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An Unusual Case of Rheumatoid Arthritis with Hypothyroidism Presenting with Inflammatory Myopathy (Polymyositis)

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Abstract

In this case, the patient was diagnosed with rheumatoid arthritis 5 years back. She had also developed symptomatic autoimmune hypothyroidism before 2 years which was managed by levothyroxine. She presented this time with inflammatory myopathy. The search of literature revealed very few cases having all these together. Inflammatory myopathies are heterogeneous group of disorders which include polymyositis (PM), dermatomyositis, and inclusion body myositis. Many features of these disorders overlap. These three conditions (rheumatoid arthritis, hypothyroidism, and PM) have similarities in genetic etiology and presentation. The association between them is discussed here.

Keywords: Polymyositis, inflammatory myopathy, rheumatoid arthritis, hypothyroidism.

Background

Autoimmune diseases are often coexistent. It can be due to genetic susceptibility and same human leukocyte antigen (HLA) associations. Rheumatoid arthritis is a progressive inflammatory disease which can lead to deformities if untreated. The treatment of rheumatoid arthritis mainly includes disease-modifying antirheumatic drugs (DMARDs) and concurrent short duration corticosteroids. Autoimmune thyroiditis is also a progressive inflammatory disorder, Hashimoto thyroiditis is most common in middle age females. Association between the right atrium (RA) and thyroid disorders (autoimmune and non-autoimmune) is found in 6%–34% of patients [26] and, when only considering thyroid antibodies as criteria, irrespective of thyroid function, the prevalence is as high as 38% in RA cases. The inflammatory myopathies are heterogeneous group of diseases which feature muscle inflammation, weakness, and sometimes associated with pain. Each subtype shows distinct clinical, histopathological, and pathophysiologic features; however, sometimes, symptoms overlap. Incidence of myositis is in the range of 0.1–1/100,000 person-years. Incidence is almost double in women compared to men. Major subtypes of inflammatory myopathies are dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM). Among them, DM is the most common form. Bohan and Peter first defined PM with characteristic features of the absence of DM rash, elevated serum enzymes, proximal muscle weakness, electromyography (EMG) findings, and muscle biopsy findings [1]. Many patients having IBM are misdiagnosed as PM. Causes of many cases of the inflammatory myopathies are idiopathic. Coexistence of all three disorders - RA, hypothyroidism, and PM is extremely rare and hence reported here.

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Case Report

The patient was a 52-year-old female who was a known case of rheumatoid arthritis, was admitted with chief complaints of difficulty in swallowing, weakness, pain in neck, and proximal muscles. Her symptoms started before 9 months; first, she developed difficulty in swallowing for solid food which worsened over time and it had slowly been progressive in course with choking character. She also developed difficulty in speech with slowly progressive course. Later, she had difficulty in raising her both upper limbs above shoulders, climbing the stairs, and standing from the sitting position, suggesting proximal muscles' involvement. There was no abnormality on neurological examination in the form of peripheral or central nerves, and no fasciculation was seen. The patient was found to be hypokalemic on admission. She had significant history of rheumatoid arthritis. It had started with complaint of polyarthralgia 5 years ago for which she was admitted due to exacerbated polyarthralgia, multiple subcutaneous nodules, skin eruptions, and fever. The level of serum creatinine kinase (CK) was within normal range, but C-reactive protein (CRP) was elevated and CH 50 was decreased. The laboratory examination showed positive cryoglobulin and high titer of rheumatoid factor, which led to the diagnosis of RA which was treated with DMARDs and steroid therapy. She also had a history of autoimmune thyroiditis which was managed by thyroxine, her latest thyroid-stimulating hormone level was 0.7303 μ IU/ml on 22/1/2018 (normal range 0.4–4.2). Her current physical examination showed diminished power (+3) in the proximal muscles of both upper and lower extremities. Her distal musculature showed normal power and tone. She had normal deep tendon reflexes on both sides. She did not have any significant skin changes or periorbital heliotrope rash. Gottron's papules were not evident either. There was no evidence of goiter on examination. Her computed tomography scan of thorax and abdomen was normal. Her echocardiography showed normal RA, right ventricle (RV), left atrium, and left ventricle (LV) size with normal LV systolic

