonged relaxation phase of bilateral ankle jerk causing a "hung up" reflex (Woltman's sign) with similar findings of knee jerk, while the sensory examination was normal along with no bowel or bladder involvement. Laboratory investigation revealed a free triiodothyronine (fT3) level of <1.54 pmol/L (normal range: 2.63-5.71 pmol/L), free thyroxine (fT4) level of <5.16 pmol/L (normal range: 9.30-19.09 pmol/L), and the activity of thyroid stimulating hormone (TSH) was more than 100 mIU/L (normal range: 0.4-4.2 mIU/L). Anti-thyroid peroxidase (anti-TPO) antibody was elevated being 62.73IU/ (normal range 0-60IU) and Creatine phosphokinase (CPK) level was 12870 IU/l (normal level: <170 U/l). Hemoglobin was 11.0gm/dl, Lipid profile evaluation showed hypercholesterolemia (240 mg/dl) and hypertriglyceridemia (180 mg/dl). Electrocardiography showed low-voltage complexes and sinus bradycardia. Two-dimensional echocardiography showed grade 2 diastolic dysfunction. Blood sugar, liver function tests, renal functions and urine examination test were within normal limits.Nerve conduction velocity study was normal and Electromyography showed small-amplitude myopathic motor unit potential. Muscle biopsy from calf muscles showed bundles of hypertrophic skeletal muscle fibre with evidence of vacuolisation and split fibres indicating pseudohypertrophy of calf muscles . Based on the above findings, a diagnosis of Hoffman's syndrome was made.



Figure 2:Pseudohypertrophy of calf muscles and improvement after thyroxine replacement

TABLE 1: PRE AND POST TREATMENT VALUES OF

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SERUM TSH AND CPK

	TSH (mIU/L)	fT3 (pmol/L)	fT4(pmol/L)	CPK(IU/L)
NORMAL	0.4-4.2	2.63-5.71	9.3-19.09	24-135
Before treatment	>100	<1.54	<5.16	12870
After 6 weeks	77	5.93	19.34	333
After 3months	10	6.12	24.58	170

mIU/L: milli-international units of biological activity per Litre of serum pmol/L:Picomoles per Litre of serum

DISCUSSION

Primary hypothyroidism accounts for 95% of the cases of thyroid insufficiency. The main etiology is Hashimoto's thyroiditis,[5] an autoimmune chronic thyroiditis which is characterized by high levels of thyroid peroxidase antibodies (anti-TPO) and thyroglobulin antibodies (anti-Tg). Both of these antibodies are found in almost 100% of patients with Hashimoto's thyroiditis. The anti-TPO Antibody is of higher affinity and found in higher concentrations and is the best choice if only a single test is ordered.[6] The primary hypothyroidism presenting as pseudohyperthrophy of muscle is very rare.[7] It has been postulated that the mechanism causing pseudo hypertrophy of muscles in Hoffman's syndrome could include an increase in connective tissue, increase in size and the number of muscular fibers. There is also change in the form of muscle fibres from fast twitching type II to slow twitching type-I fibers,[8] responsible for slowed muscle contraction and relaxation, known as hypothyroid myopathy, which often reverses on treatment. Abnormalities in oxidative enzymatic activity and accumulation of glycosaminoglycans leading to muscle hypertrophy are also seen.[9] The most common muscles groups involved are the tongue, arm and leg muscles. The muscle hypertrophy and muscle weakness will recede following treatment with thyroid hormones.

The creatine phospokinase(CPK) levels usually elevated in thyroid myopathy some times 100 times greater than normal level, however there is no relation between the level of serum CPK and the degree of weakness . The CPK is the best marker of myopathies. Muscle degeneration is thought to be the cause of elevated CPK. Other possible cause includes decreased CPK clearance .The fall of enzyme levels with the treatment occurs slowly, varying from weeks to months or even years. Hoffmann's syndrome is a specific, rare form of hypothyroid myopathy, which causes proximal muscle weakness and pseudo hypertrophy of muscles, due to connective tissue deposition . Usually this is sporadic, though reports of Hoffman's syndrome occurring in family members throw light on a genetic basis for the disease .

Calf muscle hypertrophy can have a variety of causes like genetic dystrophies, myositis, Sarcoid infiltration and neurogenic hypertrophy .The differentiation between these entities is done by clinical features, serum markers like TSH, EMG studies and response to thyroxin replacement. However, Hoffmann's's Syndrome can also present without other manifestations of hypothyroidism, and high degree of suspicion is needed. Hoffmann's's syndrome has quite good prognosis . Worsening of symptoms in some cases at the beginning of treatment may occur, probably caused by rise in metabolic demand induced by thyroxine. In these cases, the concomitant use of steroids during some time of the treatment, as membrane-stabilizing effect can be beneficial .

CONCLUSION

Hypothyroidism is a very common endocrine disorder and clinicians should be aware of this atypical and rare presentation of this syndrome that will lead to correct diagnosis & it represents those few forms of myopathy that completely reverses on prompt therapy and, hence has a good outcome. Our patient presented with predominant proximal muscle weakness and hypertrophy of calf muscles. His CPK levels were elevated more than 100 times the normal, and Anti-TPO antibody titers were also elevated. EMG showed myopathic motor unit potentials (MUAPs) with small amplitude in proximal muscles, and nerve conduction study was normal. Our patient was administered a starting dose of 100 μg/day of levothyroxine which was later escalated to 125 μg/day. On routine follow-up, the clinical manifestations were relieved,well being improved,also the muscle power was regained with significant reduction in muscle bulk, and on investigations CPK and TSH enzymes [Table 1] levels returned to normal with hormone replacement therapy.

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