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Two Cases of Dermatomyositis with Anti-cN1A Antibody Positivity

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Case Report

History

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ABSTRACT

Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of autoimmune-mediated disorders. One of the most important developments in recent years regarding IIMs is the clinical use of myositis-specific antibodies and myositis-associated antibodies. The identification of anti-cytosolic 5'-nucleotidase 1A (anti-cN1A), one of the myositis-associated antibodies, represents significant progress in understanding inclusion body myositis (IBM), with research focusing on its role in predicting survival, diagnostic potential, clinical phenotype, and histopathological correlations. With the increasing use of autoantibodies in recent years, it is essential to understand their specificity and sensitivity properties. We presented two cases of dermatomyositis with positive anti-cN1A antibodies, which are known to have high specificity in IBM. One of the cases is a male patient, and IBM was included in the differential diagnosis because of anti-cN1A antibody positivity and resistance to first-line immunosuppressive therapy. The other case is a female patient diagnosed with dermatomyositis twelve years ago, with a myositis antibodies panel performed during a disease flare revealing anti-cN1A antibody positivity.

Keywords: inclusion body myositis; dermatomyositis; myositis specific autoantibodies; myositis associated antibodies; anti-cN1A antibodies

Anti-cN1A Antikoru Pozitifliği Olan İki Dermatomiyozit Vakası

Olgu Sunumu

Süreç

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ÖZET

İdiyopatik İnflamatuvar Miyopatiler (İİM), otoimmün aracılı heterojen bir grup hastalıktır. İİM'ler ile ilgili son yıllarda en önemli gelişmelerden biri, miyozit spesifik antikorlar ve miyozit ilişkili antikorların klinik kullanımıdır. Miyozit ile ilişkili antikorlardan biri olan anti-sitozolik 5'-nükleotidaz 1A (anti-cN1A)'nın tanımlanması ile inklüzyon cisimcikli miyozitin anlaşılmasında önemli bir ilerleme kaydedilmiştir ve bu alanda yapılan araştırmalar, bu antikorun prognoz, tanıdaki kullanımı, klinik fenotip ve histopatolojik korelasyonları öngörmedeki rolüne odaklanmaktadır. Son yıllarda otoantikorların artan kullanımı nedeniyle, bu antikorların spesifisite ve sensitivite özelliklerinin anlaşılması önemlidir. Bu çalışmada inklüzyon cisimcikli miyozite spesifisitesi yüksek olduğu bilinen anti-cN1A antikorunun pozitif saptandığı iki dermatomiyozit vakası sunduk. Birinci vaka anti-cN1A antikor pozitifliği olan ve başlangıç immünsüpresif tedaviye direnç göstermesi nedeniyle inklüzyon cisimcikli miyozitin ayırıcı tanıya alındığı erkek hastadır. İkinci vaka ise on iki yıl önce dermatomiyozit tanısı almış ve hastalık alevlenmesi sırasında bakılan miyozit antikorları panelinde anti-cN1A antikor pozitifliği saptanmış kadın hastadır.

Anahtar Kelimeler: inklüzyon cisimcikli miyozit; dermatomiyozit; miyozit spesifik antikorlar; miyozit ilişkili antikorlar; anti-cN1A antikorları

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Introduction

Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of autoimmune-mediated disorders characterized by chronic muscle inflammation and extramuscular involvement affecting the skin, pulmonary, cardiovascular, and gastrointestinal systems. Dermatomyositis, polymyositis, inclusion body myositis (IBM), anti-synthetase syndrome, immune-mediated necrotizing myopathy, and overlap myositis are classified within this group.[1] These conditions are distinguished from each other through clinical features, laboratory findings, pathology, electromyography (EMG), and imaging methods.[1, 2]

One of the most important developments in recent years regarding IIMs is the clinical use of myositis-specific antibodies and myositis-associated antibodies. These autoantibodies are helpful in recognizing the clinical phenotype, predicting organ involvement, and determining prognosis.[3] The identification of anti-cytosolic 5'-nucleotidase 1A (anti-cN1A), one of the myositis-associated antibodies, represents significant progress in understanding IBM, with research focusing on its role in predicting survival, diagnostic potential, clinical phenotype, and histopathological correlations.[4, 5]

With the increasing use of autoantibodies in recent years, it is essential to understand their specificity and sensitivity properties. Studies have shown that anti-cN1A antibodies can also be detected in other autoimmune diseases, such as primary Sjögren's syndrome and systemic lupus erythematosus (SLE). On the other hand, anti-cN1A antibody positivity is significantly lower in other IIMs compared to IBM, suggesting its potential role in distinguishing IBM from conditions like dermatomyositis.[5]

Here, we report two cases of dermatomyositis with anti-cN1A antibody positivity, questioning its specificity for IBM. One of the cases is a male patient, and IBM was included in the differential diagnosis because of anti-cN1A antibody positivity and resistance to first-line immunosuppressive therapy. The other case is a female patient diagnosed with dermatomyositis twelve years ago, with a myositis antibodies panel performed during a disease flare revealing anti-cN1A antibody positivity.

