**An atypical presentation of hypothyroidism with proximal extremities weakness**

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**Abstract**

Myopathy-related symptoms are rare manifestations of hypothyroidism. Clinicians should consider hypothyroid myopathy as one of possible diagnosis for patients with proximal weaknesses. We report a 34-year-old woman, presenting with a new atypical musculoskeletal manifestation of hypothyroidism mimicking polymyositis.

**Introduction**

Pathological thyroid hormone deficiency known as hypothyroidism is commonly found in general population. More frequently in women and elderly, a European meta-analysis reported that the prevalence of overt and clinical hypothyroidism considers 0.37% and 3.8% as well as 226/100,000 predicted incidence (1, 2). Symptoms are mostly non-specific including constipation, fatigue and cold non-intolerance, thus, the detection of high thyroid-stimulating hormone (TSH) and low free thyroxin (fT4) concentrations is the key diagnostic approach (3). Less common symptoms include dry skin, myxoedema, hoarseness, normochromic and normocytic but infrequently macrocytic anaemia, increased thrombosis risk as well as neurological (encephalopathy and carpal tunnel syndrome). Musculoskeletal manifestations present in 25-79% of adults suffering hypothyroidism such as myalgia, increased serum creatine kinase (CPK) levels, stiffness and cramps (2).

Herein, we introduce a case of a 34-year-old woman, presenting with a new atypical musculoskeletal manifestation of hypothyroidism mimicking polymyositis.

**Case presentation**

A 34-year-old woman without any past medical history presented to emergency room with intensified generalized weakness over the past 2 months. She complained of proximal weakness in both upper and lower limbs to the extent of being hardly able to hair combing. She also complained of constipation and generalized abdominal pain over past 2 months. In addition, she didnot have any family history of rheumatologic disorders. In physical exam, evaluating the force of limbs out of 5, the upper limb in proximal part got 3 and the distal part scored 5. The lower limb proximal and distal parts ranked 3 and 5 respectively. Moreover, the force of cervical flexor muscle reached 4.

Laboratory results of the first day of admission were as follows (Table 1): CPK: 5120, LDH (lactate dehydrogenase): 934, Aldolase: 14.5 (<7.6), Urea: 45, creatinine: 1.5, CRP (c-reactive protein) <3 (negative: <6, Equivocal: 6-9, positive: >9), ESR (erythrocyte sedimentation rate) 1h: 13, TSH (thyroid stimulating hormone) >100, T4 (thyroxine) <0.5, Anti TPO: 906(<5.61), COVID-19 RT-PCR: Negative. Ultrasonography indicated Fatty liver grade 1 and the other parts of abdomen and pelvis was normal.

Assessing malignancies, endoscopy indicated proximal predominant erosive gastritis and colonoscopy was normal. Spiral abdominopelvic computerized tomography (CT) scan was did not show any tumor or abnormality.

High levels of CPK, aldolase, and LDH at first presentation (Table 1), as well as her first clinical presentation let to a possible diagnosis of inflammatory myopathies such as polymyositis, and immune-mediated necrotizing myopathy. Additionally, according to high TSH levels, we started levothyroxine 150 microgram/day.

To further evaluate inflammatory myopathies, EMG-NCS and more laboratory tests were conducted: Creatinine: 1.3, Protein in 24h urine: 35, urea in 24h urine: 14, Cr: 1140, 24h urine volume: 2000, anti-ds-DNA (Anti-double stranded DNA<10 (negative<100, positive>=100), C3: 108 (90-180), C4: 33 (10-40), CH50: 94 (>=90), FANA (fluorescent antinuclear antibody): Negative (no reaction at 1:100). The first EMG-NCV indicated normal sensory/motor NCS and needle exam indicated no myopathy pattern and no spontaneous discharge. To verify the results of the first EMG-NCV, the second was conducted during the first follow-up after two weeks showing normal outcomes as well.

