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Case Reports

Hypothyroidism Presenting as Hoffman's Syndrome – A Case Report

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Abstract

Hoffman syndrome is characterized by pseudohypertrophy of muscles, muscle's weakness & stiffness complicating hypothyroidism. We describe the disorder in a 45 years old female admitted with complaints of myalgia, proximal muscle weakness & calf muscle hypertrophy since 11 months. Thyroid function tests, marked elevation of muscle enzyme, electromyogram & muscle biopsy established the diagnosis of thyroid myopathy with Hoffman's syndrome. Therapy with levothyroxine resulted in marked clinical & biochemical improvements.

***Keywords**: Hoffman syndrome; Thyroid myopathy; Hypothyroidism.*

Introduction

Hoffman's syndrome was first described by Hoffman in 1897 in an adult who developed muscle stiffness and difficulty in relaxation of muscles after thyroidectomy.[1] It is characterized by the presence of hypothyroidism with muscle stiffness & pseudohypertrophy. Whereas muscle hypertrophy with weakness & slowness of movement in cretinous children is known as Kocher Debre Semelaigne Syndrome.[2, 3] However the two conditions tend to merge into each other & may even occur although at different times in the same patient.[4] In India only few cases have been reported so far [2,5,6] & to the best of our knowledge, the present case is the first case reported from this part of the country.

Case Report

A 42 years old married woman was admitted with complaints of muscle cramps, myalgia, proximal muscle weakness, fatigability, hoarseness of voice & difficulty in walking since 11 months. There was no history of dyspnoea, chest pain, jaundice, oliguria, constipation, cold intolerance, prolonged fever, hematuria, drug intake, hypertension or diabetes mellitus. Her developmental history & milestones were consistent with age. None of the family members from maternal & paternal side suffered from such illness. On examination, she weighed 74 kg with height of 168 cm & was conscious & oriented. She had puffiness of face, enlarged tongue, dry rough skin with non pitting bilateral ankle edema. She looked lethargic & her activities were slow. Thyroid was non tender & non enlarged. Pulse was 54 beats/min, regular, with no special character & all the peripheral pulses were palpable & synchronous. BP was 130/80 mm Hg and JVP normal. Examination of CVS, abdomen & respiratory system was unremarkable. Fundus examination was normal. CNS examination revealed pseudo- hypertrophy of calf muscles with normal tone. Power was grade 4 in the proximal muscles in the lower limbs & grade 5 else where. Deep tendon reflexes especially ankles showed delayed relaxation. Plantar reflexes were flexor. There was no sensory impairment or cerebellar signs. All cranial nerves were normal. Laboratory investigations on admission revealed Hb 12.5 g/dl, TLC 6700/mm^3, DLC P_{62}, L_{38}, E_0,B_0, ESR 38 mm at the end of first hour, peripheral blood film showed normocytic normochromic anemia, urine analysis normal, & RBS 81 mg/dl, blood urea 32 mg/dl, serum creatinine 1.2 mg/dl, serum Na^+ 135 mmol/L, Serum K^+ 4.6 mmol/L, Uric acid 5.1 mg/dl, S.cholesterol 320 mg/dl, S. Bilirubin 0.6 mg/dl, S. Protein 5.8 g/dl, S. triglycerides 260 mg/dl, SGOT 45 IU/L, SGPT 50 IU/L, alkaline phosphatase 113 IU/L, S.Calcium 9.1 mg/dl, S. Phosphorus 4.3 mg/dl, S. LDH 692 U/L (N 100-190 U/L), Rheumatoid Factor & antinuclear antibody being negative, CPK 512 U/L (N 25-90 U/L), S. Aldolase 13.9 U/L (N = 0-6 U/L). X ray chest showed cardiomegaly with ECG showing bradycardia & low voltage complexes. 2D Echocardiography showed diastolic dysfunction with 49% ejection fraction. U/S abdomen was noncontributory. Thyroid function tests revealed TSH 23.2

