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Case Report

Case Report on Myositis: A Challenge in Classifying Idiopathic Inflammatory Myositis

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ABSTRACT

Idiopathic Inflammatory Myopathies (IIM) are rare chronic inflammatory diseases whose etiologies are not clearly known, which particularly involve muscles, and which can also affect many other organs. There are many subgroups of inflammatory myositis under the roof of IIM, and there are intermediate form cases which do not comply with these.

A 85-year-old female patient presented to our clinic with the complaints of prevalent muscle pain that started 15 days ago and increased progressively, weakness in arms and legs, and difficulty to swallow. Muscle biopsy was performed in the patient whose elevated muscle enzymes and electromyography and Magnetic Resonance Imaging (MRI) findings were consistent with inflammatory myositis. Although the histopathological examination of muscle biopsy was consistent with inflammatory myositis, it did not completely comply with any of the known forms. As the patient's dysphagia increased and aphonia developed in the follow-up, pulse steroid, intravenous immune globulin, and azathioprine treatment in the aftermath was started. In the posttreatment 24th month, the case is being followed up in remission.

Differential diagnosis of myopathies includes infection, malignance, drug use, autoimmune diseases, IIM, etc. Although our knowledge of IIM is increasing, a final diagnosis could not be established for some cases with clinical symptoms, laboratory tests, MRI, and even with biopsy. As in our case, there may be cases which do not comply with IIM subgroup boundaries, and new research is needed for the clarification of these boundaries.

Keywords: Idiopathic inflammatory myopathies; Polymyositis; Dermatomyositis; Immune-mediated necrotizing myopathy; Inclusion body myositis

INTRODUCTION

Idiopathic Inflammatory Myopathies (IIM) are rare chronic inflammatory diseases whose etiologies are not clearly known, which particularly involve muscles, and which can also affect many other organs. IIM is a group of diseases whose pathogenic processes, clinical symptoms, disease courses, treatment responses, and prognoses differ. The subgroups of this disease group are Polymyositis (PM), Dermatomyositis (DM), Immune-mediated Necrotizing Myopathy (NM), Anti-Synthetase Syndrome (ASS), and Inclusion Body Myositis (IBM). Considering all classification criteria, amyopathic dermatomyositis, sporadic inclusion particle myositis, overlap myositis, and cancer-associated myositis are included in this group [1].

The main complaint in IIM is weakness, which is more prevalent in proximal muscles. Diagnosis of IIM is established after the exclusion of other diseases that could lead to myopathy, with laboratory findings including auto-antibodies, Electromyography (EMG), and Muscle magnetic Resonance Imaging (MRI) [2]. Although all these examinations are performed and IIMs are known, still there are difficulties experienced in the diagnosis of some cases.

There are various inflammatory myositis under the umbrella of IIM, and there are inconsistent intermediate forms as well. Here, in order to draw attention to this fact, we are presenting an inflammatory myositis case which has many common points with the diseases included in the IIM group but does not totally overlap with any of the diseases in the IIM group.

CASE PRESENTATION

A 85-year-old female patient presented to our clinic with the complaints of prevalent muscle pain that started 15 days ago and increased progressively, weakness in arms and legs, and difficulty to swallow. The patient did not have a history of drug use and any known chronic diseases. She did not have fever, arthralgia or arthritis, cough, shortness of breath, rash, paresthesia, abdominal pain, or other symptoms. In the neurological examination, cranial nerve and sensory examinations were normal, and bilateral upper and lower extremities muscle power was determined as proximal 1/5 and distal 2/5. Deep tendon reflex was normoactive. No pathological symptoms were found in the physical examination.

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In laboratory tests, the following values were found: Creatine Kinase (CK) 1026 U/L (0-145 U/L), AST 119 U/L (0-35 U/L), ALT 62 U/L (0-35 U/L) C-Reactive Protein (CRP) 81 mg/L (0-5 mg/L), sedimentation 93 mm/hour, and LDH 661 U/L (0-247 U/L). Antinuclear Antibodies (ANA), Anti-Extractable Nuclear Antibodies (ENA) and a myositis antibody panel, which included serologies for PM-SCL, Jo-1, Ku, PL-7, PL-12, MDA5, NXP2, EJ, SRP, MI2 alpha, MI2 beta, SAE1, TIF1g, PM/Scl75, OJ were negative.

In the electromyography examination, there were myopathi type MUP changes which were accompanied by intense denervation in the upper and lower muscle groups. In spinal MRI, in the paravertebral muscle structures included in the section and in left humerus and left thigh MRI, diffuse T2 hyperintense signal changes in muscle plains and significant edema in the subcutaneous soft tissue were seen. Due to prevalent paraspinal involvement, HMG-CoA reductase ab <20 CU, SRP IFA Screen was determined to be negative in the necrotizing myopathy panel sent. In the Positron-Emission Computer Tomography (PET-CT) performed in terms of paraneoplastic myopathy, diffusely increased F18-FDG uptakes were observed in both extremities and shoulder muscles, piriformis muscles in the pelvis, and muscle tissues, more prominently in obturator internus and externus muscles.

