JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1716320
J Contemp Med 2025;15(4):190-192

Case Report / Olgu sunumu

Winged Scapula and Mild Weakness in a Patient with SYNE2 Mutation-Associated Myopathy

SYNE2 Mutasyonu ile ilişkili Miyopatili Bir Hastada Kanat Skapula ve Hafif Güçsüzlük

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Abstract

Emery-Dreifuss muscular dystrophy (EDMD) is a rare disease characterized by scapulo-humero-peroneal muscle weakness, joint contractures, and cardiomyopathy. EDMD5 is an uncommon subtype caused by SYNE2 gene mutations. A 49-year-old male presented with lifelong difficulty running and rising from a squat. Examination revealed mild proximal lower limb weakness and bilateral winged scapula with left-sided predominance. Electromyography showed motor unit action potentials of reduced amplitude and short duration. Muscle biopsy indicated fiber atrophy with preserved staining for key muscular proteins. The findings in this case illustrate that clinical severity in EDMD5 may vary among individuals, as shown by the presence of mild weakness and a winged scapula.

Keywords: Emery-Dreifuss muscular dystrophy, EDMD5, myopathy, SYNE2 mutation, winged scapula

Öz

Emery-Dreifuss musküler distrofi (EDMD), skapulo-humero-peroneal kas güçsüzlüğü, eklem kontraktürleri ve kardiyomiyopati ile karakterize nadir bir hastalıktır. EDMD5, SYNE2 gen mutasyonlarına bağlı olarak gelişen nadir bir alt tiptir. Kırk dokuz yaşındaki erkek hasta, yaşamı boyunca koşma ve çömelme pozisyonundan kalkmada güçlük öyküsü ile başvurdu. Muayenede, proksimal alt ekstremite kaslarında hafif güçsüzlük ve sol tarafta belirgin olmak üzere bilateral kanat skapula saptandı. Elektromiyografide amplitüdü küçülmüş ve süresi kısa motor ünite aksiyon potansiyelleri gözlendi. Kas biyopsisinde temel kas proteinlerine yönelik boyanmanın korunduğu, ancak lif atrofisinin mevcut olduğu görüldü. Bu olguda gözlenen hafif güçsüzlük ve kanat skapula bulguları, EDMD5'te klinik şiddetin bireyler arasında değişkenlik gösterebileceğini ortaya koymaktadır.

Anahtar Kelimeler: Emery-Dreifuss musküler distrofi, EDMD5, miyopati, SYNE2 mutasyonu, kanat skapula

INTRODUCTION

Emery-Dreifuss muscular dystrophy (EDMD) is less common than Duchenne and Becker muscular dystrophies and is typically characterized by weakness in the scapulo-humero-peroneal muscles, cardiomyopathy, and contractures of the extremities.[1,2] Mutations in the EDMD gene, encoding emerin, and the LMNA gene, encoding lamin A/C, are responsible for the most prevalent subtypes of EDMD: EDMD1 and EDMD2, respectively.[1,2] Other genes such as SYNE1 and SYNE2, which encode nesprin-1 and nesprin-2, have also been implicated in rare EDMD subtypes. EDMD5, one of the rare subtypes of EDMD, has been reported in only a limited number of cases, which hampers the full characterization of its clinical features.[1-3] This report describes a patient with EDMD5, a rare subtype of Emery-Dreifuss muscular dystrophy caused by a SYNE2 mutation.

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Received *(Geliş Tarihi)*: 09.06.2025 **Accepted *(Kabul Tarihi)*:** 03.07.2025

CASE

A 49-year-old male presented to the neurology clinic with lifelong difficulties in running and rising from a squatting position. His medical history was unremarkable, and he was not taking any medications. While his family history revealed no significant findings, his parents were consanguineous, being third-degree relatives. On examination, he exhibited mild proximal weakness in the lower extremities and bilateral winged scapula, more prominent on the left side (**Figure 1A**). Muscle strength was assessed using the Medical Research Council scale. Strength in bilateral shoulder abduction and elbow flexion was graded as 4, and proximal strength in the proximal lower limb muscles was also 4 bilaterally. Strength in all other muscle group was normal. No joint limitations were observed. Sensory examination and deep tendon reflexes were within normal limits. Serum alanine aminotransferase, aspartate aminotransferase, and creatine kinase levels were 45 U/L, 68 U/L, and 346 U/L, respectively. Nerve conduction studies of the median, posterior tibial, and sural nerves yielded normal results. Needle electromyography showed no positive sharp waves, fibrillation potentials, or myotonic discharges in the left biceps brachii and deltoid muscles. However, motor unit action potentials in these muscles exhibited reduced amplitude and short duration (**Figure 1B**).