Microscopic findings of biopsy of quadriceps skeletal muscle shows skeletal muscle with mild variation in size of myofibers, few nuclear centralizations and mild increased sacrolemmal nuclei, also a few degenerated and pale myofiber with a few lymphocytic inflammations around small vessels are seen (Figure 1). According to pathological reports, diagnosis was nonspecific myopathy.

During her admission, CPK, LDH, and creatinine concentrations retained higher than reference range (Table 1), however, the showed gradual decrease after starting thyroid hormone therapy. Considering microscopic findings, this case was suggestive for myopathy of hypothyroidism and the patient was discharged prescribed with levothyroxine 150 microgram/day. Her follow-up in two months had normal muscle enzymes and physical examination, and all the symptoms disappeared along with TSH decrease.

**Discussion**

Muscle involvement is a prevalent problem in both congenital and adult hypothyroidism, which can vary intensively (4). Regardless of the fact that these were rarely the initial symptoms of the disease, in a limited sample, 79% of patients with recently diagnosed hypothyroidism experienced of weakness, fatigue, cramps, and myalgias (5).

Non-specific muscle stiffness or diffuse muscle pain, are frequent symptoms in hypothyroidism, which may be in correlation with an increase in the levels of muscle enzymes (6). Proximal muscle weakness gradually increases in time. Hypothyroid myopathy can occasionally be more severe and accompanied by a noticeable rise in muscle enzymes (7-9). The serum CPK level rised in 57 to 90% of individuals with hypothyroid myopathy, long before the onset of typical clinical symptoms of hypothyroidism. Although the level of CPK and the level of TSH have been indicated to correlate in some cases, the level of CPK is not directly related to the severity of clinical symptoms (10).

The exact mechanism of hypothyroid-associated-myopathy remains uncertain. T4 deficiency causes disturbances in glycogenolysis and mitochondrial oxidative metabolism. Consequently, resulting in muscular dysfunction (11). One of the manifestations is specific atrophy of type 2 fibers, which are more reliant on glycolysis for their energy source. Rhabdomyolysis of muscle cells can happen with severe or persistent oxidative damage (12). Several cases of extremely severe rhabdomyolysis associated with hypothyroidism have been documented (13-15).

A hypothyroid evaluation is necessary if any of the aforementioned symptoms or signs cannot be explained by other identified causes. EMG could be helpful in order to distinguish hypothyroid myopathy from inflammatory myositis or other neuromuscular disorders. Nearly 50% of hypothyroid individuals with proximal muscle weakness have normal EMGs, and the rest may show myopathic alterations with increased low-amplitude, polyphasic potentials, and rarely increased insertional activity (6, 16, 17). Muscle biopsy is usually normal or may contain a few non-specific changes such as Mild, focal necrosis, degeneration of muscle fibers and mild inflammatory infiltrates. Indeed, Extensive inflammatory changes can suggest an alternative diagnosis such as polymyositis (16, 18).

Thyroid hormone replacement therapy is efficient in treating hypothyroid myopathy. Within a few weeks, the serum CPK level would return to normal range after a rapid decline, even earlier than TSH (16). Notably, clinical symptoms considering muscular weakness, recover more slowly (6).

In this report, a 34-year-old woman presented with proximal weakness for 2 months in both upper and lower limbs, letting to diagnosis of both inflammatory of hypothyroid myopathy. Further assessment revealed a TSH level more than 25, a CPK total of 5120, and an LDH of 935. These findings strongly imply hypothyroidism-related rhabdomyolysis. Confirming, the EMG-NCV revealed no inflammatory pattern. To more extent, biopsy of skeletal muscle also supported the proposed diagnosis. Normal physical examinations, muscle enzymes and disappearance of symptoms after two months of levothyroxine therapy also confirmed hypothyroid myopathy. Thus, considering hypothyroidism as one of possible differential diagnosis in patients presenting with myopathy symptoms should be considered along with inflammatory or neurological diseases.

**Conclusion**

Hypothyroidism with the first presentation mimicking inflammatory myopathies, called hypothyroidism myopathy, is very rare. Practitioners should precisely consider hypothyroidism as one of the first differential diagnosis while facing high muscle enzymes and recent proximal weakness in order to avoid further unnecessary evaluations and cost in the clinic.