As the patient developed dysphagia, aphonia, and shortness of breath, without waiting for biopsy, she was administered intravenous methylprednisolone 500 mg/day for three days. Biopsy was performed through left deltoid muscle on the second day of pulse steroid treatment. The muscle injury signs such as size and shape difference, rare nuclear internalization, and vacuoles were found in myofibrils on sections (Figure 1a). A mild increase in interstitial connective tissue intensity, degeneration, and regeneration were detected on Modified trichrome staining (Figure 1b). A small number of immature fibers were detected on neonatal myosin staining (Figure 1c). There was mild inflammatory infiltration which mainly composed of T lymphocytes and macrophages located in endomysium such as polymyositis (Figure 1d). Material and amyloidosis were not detected on PAS, dPAS, Oil Red O and Crystal Violet staining. Mitochondrial pathology was not detected on NDH-TR, SDH, and COX staining technique. Type 2/1 ratio decreased on immunohistochemical slow myosin staining. It was defined to be polymyositis according to histomorphological, histochemical and immunophenotypic findings. When the patient's muscle histopathology and clinical findings were evaluated together, she was accepted as IIM intermediate form under the umbrella of PM.

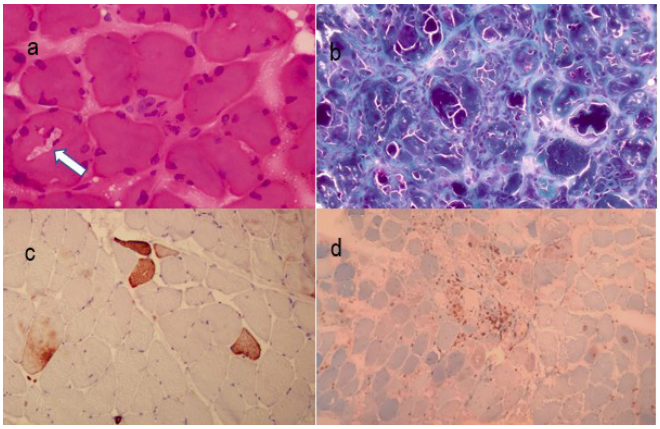

Figure 1: a): A rimmed vacuole was noted (arrow) in the biopsy (HE X 400). b): Biopsy demonstrating atrophic and hypertrophic muscle fibers as well as inflammatory cell infiltration (modified trichrome X 100) c): Note the necrotic/regenerating fibers expressing neonatal myosin (DAB X 200). d): Biopsy showing many CD3- positive T lymphocytes in endomysium (DAB X 100).

Following pulse steroid, steroid treatment was continued orally as 1 mg/kg/day. As clinical recovery was not achieved despite improvement in laboratory values, Intravenous Immune Globulin (IVIG) was started at a dosage of 2 g/kg, and steroid was gradually started to be reduced. The patient, who was evaluated with bilateral muscle power lower and upper extremity proximal 4/5 and distal 5/5, was taken into rehabilitation program and discharged. Improvement in symptoms was observed in the 3rd month follow-up. 24th month laboratory values were determined to be normal with values of CK 18 U/L, LDH 220 U/L, AST 15 U/L, CRP:3.5 mg/l, sedimentation 21 mm/hour. The patient is being followed up in remission.

RESULTS AND DISCUSSION

IIM is a heterogenous group of diseases that occur in autoimmune nature and primarily affect muscles. IIM can be seen in all age groups and genders. The average age of PM onset is 50-60 years, while there are two peaks in DM, which are the ages of 5-15 years and 45-65 years. IBM is usually seen in individuals over the age of 50 years, and it is rare in young individuals [2]. Our case was diagnosed at the age of 83 years, and she was at a more advanced aged than expected in terms of PM and DM.

A significant portion of all myositis (11%-40%) can accompany autoimmune diseases such as systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and Sjogren's syndrome [2-3]. In our case, no secondary disease accompanying myositis was observed. In addition, other causes that may lead to myositis such as infection, drug use, or malignancy did not exist.

Muscle weakness in PM and DM usually start in a subacute way developing in a few weeks or chronically developing in months. In rare cases, it can display an acute onset [4]. While symmetric proximal muscle involvement is expected in PM and DM, asymmetric proximal and distal involvement is observed in IBM, and it progresses insidiously. Clinical symptoms of our case had started in two weeks, and proximal and distal muscles were affected. No asymmetric involvement as in IBM was observed.