The muscle biopsy of the right biceps brachii revealed muscle fiber atrophy, with normal staining for dystrophin, emerin, dysferlin, and sarcoglycans. Genetic analysis identified a heterozygous variant in the SYNE2 gene (NM_182914.2: c.1074G>T;p.Glu358Asp), which was also detected in his father but not in his mother. One month prior to his neurology clinic visit, the patient was hospitalized with widespread pain, weakness, and dyspnea, symptoms that were most likely attributed to pneumonia. Electrocardiography (ECG), Holter ECG, echocardiography, and coronary angiography performed during his hospitalization showed normal results. His symptoms resolved within two weeks with symptomatic treatment alone. The patient gave written consent for the presentation of this case.

DISCUSSION

EDMD is a myopathy characterized by progressive muscle weakness, particularly affecting the scapulohumeral muscles in the upper extremities and the peroneal muscles in the lower extremities. It may be accompanied by cardiomyopathy, cardiac arrhythmias, or joint contractures.[1,2] The diagnosis is based on clinical features, electrodiagnostic studies including needle electromyography, and genetic testing. The presence of heart diseases such as cardiac arrhythmias in patients with EDMD highlights the importance of timely diagnosis and close follow-up of the disease.

EDMD has several subtypes based on the underlying genetic mutations. Mutations in genes such as LMNA, EMD, SYNE1, and SYNE2 have been implicated in EDMD and related myopathies.[1-4] The SYNE1 and SYNE2 genes encode nesprin-1 and nesprin-2, respectively.[1,2] EDMD4 and EDMD5 can develop in SYNE1 and SYNE2 mutations, respectively.[1-3] Weakness in these EDMD subtypes can vary from mild weakness to severe weakness.[1-3] In this present case, there was mild weakness in the proximal lower extremities. As in this present case, it was reported that no contractures were observed in EDMD5 compared to EDMD4.[1,2] Furthermore, mutations in the SYNE2 gene may play a role in the pathogenesis of EDME by impairing the mechanical connection between the nuclear envelope and the cytoskeleton.[5] Heterozygous missense variants identified