Case 1

A 37-year-old male visited our clinic presenting with a rash on his face (Figure-1), nodular lesions on the scalp, and hard nodular lesions on the abdominal surface as well as the medial aspect of the right thigh. The patient reported no accompanying symptoms. Initial tests revealed positive Antinuclear Antibody (ANA) at a titer of 1/160 with a speckled pattern and negative anti-double stranded DNA (anti-dsDNA). Skin biopsies were compatible with the tumid form of lupus erythematosus.

The patient was preliminarily diagnosed with cutaneous lupus erythematosus and treated with azathioprine, hydroxychloroquine, and steroids. However, there was no improvement in skin symptoms after six months of treatment. Due to the development of oropharyngeal dysphagia, proximal muscle weakness in the upper and lower extremities, and a weight loss of 10 kg in the last month, the patient was re-evaluated. Physical examination revealed 3/5 bilateral upper extremity proximal muscle strength, 4/5 distal muscle strength, 4/5 bilateral lower extremity proximal muscle strength, and 5/5 distal muscle strength. The patient had hyperemic skin lesions on the face, forehead, cheeks, and around the eyes. Laboratory investigations showed elevated levels of aspartate aminotransferase (AST) 62 IU/L, creatine kinase (CK) 588 U/L, lactate dehydrogenase (LDH) 407 U/L, C-reactive protein (CRP) 29 mg/L. The erythrocyte sedimentation rate (ESR) and alanine aminotransferase (ALT) were within normal levels.

Due to oropharyngeal dysphagia with a risk of aspiration pneumonia and significant weight loss, the patient was urgently started on 1-gram intravenous methylprednisolone for three days, followed by maintenance treatment with 60 mg/day of oral prednisolone and 2 g/day of mycophenolate mofetil (MMF). A needle EMG revealed significant myogenic involvement, especially in the proximal muscles, and the patient was initially diagnosed with IIMs. A barium swallow study was conducted due to dysphagia, which revealed tracheal aspiration in the form of overflow from the hypopharynx. A Positron Emission Tomography - Computed Tomography (PET/CT) scan was conducted for malignancy screening and to visualize muscle involvement, which revealed mild fluorodeoxyglucose (FDG) uptake in the muscle tissue. Prostate examination, gastroscopy, colonoscopy, thyroid ultrasound, scrotal ultrasound, and PET/CT did not reveal any malignancy.

The myositis-specific and myositis-associated antibodies panel was analyzed using the immunoblot technique from serum samples. The panel showed anti-SSA: 3+ and anti-cN1A antibody: 1+. Other autoantibodies were negative. Due to the positive detection of the anti-cN1A antibody and the dominant clinical manifestation of oropharyngeal dysphagia, IBM was included in the differential diagnosis. A biopsy taken from the deltoid muscle showed perifascicular atrophy and fibrosis, without inclusion bodies, which were consistent with the histomorphological findings of dermatomyositis (Figure-2).

The case was reassessed with the potential diagnosis of dermatomyositis and the skin biopsies performed during the patient's initial presentation were reevaluated. All the histologic findings were also consistent with dermatomyositis. The patient was then diagnosed with dermatomyositis. Due to the lack of improvement in extremity muscle strength, persistent oropharyngeal dysphagia, and the anticipated poor prognosis observed during treatment with MMF and high-dose steroids, MMF was discontinued. The patient was started on cyclophosphamide, rituximab, and intravenous immunoglobulin (IVIG) therapy. Significant improvement was observed in symptoms of oropharyngeal dysphagia at the end of the first month under this therapy. Oral feeding was initiated, and weight gain was achieved. Bilateral muscle strength was 5/5 in the upper and lower extremities. Muscle enzymes returned to normal.