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micro units/ml (N 0-4.5), T4 3.1 µg/dl (Normal 5-12 µg/dl), T3 45.2 ng/dl (Normal 70-190 ng/dl). Antithyroid levels 1002 µ/ml (Normal 40 µ/ml), antiperoxidase 905 µ/ml (Normal = 35 µ/ml). Ultrasound thyroid showed atrophy. Electromyogram (EMG) showed polyphasic action potentials consistent with thyroid myopathy and nerve conduction velocities were normal. The muscle biopsy taken from hypertrophied calf muscles showed muscle fibre hypertrophy, increased nuclei, mucoid deposits at places with increased interfibreground substance thus conforming the diagnosis of hypothyroid myopathy with Hoffman's syndrome. The patient was treated with levothyroxine starting from 25 µg/day & increased to 100 µg/day. The patient showed significant improvement in the symptoms within 4 weeks. All the above investigations were repeated at 6 months interval, which showed marked improvement in the symptomatology & biochemical parameters including muscle enzymes but there was insignificant improvement of muscle hypertrophy despite 6 months of 200 µg thyroxin therapy. But the patient lost weight to 71 kg. The patient is doing well & is on regular follow up.

Discussion

The signs & symptoms related to hypothyroid myopathy include cramps, muscular weakness, myalgia, stiffness, myxedema & hyporeflexia. Muscle hypertrophy, wasting, rhabdomyolysis are unusual features.[7,8] Proximal muscle hypertrophy in adult hypothyroidism is known as Hoffman's syndrome.[7,9] The entire musculature is affected to some extent but the most obvious enlargement is in the tongue, arms & legs. The main etiology is Hashimoto's thyroidits, an auto immune chronic thyroiditis characterized by high levels of antiperoxidase (anti TPO) & antithyroglobulin as documented in our case. Antithyroglobulin is present in 80-90% of cases & anti – TPO in 90-100% of cases.[10] The muscle involvement in hypothyroidism is characterized by changes in muscle fibres from fast twitching type II to slow twitching type I fibres, deposition of glycosaminoglycans, poor contractility of actin-myosin units, low myosin ATPase activity & low ATP turnover in skeletal muscle.[7] Histological changes include type 2 fibre hypertrophy or atrophy, myofibre necrosis & regeneration & prominent core-like areas containing amorphous granulofilamentous material.[11] The presence of cores correlated with the severity of hypothyroidism, muscle hypertrophy, cramps & duration of hypothyroid state.[12] Delayed relaxation of tendon jerks & proximal muscle weakness correlate with the biochemical severity of hypothyroidism (Serum T4 < 3.1 µg/dl. The rate limiting step in muscle relaxation is reuptake & calcium by sarcoplasmic reticulum, which is dependent on ATPase content of the muscle fibre. Calcium ATPase activity of the fast twitch of muscle fiber is decreased in hypothyroidism resulting in delayed relaxation. EMG findings in hypothyroidism include slow muscle fibrillations, positive sharp waves & complex repetitive discharges.[13] Muscle biopsies in most of the studies have not revealed any abnormalities.[5,14] The muscle biopsy in our case showed hypertrophy of muscle fibres with increased nuclei, few necrotic fibres & mucoid deposits at places & the findings are similar to those observed by Mishra & Mastropasqua.[2,14] Raised CPK-MM, typical myopathic EMG, low T_4 & T_3, high TSH and their reversibility with levothyroxine favour the diagnosis of hypothyroid myopathy. There is marked improvement in the clinical symptomatology & biochemical parameters with replacement thyroxin therapy. But insignificant improvement of hypertrophied calf muscles in our case is similar to that of Astram et al.[15] Secondary sexual characteristics are not altered.[11] Other less common association of the disorder include peripheral neuropathy, facial weakness, cerebellar ataxia & dementia.

Conclusion

This rare case presentation of Hoffman syndrome in hypothyroidism is highlighted in order to focus the attention of the clinicians on the occurrence of this rare complication in the absence of overt manifestations of hypothyroidism. Hypothyroidism should be considered in the differential diagnosis of proximal muscle weakness.

Conflict of interest: None.

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