CASE REPORT AND LITERATURE REVIEW

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INTRAVENOUS IMMUNOGLOBULIN THERAPY IN A CASE OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH DERMATOMYOSITIS

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Abstract

Idiopathic inflammatory myopathy is a systematic autoimmune disease characterized by chronic muscle inflammation. Dermatomyositis (DM) is an idiopathic inflammatory myositis characterized by muscle pain, muscle weakness, and skin rash. It is important to screen patients with DM for an underlying malignancy. Interstitial lung disease is a major prognostic determinant that increases morbidity and mortality in these patients. Here, we present the successful treatment of a 51-year-old case of DM with interstitial lung involvement with intravenous immunoglobulin. The patient had a history of surgery due to a mass in the rectum and was admitted with complaints of weight loss, muscle weakness, skin rash, and shortness of breath at follow-up.

Keywords: Dermatomyositis, intravenous immunoglobulin, interstitial lung disease

INTRODUCTION

Idiopathic inflammatory myopathy (IIM) is a heterogeneous group of systematic autoimmune diseases characterized by chronic muscle inflammation. Dermatomyositis (DM) is an idiopathic inflammatory myositis characterized by muscle pain, muscle weakness, and rash. It is seen that it peaks between the ages of 45 and 60 in adults (1).

Patients with DM are more likely to have an underlying malignancy. In DM patients over 50 years of age, 30% develop cancer during their clinical course. DM is considered as a part of the paraneoplastic syndrome mediated by cancer-associated secretions and antibodies (2).

Interstitial lung disease (ILD) is a common condition (20-65% of patients) in patients with DM, similar to other connective tissue diseases. Some antibodies thought to be associated with ILD have been identified. ILD is a major prognostic determinant that causes an increase in morbidity and mortality. Severe pulmonary involvement was demonstrated in the presence of anti-MDA5 antibodies. It is a condition that should be screened for with the diagnosis of disease (3).

In this presentation, in a case referred to us for differential diagnosis with complaints of weight loss, muscle pain, weakness, skin rash, and shortness of breath, we wanted to underline the rare simultaneous DM and ILD after being followed up for a mass in the colon.

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CASE REPORT

A 51-year-old male patient was referred to our rheumatology clinic with complaints of weight loss, muscle pain, weakness in the upper and lower extremities, skin rash, and shortness of breath. The patient, who developed general muscle weakness such as inability to stand up about 1 month ago, had an erythematous rash on the upper arm and trunk in the last 10 days. The patient's history revealed that he had been operated on in an external center 2 years ago for a mass in the rectum, and the resected tissue pathology was compatible with squamous cell carcinoma. Tumor markers were found to be normal as a result of malignancy scans performed afterward, and no pathology was observed in the imaging of the patient.

In his physical examination, the manual muscle test revealed 3-/5 strength. In the upper extremity and 3+/5 in the hip flexors in the lower extremity. Deep tendon reflexes were normoactive, and sensory examination was normal. Dermatological examination revealed erythema on the extensor surfaces of the arms and erythematous maculopapular lesions on the anterior and posterior trunks. DM was considered in the foreground, and routine tests were performed. In the laboratory examination, acute phase reactants slightly increased as C-reactive protein was 14 mg/dL (normal range: 0-5 mg/dL), sedimentation was 31 mm/h (normal range: 0-20 mm/h), and aspartate aminotransferase (AST) was 59 U/L (0-40), and lactate dehydrogenase (LDH) was 619 U/L (135-225). Baseline creatine kinase (CK) levels were increased to 574 U/L (0-200). In the rheumatological examinations requested for differential diagnosis, anti-nuclear antibody (ANA) was stained in a 1:160 µmoL positive spotted pattern. In the ANA panel, anti-dsDNA, SS-A, SS-B, and anti-Jo-1 were normal. Rheumatoid factor, anti-cyclic citrulized peptide, and anti-neutrophil cytoplasmic antibodies (P-ANCA, C-ANCA) were negative.

In terms of internal organ involvement, chest X-rays, pulmonary function tests, high-resolution computed tomography, echocardiography, electrocardiography, abdominal ultrasonography, and tumor markers were requested. Electromyography of the patient revealed findings consistent with myogenous involvement. There were dense consolidated areas in the right side of the chest radiograph (Figure 1). While vital capacity was normal in the respiratory function test, the 6-min walk test distance was measured at 340 meters. Thorax tomography was performed, and the right lung upper lobe anterior segment and lower lobe superior segment were dominant; scattered ground glass densities showed nodulation in places; and a fine reticular density increase was detected (Figure 2). It was evaluated by bronchoscopy in terms of malignancy and infection, and no neolasic changes were observed because of the biopsy. Magnetic resonance imaging of bilateral lower extremity muscles showed patchy edematous areas in the quadriceps muscle (rectus femoris, vastus lateralis, and semitendinosus). Based on these clinical, laboratory, and imaging findings, we concluded that the patient had DM with prominent ILD involvement.