function. The left ventricular ejection fraction was 65% (M mode), but there was reduced LV diastolic compliance. Doppler study showed mild mitral and tricuspid regurgitation. There was mild pulmonary artery hypertension with RVSP = 41 mmHg. Her complete blood count showed leukocytosis with increased polymorphs. Her Vitamin B12 level was in normal range. Her Vitamin D3 was low 6.6 ng/ml (30–100). Her upper gastrointestinal endoscopy showed lower end Grade 1 esophagitis, hiatus hernia, and multiple hemorrhagic spots in the stomach. Her ultrasound abdomen was normal. She had gross proteinuria (+++) and hematuria (++) on urine examination on February 24, 2018. Her CRP was elevated 9.8 mg/L (normal range 0–3.3). Her creatinine level was 0.23 mg/dl (normal range 0.55–1.02 mg/dl) and creatine phosphokinase level was 165.08 (34–145). Her lactate dehydrogenase (LDH) level was 152.83 U/L (normal <247 U/L) and her serum glutamic pyruvic transaminase level was 93.02 U/L (normal <35 U/L), serum glutamic oxaloacetic transaminase was 45.37 U/L (<31). She was positive for antinuclear antibodies (ANA); however, other antibodies including anti-Ro 1, anti-Mi 2, anti-centromere, anti-Scl 70, Ro 52, JO 1, anti-nucleosome, and anti-histone were negative. Her deltoid biopsy showed endomysial inflammatory infiltrate, few atrophic fibers, and mild endomysial fibrosis which were highly suggestive of PM. The patient was admitted for 5 days and treated with injection Methylprednisolone 500 mg twice daily, tablet amlodipine 5 mg once daily, syrup potassium chloride 10 ml thrice daily, injection Deriphyllin 110 mg thrice daily, tablet spironolactone 25 mg twice daily, and hydroxychloroquine sulfate (400 mg/day). She was continued on oral methylprednisolone (40 mg/day) and hydroxychloroquine (400 mg/day). Prednisolone was tapered at rate of 5 mg/month, and after 3 months, azathioprine treatment was continued for maintenance. She had considerable improvement in muscle strength (4/5) after 5 months of therapy (Fig. 1 and 2).

Disucssion

Rheumatoid arthritis and thyroid disorders association

Rheumatoid arthritis and autoimmune thyroid disorders have some similarities pathogenesis which include HLA-DR-B1, cytotoxic T-lymphocyte-associated antigen 4, protein tyrosine phosphatase non-receptor type 22, FC receptor-like 3, and interleukin 2 receptor alpha. High cyclic citrullinated peptide (CCP) levels in RA patients with thyroid disorders are more commonly found in HLA-associated variant. High anti-CCP ≥100 EU/mL in such patients indicates the role of genetic factors in the pathogenesis of both conditions (rheumatoid arthritis and hypothyroidism) and also explains the less response to the RA treatment in such patients. In a study, thyroid disorders were found 3 times more prevalent in female patients with RA than the similar control group. Hypothyroidism and Hashimoto's thyroiditis were found in majority of these women [29]

Rheumatoid arthritis and PM association

RA patients who have weakness of limbs can insidiously develop inflammatory myopathy. Patients with rheumatoid arthritis who are on long-term steroid therapy can have similar presentation as PM due to similar pattern of muscle weakness in both conditions. However, EMG studies are useful in differentiating these two conditions. Some studies demonstrate that rheumatoid factor and anti-CCP antibody are commonly seen in patients of idiopathic inflammatory myopathy. However, they have less levels of rheumatoid factor and anti-CCP antibodies compared to other connective tissue diseases [13]. Hence, they can be misdiagnosed as rheumatoid arthritis.

Association between hypothyroidism and PM

Hypothyroidism is associated with muscle weakness in almost 38% of cases. First recorded muscle weakness in hypothyroidism was by Ord, in 1880. Many articles have described a hypothyroid myopathy mimicking PM. Hypothyroidism with musculoskeletal symptoms and dermal mucinosis can mimic PM. Patients who have both PM and thyroid dysfunction are more likely to have higher levels of CRP and IgG as well as higher incidences of fever and erythra. Elevated CK is also seen in hypothyroid patients. Cases of rhabdomyolysis secondary to thyrotoxicosis in hyperthyroid patients also show elevated muscle enzymes. Usually, EMG is normal in hypothyroid patients; however, positive sharp waves and fasciculations may be seen like in PM. There is dysfunction of suppressor T-cells in hypothyroidism and PM as well it may suggest a common pathogenesis. Furthermore, both hypothyroidism and inflammatory myopathy are associated with HLA B8 and DR3. Hence, both of the diseases can be associated and can coexist. Hence, proper evaluation using muscle biopsy and EMG is necessary. The muscle weakness can be easily confused with hypothyroid myopathy or RA-related weakness. Furthermore, such cases can be confused with myasthenia gravis, so diagnosis of PM can be easily missed. Proper investigations including muscle enzymes (aspartate transaminase, alanine transaminase, CK, LDH, and aldolase), EMG, muscle biopsy (PM shows endomysial inflammation with CD8 T-cells, macrophages, and myeloid dendritic cells), magnetic resonance imaging (areas of muscle inflammation and necrosis are seen as intramuscular short tau inversion recovery as hyperintense regions). Replacement of muscle tissue with fibrofatty tissue may be seen on T1-weighted images in inflammatory myopathy and antibodies (ANA, anti-JO 1, anti-MI 2, anti-SRP, anti-ARS, PM Scl, anti-U1 RNP, and anti-U2 RNP can be used to diagnose and differentiate inflammatory myopathies) should be done. As the steroids are the first line of treatment for many autoimmune conditions, they can be initiated in such patients (prednisolone 1 mg/kg/day tapered after 6 weeks). Steroid-resistant patents should be treated by alternative therapy (azathioprine, methotrexate, rituximab, cyclophosphamide, or IVIG) for treatment on presenting condition of PM. Proximal muscle strength and muscle enzyme levels can be used to assess the response of the therapy. There are not many cases reported in the literature which have all the three conditions coexistent. This case shows a unique presentation and also proves the common etiological factors in pathogenesis in the autoimmune conditions. The genetic association of these conditions should be further investigated.

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