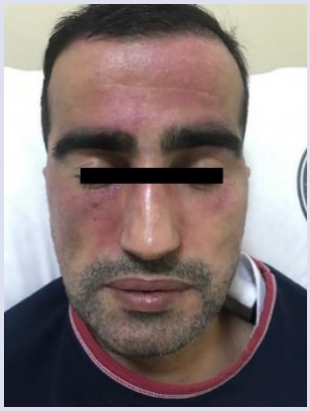

***Figure-1**: Rash on patient's face at presentation.*

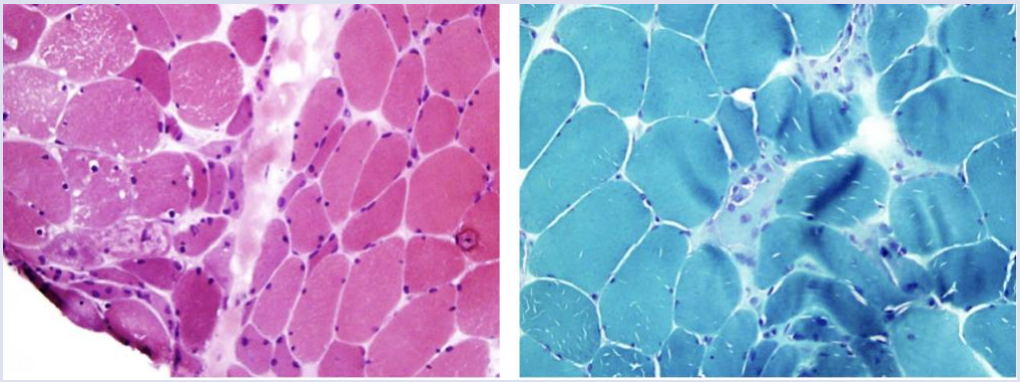

***Figure-2**: Histomorphological findings of muscle biopsy. A, Perifascicular atrophy (Hematoxylin-eosin staining x200). B, Necrotic muscle fibers (modified Gomori trichrome staining x200)*

Case 2

A 43-year-old female patient first presented to the internal medicine department twelve years ago with a rash on her face and edema in her eyes and feet. She also reported diffuse pain in her arms and shoulders and had difficulties raising her arms and climbing stairs. Laboratory tests showed elevated levels of CK (18000 U/L), LDH (1892 U/L), AST (960 IU/L), and ALT (560 IU/L). A needle EMG showed diffuse myogenic involvement. The anti-SSA and anti-histidyl-tRNA synthetase (anti-Jo-1) antibodies were positive. Muscle biopsy showed perifascicular atrophy and perimysial lymphoid infiltration, and she was diagnosed with dermatomyositis. She was treated with pulse glucocorticoids, followed by oral prednisolone, azathioprine 100 mg/day, and hydroxychloroquine 200 mg/day for the next five years until she had a flare similar to that she experienced when her disease first emerged. She was hospitalized again and treated with pulse glucocorticoids, MMF (2 g/day), and rituximab. Four years later, despite the treatment, the patient developed proximal muscle weakness and elevated CK levels. A new panel of myositis-specific and myositis-associated antibodies was examined in serum samples using the immunoblot method, which showed anti-SSA: 2+, anti-Jo-1: 3+, and anti-cN1A antibody: 3+. Although anti-cN1A antibody positivity was detected, the clinical presentation remained inconsistent with IBM. With a diagnosis of dermatomyositis, the treatment was subsequently switched to IVIG and tofacitinib (10 mg/day). The patient remains in remission under this regimen.

Discussion

Here, we present two cases of dermatomyositis with positive anti-cN1A antibodies, which are known to have a high specificity for IBM. The first case was initially diagnosed as cutaneous lupus erythematosus based on rash, skin biopsy results, and ANA positivity. During follow-up, with the development of oropharyngeal dysphagia, proximal muscle weakness, and elevated muscle enzyme levels, IIMs were considered in the diagnosis. After the myositis antibody panel was positive for both anti-cN1A and anti-SSA, along with distal muscle weakness (less severe than proximal weakness), oropharyngeal dysphagia, and resistance to first-line immunosuppressive treatment, IBM was included in the differential diagnosis. Based on the patient's age, symmetric proximal muscle weakness rather than distal weakness, and muscle biopsy findings inconsistent with IBM, we excluded the diagnosis of IBM, confirming the diagnosis of dermatomyositis. The second case involved a female patient with a history of dermatomyositis, in which anti-cN1A positivity was detected during a disease flare.

There were no findings suggestive of IBM based on the clinical findings and muscle biopsy results.

Idiopathic inflammatory myopathies are a group of diseases that commonly present with muscle weakness; however, the subgroups exhibit significant heterogeneity. The identification of myositis-specific and myositis-associated antibodies has shown that this heterogeneity is both clinical and serological. With the increasing use of these antibodies in clinical practice, it is essential to understand their characteristics.[6] These cases highlight dermatomyositis with anti-cN1A positivity, questioning its specificity for IBM.