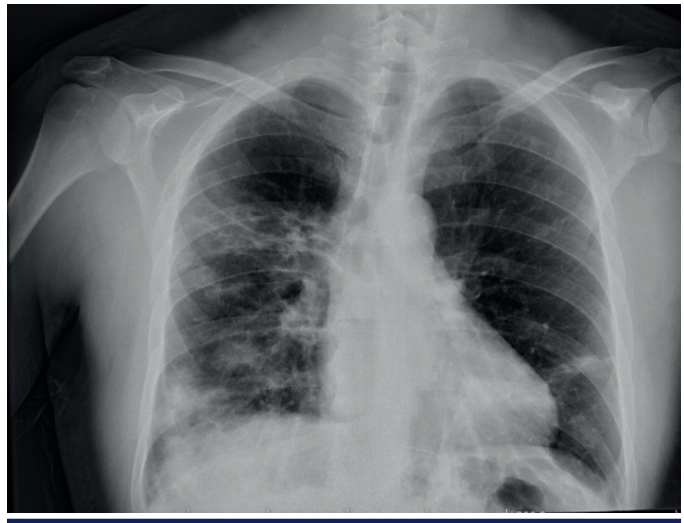

Figure 1. Dense consolidated areas in the right lung

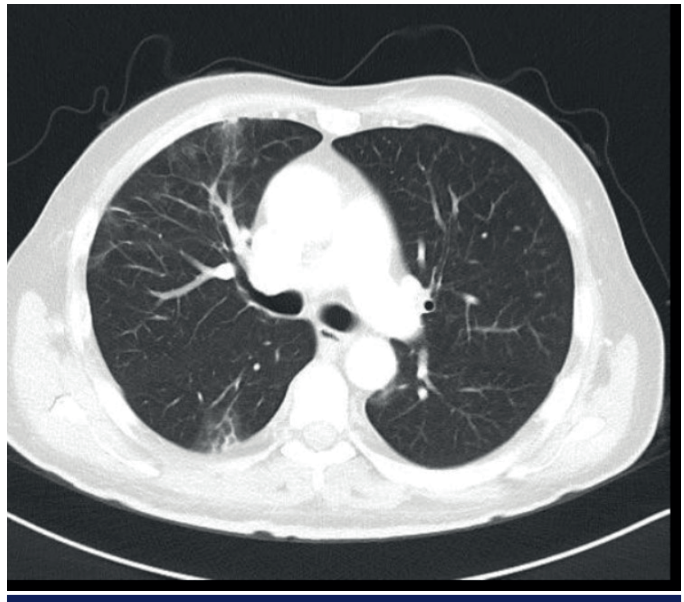

Figure 2. In the evaluation of the lung parenchyma areas, ground glass densities and fine reticular density increases are observed, which is more prominent in the lower lobes of both lungs

Systemic corticosteroid (1 mg/kg/day) treatment was initiated. On the 3rd day of treatment, intravenous immunoglobulin (IVIG) treatment (at 2 g/kg for 5 days) was administered for

lung involvement. On the 7th day of treatment, CK: 142 U/L and LDH: 219 U/L were in the normal range. Clinically, at the end of the 10th day, the patient had regression of skin lesions and increased muscle strength (3+/5, hip flexors 4/5). The steroid dose was gradually reduced. IVIG treatment was continued for 3 months, once a month. At the end of three months, no side effects related to IVIG treatment were observed. In the thorax tomography of the patient, regression was observed in the ground glass areas (Figure 3). The patient's skin lesions did not recur. The exercises for the patient whose muscle strength was 4/5were continued. After IVIG, maintenance treatment was continued with methotrexate (10 mg/week) and steroids (8 mg/day).

Written and verbal consent was obtained from the patient and his relatives.

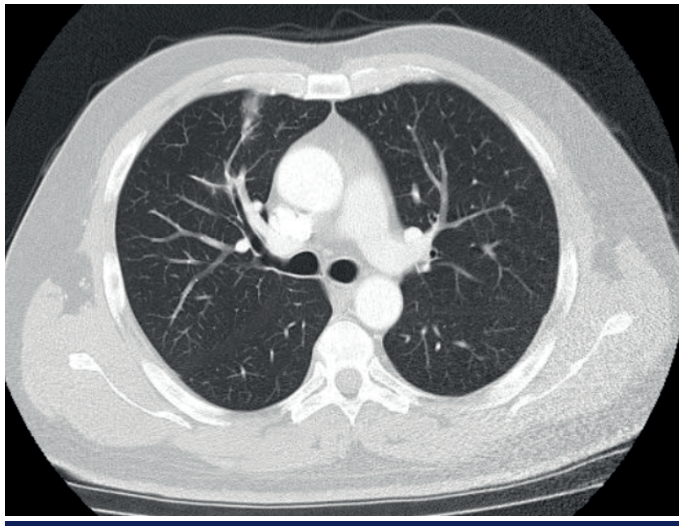

Figure 3. The findings observed in the upper lobe in the tomography taken after the treatment were evaluated as regressed

DISCUSSION

DM is an extremely rare IIM that often presents with progressive, symmetrical, proximal muscle weakness and characteristic cutaneous findings. Skin manifestations may also develop in the absence of muscle disease. It is characterized by pink-purple papules (gottron papules) on the interphalangeal and metacarpophalangeal joints and pink-purple erythema (heliotropic rash) with or without edema involving the periorbital skin (4).