In the primary evaluation of IIM, CK elevation is observed as 80-90%. CK elevation in PM and DM can be seen up to 50-fold. Normal CK level is more frequently observed in DM than in PM [2]. While CK level can be normal in IBM, CK level can increase up to 100 times higher in NAM [5]. In our case, CK levels followed a high course from the beginning, and they reached up to 5-10 times higher than normal levels.

Autoantibodies in IIM are divided into two as Myositis-Specific Autoantibodies (MSA) and Myositis-Associated Autoantibodies (MAA). While MSAs can be seen in 50%-60% of IIMs, MAA can be observed in other autoimmune diseases [6]. MSAs are divided into three groups as anti t RNA synthetases, anti-signal Recognition Particle (anti-SRP), and other antibodies against cytoplasmic or nuclear components involved in the regulation of protein synthesis and translocation, gene transcription, and viral recognition including anti-Mi-2 anti-PM-Scl and anti-CADM-140 [7]. MSAs and MAAs in our case were determined to be negative.

Muscle biopsy is important in terms of both establishing the diagnosis of IIM and excluding other myopathy causes. Although our case had symptoms consistent with IIM, no full consistence with any of the IIM subgroups was determined. As inclusion/vacuole formations in some myofibers were not prevalent and clinical symptoms were not consistent with IBM, they were not evaluated as IBM. Although 29% of IBM cases are clinically consistent, they are not diagnosed with PM as vacuole is not observed. To add to the complexity, patients who have steroid-responsive PM may have a few rimmed vacuoles. Although better visualized on immunostaining of phosphorylated tau (with SMI-31), eosinophilic cytoplasmic inclusions are rarely seen in IBM [8]. In our case, performing of biopsy on the second day of steroid treatment as a clinical necessity can be misleading in terms of histopathological evaluation.

In the last decade, immune mediated necrotizing myopathy, which is a subtype that is seen without lymphocytic infiltration as in muscle biopsies of other IIMs and where muscle fiber necrosis stands out, has been defined [9]. In two-thirds of these patients, anti-SRP antibodies or anti-3-hydroxy-3-methylglutaryl-coenzyme a reductase (HMGCR) antibodies are determined, and in negative ones, an underlying malignancy can be detected. Patients who have HMCGR antibody can be divided into two as those exposed to statin and those not exposed to statin. Those who are not exposed to statin are younger, their CK levels are elevated, and their response to treatment is poorer [10]. Though not very prevalent, necrotic fibers were prominent in the muscle biopsy of our case,

and T lymphocyte infiltration was observed. Her histopathological findings were not consistent with NAM, anti SRP and anti HMCGR antibodies were negative, and she had no history of exposure to statin.

The first three years after the diagnosis of IIMs, especially the first year, are very risky in terms of malignancy development. Paraneoplastic myositis is similar to IIM, but there are also differences between them. Paraneoplastic myositis is seen in advanced ages, and along with more severe muscle involvement such as dysphagia and ulceration in the skin, skin involvement is observed more. Muscle biopsies are not very different in myositis seen without malignancy [11]. In some studies, vacuole fibers and intense complementary C5b-9 accumulations are observed [12]. Response to steroid is very good in paraneoplastic myositis. The onset of the disease in our case in advanced age, presence of dysphagia, and observation of inclusion/vacuole in some myofibrils are consistent with paraneoplastic myositis. In the evaluation of the patient in terms of malignancy supported with PET/CT, no anomaly was detected, and no malignancy developed until the 24th month follow-up.

CONCLUSION

Our case is an inflammatory myositis case which is seen in advanced ages, in which symmetric proximal and distal lower and upper extremity muscles and paraspinal muscles are involved, which has an acute onset, and whose autoantibodies are negative. In muscle biopsy, necrotic and regenerated fibers consistent with inflammatory myositis and interstitial T lymphocyte infiltration in endomysium were observed. With these findings, the case was evaluated as intermediate inflammatory myositis under the umbrella of PM and treated accordingly. It should be noted that performing biopsy after starting steroid can affect the result of the biopsy to some extent.

Differential diagnosis of myopathies includes many factors such as infection, malignancy, drug use, autoimmune diseases, IIM, etc. The clinical symptoms, histopathological findings, autoantibody profiles, treatment to response, and prognoses of IIM subgroups can vary. Classification criteria for IIM have been developed for approximately 50 years. Although our knowledge of IIM has advanced, these diagnostic boundaries may not be sufficient with clinical findings, laboratory tests, and even with biopsy for some cases. The existence of some intermediate forms draws attention to the gap in this issue, and further research is needed in this regard.

PATIENT CONSENT

The patient provided informed written consent prior to inclusion of her data in this report.

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CONFLICT OF INTEREST

None

ETHICAL APPROVAL

Not applicable

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