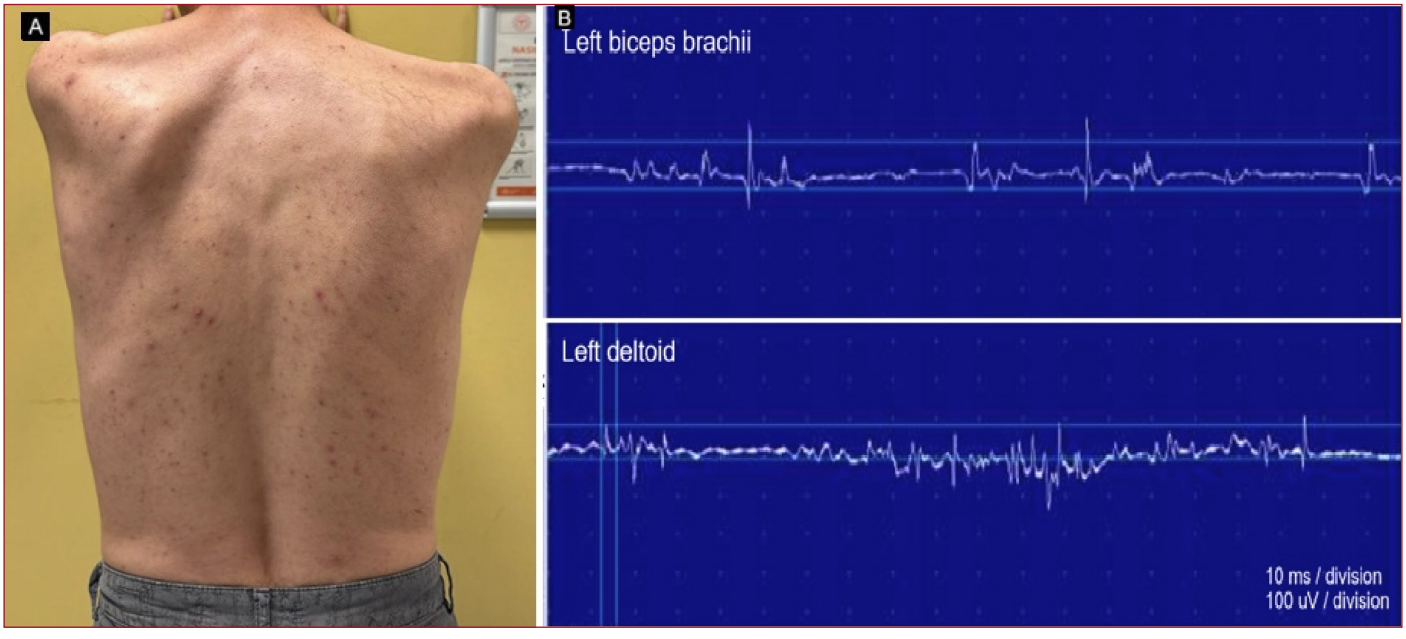

Figure 1. (A) Bilateral winged scapula with left-sided predominance **(B)** Myopathic motor unit action potentials in biceps brachii and deltoid muscles.

in patients with EDMD or EDME-like phenotypes have been associated with abnormal nuclear morphology and disrupted interactions among emerin, nesprin, and lamin proteins.[5] Taken together, these findings may help explain the mild clinical presentation observed in our patient.

Muscle weakness in EDMD primarily affects the scapular and humeral muscles, leading to winged scapula.[1,2] While winged scapula typically presents symmetrically in most myopathies, asymmetric involvement may be seen in certain hereditary myopathies, such as facioscapulohumeral dystrophy.[6] In the present case, although the winged scapula was bilateral, it was more prominent on the left side. Therefore, clinicians should be aware that hereditary myopathies with asymmetric features, although rare, may occur. In addition, this case did not show joint contractures or severe muscle weakness, findings often reported in other EDMD subtypes. This supports the view that EDMD has a broad clinical spectrum.

Life-threatening complications can occur in EDMD.[1,2,4] Cardiac involvement such as cardiomyopathy, arrhythmias, or heart failure has been reported, particularly in EDMD5.[1,2,4] However, no cardiac pathology was detected in the present case. Respiratory muscle weakness has been observed in animal models lacking SYNE1 and SYNE2, suggesting the potential role of these genes in motor innervation and respiratory function.[7] The episode of dyspnea and generalized weakness in our patient may support this association. In patients with EDMD5, intercurrent infections such as pneumonia may predispose to episodes of dyspnea and diffuse muscle weakness.

CONCLUSION

This case highlights that the presence of mild weakness and a winged scapula in this patient reflects the variability in the severity of muscle involvement among individuals with EDMD5. Additionally, this case suggests that some EDMD subtypes may present with mild clinical features in the absence of cardiac involvement or joint contractures.

ETHICAL DECLARATIONS

Informed Consent: The patient signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Madej-Pilarczyk A. Clinical aspects of Emery-Dreifuss muscular dystrophy. Nucleus. 2018;9(1):268-74.
2. Heller SA, Shih R, Kalra R, Kang PB. Emery-Dreifuss muscular dystrophy. Muscle Nerve. 2020;61(4):436-48.
3. Lee SJ, Lee S, Choi E, Shin S, Park J. A novel SYNE2 mutation identified by whole exome sequencing in a Korean family with Emery-Dreifuss muscular atrophy. Clin Chim Acta. 2020;506:50-4.
4. Hata Y, Hachiwaka R, Ichimata S, Yamaguchi Y, Nishida N. An autopsy case of sudden unexpected death of a young adult with progressive intraventricular conduction delay. Pathol Res Pract. 2022;240:154226.
5. Zhang Q, Bethmann C, Worth NF, et al. Nesprin-1 and -2 are involved in the pathogenesis of Emery Dreifuss muscular dystrophy and are critical for nuclear envelope integrity. Hum Mol Genet. 2007;16(23):2816-33.
6. Lin XD, He JJ, Lin F, et al. A "Triple Trouble" Case of Facioscapulohumeral Muscular Dystrophy Accompanied by Peripheral Neuropathy and Myoclonic Epilepsy. Chin Med J (Engl) 2018;131(18):2164-71.
7. Zhang X, Xu R, Zhu B, et al. Syne-1 and Syne-2 play crucial roles in myonuclear anchorage and motor neuron innervation. Development. 2007;134(5):901-8.