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**CONFLICT OF INTEREST**

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. The Authors declare that there is no conflict of interest.

**ETHICAL APPROVAL**

Written informed consent was obtained from the patient in our study. The purpose of this research was completely explained to the patient and was assured that their information will be kept confidential by the researcher. The present study was approved by the Medical Ethics Committee of the academy.

**CONSENT STATEMENT**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images in accordance with the journal's patient consent policy. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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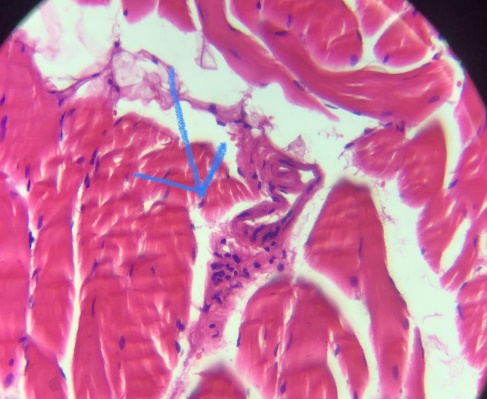
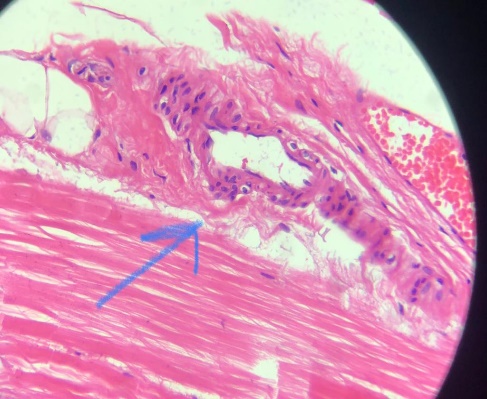
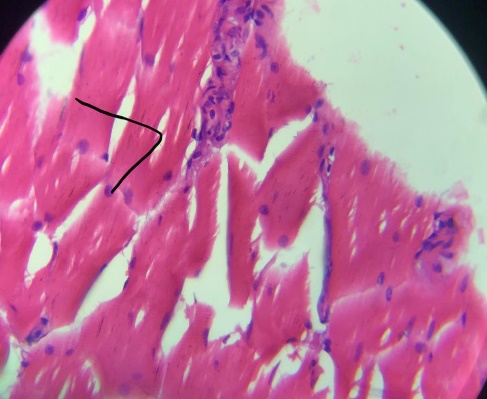
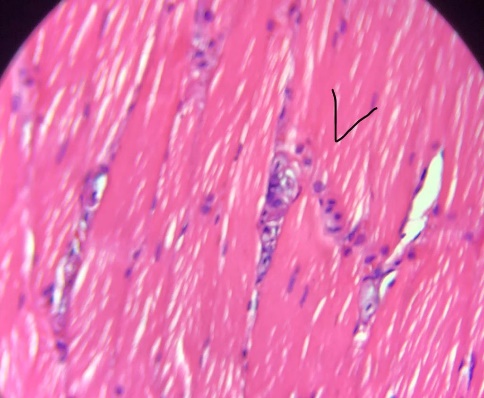
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|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Test, Unit** | **Result** | | | | | | | **Reference Range** |
| **Blood biochemistry** | | | | | | | | |
|  | Admission | 1st Day | 2nd Day | 3rd Day | 4th Day | 5th Day | Discharge |  |
| BS, mg/dL | 106 |  |  |  |  |  |  | 70-120 |
| AST, U/L | 161 |  |  |  |  |  |  | Up to 35 |
| ALT, U/L | 84 |  |  |  |  |  |  | Up to 45 |
| ALP, U/L | 133 |  |  |  |  |  |  | 98-279 |
| LDH, U/L | 934 | 907 | 969 | 861 | 757 | 671 | 741 | 225-500 |
| C-Reactive Protein | <3 |  |  |  |  |  |  | negative: <6,  Equivocal: 6-9,  positive: >9 |
| Creatinine, mg/dL | 1.5 | 1.6 | 1.5 |  | 1.5 | 1.4 | 1.3 | 0.6-1.2 |
| Urea, mg/dL | 45 |  | 29 | 22 | 30 | 32 | 34 | 10-50 |
| Uric Acid, mg/dL | 3.9 |  |  |  |  |  |  | Male 3.4-7  Female 2.4-5.7 |
| Na, mmol/L | 133 | 143 | 138 |  | 139 | 138 | 138 | 135-148 |
| K, mmol/L | 3.8 | 4.1 | 4 |  | 4.5 | 3.9 | 4.3 | 3.5-5.3 |
| Ca, mg/dL | 10.3 |  |  |  |  |  |  | 8.8-10.2 |
| P, mg/dL | 3.6 |  |  |  |  |  |  | 2.5-5 |
| Mg, mmol/l | 2.4 |  |  |  |  |  |  | 1.9-2.5 |