Autoantibodies targeting cN1A, an enzyme involved in nucleic acid metabolism and expressed in skeletal muscle, are present in IBM patients.[4,7] IBM typically occurs in men over the age of 50 years, affects both proximal and distal muscle groups, often with asymmetric involvement, and may also involve the facial muscles. Dramatically elevated muscle enzyme levels were not observed, and dysphagia developed in > 50% of the patients. In terms of clinical findings and resistance to immunosuppressive therapy, IBM differs from other IIMs.[1,2] With the detection of anti-cN1A antibodies in IBM patients, it has been recognized that autoimmune mechanisms may also play a role in its pathogenesis in addition to degenerative mechanisms.[4,7]

Various techniques, such as Immunoblotting, Enzyme-Linked Immunosorbent Assay (ELISA), Cell-Based Immunofluorescence Cytochemistry, and Addressable Laser Bead Immunoassay (ALBIA) have been reported in the literature for the detection of anti-cN1A antibodies. Depending on the technical differences and variations in cutoff values, the sensitivity and specificity vary.[5] A meta-analysis including seven studies conducted between 1990 and 2020 compared anti-cN1A positivity between IBM and PM/DM, autoimmune diseases, and neuromuscular disorders. The evaluation of 599 IBM patients and 1,676 patients with other conditions revealed that the positive predictive value (PPV) of the tests was 0.25 in the general population and increased to 0.75 in individuals over 50 years of age, while the diagnostic significance remained insufficient.[8] In the assessment of this meta-analysis, variations in assay techniques, the lack of adjustments for factors such as age, gender, ethnicity, disease severity, comorbidities, and the limited number of studies should be considered.

In suspected cases of IIMs, an extended myositis panel is routinely used. This helps to confirm the diagnosis and provides insights into organ involvement and prognosis.

Conclusion

Due to the relative rarity of IBM, more data is needed on anti-cN1A antibodies, and the information available is based on studies with small populations. More research needs to be done to demonstrate the relationship between clinical presentation and anti-cN1A positivity in patients diagnosed with dermatomyositis. The role of antibodies in the diagnosis of rheumatologic diseases is increasing day by day, but clinical findings and biopsy remain the most important methods.

Patient Consent

Written informed consent was obtained from the patients for publication of this case report.

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None

Authorship Contribution

Design: S.U., Z.T.D.
Data Collection: K.T., K.P, G.U.
Manuscript Writing: K.T., K.P., Z.T.D.
Supervision: S.U

Conflict of Interest

The authors declare no conflict of interest.

References

1- Lundberg IE, Fujimoto M, Vencovsky J, et al. Idiopathic inflammatory myopathies. *Nat Rev Dis Primers*. 2021;7(1):86. Published 2021 Dec 2. doi:10.1038/s41572-021-00321-x

2- Allameen NA, Salam S, Reddy V, Machado PM. Inclusion body myositis and immunosenescence: current evidence and future perspectives. *Rheumatology (Oxford)*. Published online November 6, 2024. doi:10.1093/rheumatology/keae614

3- Allameen NA, Ramos-Lisbona AI, Wedderburn LR, Lundberg IE, Isenberg DA. An update on autoantibodies in the idiopathic inflammatory myopathies. *Nat Rev Rheumatol*. 2025;21 (1):46-62. doi:10.1038/s41584-024-01188-4

4- Larman HB, Salajegheh M, Nazareno R, et al. Cytosolic 5'-nucleotidase 1A autoimmunity in sporadic inclusion body myositis. *Ann Neurol*. 2013;73(3):408-418. doi:10.1002/ana.23840

5- Salam S, Dimachkie MM, Hanna MG, Machado PM. Diagnostic and prognostic value of anti-cN1A antibodies in inclusion body myositis. *Clin Exp Rheumatol.* 2022;40(2):384-393. doi:10.55563/clinexprheumatol/r625rm

6- Lundberg IE, Fujimoto M, Vencovsky J, et al. Idiopathic inflammatory myopathies. *Nat Rev Dis Primers.* 2021;7(1):87. Published 2021 Dec 2. doi:10.1038/s41572-021-00325-7

7- Pluk H, van Hoeve BJ, van Dooren SH, et al. Autoantibodies to cytosolic 5'-nucleotidase 1A in inclusion body myositis. *Ann Neurol.* 2013;73(3):397-407. doi:10.1002/ana.23822

8- Mavroudis I, Knights M, Petridis F, Chatzikonstantinou S, Karantali E, Kazis D. Diagnostic Accuracy of Anti-CN1A on the Diagnosis of Inclusion Body Myositis. A Hierarchical Bivariate and Bayesian Meta-analysis. *J Clin Neuromuscul Dis*. 2021;23(1):31-38. doi:10.1097/CND.0000000000000353