International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Hoffmann Syndrome: A Reversible Hypothyroid Myopathy in a Young Adult

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Abstract: ***Hoffmann syndrome is a rare manifestation of hypothyroid myopathy characterized by muscle weakness, pseudohypertrophy, and elevated muscle enzymes. Although alarming in presentation, it is potentially reversible with early diagnosis and treatment. We report a case of a 22-year-old male who presented with bilateral calf hypertrophy, lower limb pain, and muscle weakness. Investigations revealed severe hypothyroidism with markedly elevated creatine phosphokinase levels. The patient showed complete clinical and biochemical recovery following thyroid hormone replacement and a structured rehabilitation program. This case highlights the importance of considering endocrine causes in patients presenting with unexplained muscle hypertrophy and emphasizes the role of rehabilitation in functional recovery.***

Keywords: Hoffmann syndrome, hypothyroid myopathy, pseudohypertrophy, creatine phosphokinase, rehabilitation

1. Introduction

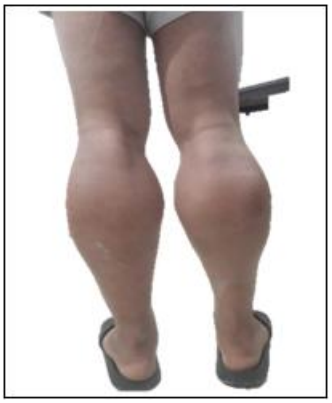
Hypothyroid myopathy is a well-recognized complication of thyroid hormone deficiency; however, **Hoffmann syndrome** represents a rare and distinctive variant characterized by muscle pseudohypertrophy, weakness, and significantly elevated serum muscle enzymes. Due to its rarity and resemblance to primary muscle disorders, diagnosis is often delayed. Early identification is crucial, as prompt thyroid hormone replacement can lead to complete reversal of symptoms. We present a rare case of Hoffmann syndrome in a young adult male, highlighting its clinical features, diagnostic challenges, and rehabilitation outcomes.

2. Case Report

A 22-year-old male presented with complaints of burning sensation and intermittent crampy pain in both lower limbs for one year, associated with progressive weight gain. There was no history of trauma, strenuous exercise, drug intake, or similar illness in the family.

On examination, the patient had a body mass index of 27.1 kg/m². Neurological examination revealed normal higher mental functions and intact sensory system. Motor examination showed muscle power of 5/5 in both upper limbs and hip flexors and abductors, while hip extensors, knee flexors and extensors, and ankle plantarflexors had a power of 4/5 bilaterally. Deep tendon reflexes revealed reduced knee jerks bilaterally, with equivocal ankle jerks. No fasciculations or muscle atrophy were noted in other muscles. Bilateral calf pseudohypertrophy was present, with a circumference of 50 cm.

Laboratory investigations revealed markedly elevated creatine phosphokinase (10,119 U/L), elevated lactate dehydrogenase (906 IU/L), raised C-reactive protein (7.04 mg/L), and severe hypothyroidism with thyroid-stimulating hormone levels of 100 µIU/L. Serum cholesterol was elevated (329 mg/dL). Complete blood count, liver and renal function tests, serum electrolytes, and urine myoglobin were within normal limits. Electromyography showed low-amplitude motor unit action potentials with a complete interference pattern and no spontaneous activity. Electrocardiography and echocardiography were normal, initially muscle biopsy was planned to rule out metabolic myopathies but clinical and biochemical findings were suggestive of **Hoffmann syndrome secondary to hypothyroidism** was made.



3. Management and Outcome

The patient was managed in a multidisciplinary setting. Thyroid hormone replacement was initiated with levothyroxine (75 µg/day). He was also advised lifestyle modification, including dietary counseling for hypercholesterolemia, weight management, and a supervised rehabilitation program focusing on gradual strengthening exercises.

On follow-up, significant biochemical and clinical improvement was observed. Lactate dehydrogenase normalized within 6 weeks, thyroid-stimulating hormone normalized by 8 weeks (2.5 mIU/L), and creatine phosphokinase levels decreased to 870 U/L by 12 weeks. Serum cholesterol reduced to 190 mg/dL. Clinically, muscle strength improved to 5/5 in all muscle groups, and bilateral calf hypertrophy regressed completely.

4. Discussion

Hoffmann syndrome is a rare form of hypothyroid myopathy characterized by proximal muscle weakness,

pseudohypertrophy of muscles, and significantly elevated muscle enzymes. Although musculoskeletal manifestations are frequently seen in hypothyroidism, the Hoffmann variant is uncommon and often underdiagnosed, particularly in younger patients. The condition was first described by Hoffmann in 1897 and is considered a rare but reversible complication of long-standing hypothyroidism[1].

Patients with Hoffmann syndrome typically present with progressive proximal muscle weakness, muscle stiffness, cramps, delayed relaxation of deep tendon reflexes, and pseudohypertrophy of the calf muscles[2]. The enlargement of the calf muscles is believed to result from muscle fiber hypertrophy, increased connective tissue, and accumulation of mucopolysaccharides within the muscle tissue[3]. These changes often lead to functional impairments such as decreased endurance, reduced exercise tolerance, and difficulty performing activities of daily living. In the present case, the patient demonstrated lower limb weakness associated with calf pseudohypertrophy, which contributed to pain, early fatigability, and reduced functional capacity, findings consistent with previously reported cases.

Marked elevation of **creatine phosphokinase (CPK)** is frequently observed in hypothyroid myopathy and may mimic inflammatory or metabolic muscle disorders. Consequently, patients may undergo extensive diagnostic evaluation before the underlying endocrine disorder is recognized[4]. Previous studies have emphasized the importance of considering hypothyroidism as a reversible cause of myopathy to avoid unnecessary invasive investigations such as muscle biopsy[2,4]. Electromyography findings are often nonspecific and typically demonstrate a myopathic pattern, including low-amplitude, short-duration motor unit potentials[1].

The primary treatment for Hoffmann syndrome is **thyroid hormone replacement therapy**, which usually results in gradual improvement in muscle strength and normalization of serum muscle enzyme levels[5]. Clinical recovery may take several weeks to months depending on the severity and duration of hypothyroidism prior to treatment initiation. In addition to pharmacological therapy, **rehabilitation plays an important supportive role** in improving functional outcomes. A structured rehabilitation program including graded strengthening exercises, endurance training, and lifestyle modification can help prevent deconditioning and restore physical function.

Early diagnosis and prompt initiation of thyroid hormone therapy, combined with multidisciplinary management, can lead to complete functional recovery in most patients. Early rehabilitation intervention further enhances recovery by improving muscle strength, reducing fatigue, and promoting independence in daily activities.

5. Conclusion

Hoffmann syndrome, though rare, should be considered in the differential diagnosis of patients presenting with muscle hypertrophy and weakness. Early diagnosis and timely thyroid hormone replacement, combined with a structured rehabilitation program, can result in complete functional and biochemical recovery.

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