The diagnosis of DM is made by combining characteristic cutaneous findings, muscle weakness, and laboratory evidence of myositis. However, a biopsy should be performed in the absence of clinical signs of muscle disease and in patients presenting with vague skin findings (5).

In this study, bilateral lower and upper extremity muscle weakness and rashes on the arms and trunk supported the clinical diagnosis of DM.

CK, LDH, aldolase, AST, and alanine aminotransferase are muscle enzymes that can be elevated in patients with inflammatory myopathy and other muscle disorders (6). Our patient had high initial CK and LDH levels, which contributed to the diagnosis in the laboratory.

The presence of an underlying malignancy in cases of DM requires age- and gender-appropriate screening, particularly in the first three years. The risk of malignancy increases in patients with severe skin involvement (especially shawl signs or skin necrosis) and high sedimentation. In addition to its association with malignancy in many organs, including the ovary, breasts, stomach, colorectum, lungs, and prostate, non-Hodgkin lymphomas can also be seen (7). Paraneoplastic DM has been reported, particularly in the elderly and men. DM may occur simultaneously with cancer, either before or after cancer (8). Our patient had a history of surgery due to a rectal tumor two years ago.

ILD is a feature of myositis, mostly in association with anti-Jo-1, but rapidly progressive ILD is associated with pulmonary failure and death, most commonly MDA5-related DM. In anti-MDA5-related DM, it is critical to identify patients who may benefit from close monitoring of their pulmonary status (9). Our patient also had symptomatic pulmonary involvement, and ANA was positive, whereas anti-Jo-1 and anti-MDA5 were negative.

Our patient also had symptomatic pulmonary involvement, and ANA was positive, whereas anti-Jo-1 and anti-MDA5 were negative. The cornerstone of initial therapy for DM is the use of glucocorticoids. If ILD is present, it is usually resistant to glucocorticoid monotherapy; therefore, combination therapy with glucocorticoids and immunosuppressants is recommended as the initial therapy. However, ILD associated with DM, including amyopathic DM, is considered an important condition because it often causes death despite intensive treatment with high-dose corticosteroids and immunosuppressive agents (10).

IVIG is a plasma product consisting mainly of monomeric IgG. In the last few decades, the indications for the use of IVIG have expanded to include the treatment of various autoimmune diseases. The standard dose of IVIG therapy is 2 g/kg in two to five daily doses, usually lasting 3-6 months (11). Although IVIG therapy appears to have rarely been used as first-line therapy in DM, it has been shown to be beneficial in glucocorticoid-

resistant conditions as initial therapy in selected patients with progressive muscle weakness or severe dysphagia at risk for aspiration. In these situations, IVIG may have a faster onset of action than glucocorticoids. IVIG has been shown to be effective in most DM patients with lung and esophageal involvement. In some patients, IVIG may reduce the dose of corticosteroid required for maintenance, which is the most effective steroid-sparing effect (12).

In a double-blind study in patients with resistant DM, IVIG combined with corticosteroids significantly improved muscle strength and decreased serum CK levels compared with placebo (13).

Other treatment options for DM include rituximab, a chimeric anti-CD20 monoclonal antibody targeting B cells. In a retrospective analysis of seven patients with ILD refractory to first-line therapy, RTX showed that clinical signs and pulmonary functions improved and uptake on CT regressed (14). However, greater clinical experience with this agent is required before firm conclusions can be drawn.

Azathioprine and methotrexate are both widely used for treating connective tissue disease because of their favorable safety profiles. No prospective studies of DM controlled using methotrexate have been conducted; however, in a few studies, it has been found that it can be used in maintenance therapy in cases where glucocorticoids fail initially (15). In this case, steroid use was gradually reduced after IVIG and methotrexate were added to the treatment, and the disease remained stable at follow-up.

CONCLUSION

IIM is a rare disorder of the muscles. In this case, we aimed to draw attention to the rare inflammatory myositis-associated interstitial lung involvement. If the diagnosis is made quickly and effective treatment is initiated, the results are satisfactory.

Ethics

Informed Consent: Written and verbal consent was obtained from the patient and his relatives.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.A.A., Ö.A., Concept: K.A.A., Ö.A., Data Collection or Processing: K.A.A., Ö.A., Analysis or Interpretation: K.A.A., Ö.A., Literature Search: K.A.A., Writing: K.A.A.

Conflict of Interest: The authors have no conflicts of interest to declare.

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