| Alb, g/dl | 4.7 |  |  |  |  |  |  | 3.6-4.8 |
| CPK Total, U/L | 5120 | 4059 | 3056 | 2668 | 2275 | 1866 | 1718 | 24-170 |
| Aldolase | 14.5 |  |  |  |  |  |  | <7.6 |
| CK-MB, IU/L | 62 |  |  |  |  |  |  | <24 |
| Troponin I ultra, ng/mL | 2.00 |  |  |  |  |  |  | Without myocardial damage: <19 |
| **Hematology** | | | | | | | | |
| WBC, µL | 9400 |  |  |  |  |  |  | 4000-11000 |
| RBC, 10^6/µL | 3.88 |  |  |  |  |  |  | 4.2-6.3 |
| Hb, g/dL | 12.2 |  |  |  |  |  |  | 12-16 |
| Hematocrit, % | 36.1 |  |  |  |  |  |  | 30-45 |
| MCV, fL | 93.0 |  |  |  |  |  |  | 80-100 |
| MCH, pg | 31.4 |  |  |  |  |  |  | 27-32 |
| MCHC, g/dL | 33.7 |  |  |  |  |  |  | 33-38 |
| Platelet, µL | 290000 |  |  |  |  |  |  | 150000-450000 |
| Neutrophil, % | 60 |  |  |  |  |  |  | -- |
| Lymphocyte, % | 36 |  |  |  |  |  |  | -- |
| **Serology and Endocrinology** | | | | | | | | |
| ESR 1h | 13 |  |  |  |  |  |  | 20> |
| COVID-19 RT-PCR | negative |  |  |  |  |  |  |  |
| Urine 24hr/ Pr, mg/24hr |  |  | 35 |  |  |  |  | 24-141 |
| Urine 24hr/ Urea, g/24hr |  |  | 14 |  |  |  |  | 13-36 |
| Urine 24hr/Cr, mg/24hr |  |  | 1140 |  |  |  |  | 600-1800 |
| Urine 24hr/Volume, ml |  |  | 2000 |  |  |  |  | -- |
| TSH | >100 |  |  |  |  |  |  | 0.27-4.2 |
| T4 | <0.05 |  |  |  |  |  |  |  |
| Anti-TPO antibody | 906.03 |  |  |  |  |  |  | <5.61 |
| Anti-ds DNA |  | 10 |  |  |  |  |  | negative: <100,  positive: >=100 |
| C3 |  | 108 |  |  |  |  |  | 90-180 |
| C4 |  | 33 |  |  |  |  |  | 10-40 |
| CH50 |  | 94 |  |  |  |  |  | >=90 |
| FANA |  | negative |  |  |  |  |  | Negative: no reaction at 1:100  Trace: positive reaction at 1:100  Positive: positive reaction at 1:320 or more |

**Table 1.** Serial laboratory results



1

2

3

4

5

**Figure 1.** Microscopic findings of biopsy of quadriceps skeletal muscle; (1,2): mild variation in size of fiber, nuclear sacrolemmal proliferation, (3,4): few lymphocytic infiltrations around small arteries, (5): basophilic change in a few fiber arteries