Case Study of Dysferlinopathy: A Clinical Perspective on a 29 Year Old Female with Progressive Lower Limb Weakness

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Introduction

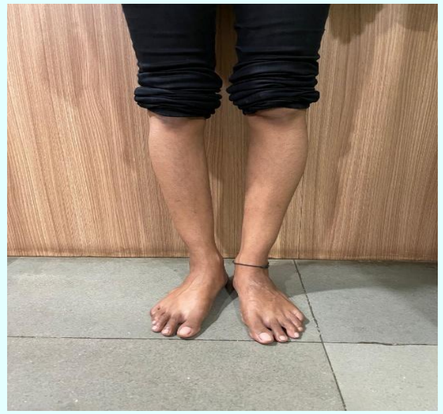
Dysferlinopathy is a rare, autosomal recessive muscular dystrophy that primarily affects skeletal muscles, leading to progressive muscle weakness. The condition is associated with mutations in the DYSF gene, which encodes the protein dysferlin. Dysferlin is essential for muscle membrane repair, and its absence or dysfunction leads to various clinical presentations, including limb-girdle muscular dystrophy type 2B (LGMD2B) and Miyoshi myopathy.

Patient Presentation

A, 29 years old women presented with insidious-onset, progressive difficulty in walking that had been worsening over two years. She reported tingling and numbness in both lower extremities, alongside pain that had persisted for an equal duration. Her symptoms were accompanied by muscle weakness, and she experienced significant difficulty in performing everyday tasks such as walking and climbing stairs. A notable aspect of her history was that she had been walking with difficulty for approximately five years due to progressive muscle weakness . Additionally, the patient mentioned a family history of muscular weakness, with two maternal aunts and one maternal uncle having experienced similar symptoms, pointing towards a possible hereditary condition.

Physical Examination

Upon examination, the patient had observable muscle weakness in both the upper and lower extremities. Power in the upper limbs (UL) was noted as 4/5 for shoulder and elbow flexion, whereas in the lower limbs (LL), she had a power rating of 4/5 for plantar flexion and 5/5 for dorsiflexion. Laboratory findings revealed elevated creatine kinase (CK) levels, with a value of 9811 U/L, indicating muscle breakdown and a probable muscular dystrophy diagnosis.



Magnetic Resonance Imaging (MRI)

MRI of both lower extremities was performed which showed fatty atrophy of the bilateral medial and lateral gastrocnemius and soleus muscles, a typical finding in patients with Miyoshi myopathy, a variant of dysferlinopathy that affects the lower limbs.

Electromyography (EMG) studies of Right gastrocnemius and Left gastrocnemius muscle shows no spontaneous activity with reduced MUAP and reduced recruitment pattern. Right quadriceps muscles shows no spontaneous activity with normal MUAP and recruitment pattern. **Nerve Conduction study** was normal, further pointing towards a muscular pathology rather than a neurogenic cause for the weakness.

Genetic report identified compound heterozygous variants of uncertain significance in exons 27 and 29 of the *DYSF* gene, which are known to cause a spectrum of muscle disorders, including Miyoshi myopathy and LGMD2B

Discussion

- In this case, the patient exhibited symptoms consistent with both LGMD2B and Miyoshi myopathy. The presence of both proximal and distal muscle weakness points to a broad dysferlinopathy spectrum, emphasizing the complex and overlapping phenotypes seen in patients with *DYSF* mutations. The reported family history of muscular dystrophy further supports the diagnosis of an inherited condition.

Management and Treatment Plan

- Currently, there is no cure for dysferlinopathy. Treatment is supportive and aimed at managing symptoms and improving the patient’s quality of life. The patient was treated with analgesics to manage the pain and was advised on the use of antacids and antiemetics to mitigate gastrointestinal side effects associated with long-term medication use.
- Physiotherapy was recommended to help maintain muscle function and prevent contractures.
- Given the progressive nature of the disease, regular follow-up was advised to monitor the patient’s muscle strength and adjust the management plan as necessary.

CONLUSION:

- This case highlights the complexity of diagnosing and managing dysferlinopathy, a rare and progressive muscle disorder
- The patient’s presentation, family history, and diagnostic findings, including elevated CK levels, MRI evidence of muscle atrophy, and genetic testing, all support the diagnosis of dysferlinopathy
- The literature reinforces the variability in clinical presentations and the importance of genetic testing for a definitive diagnosis.
- While there is no cure, supportive management with physiotherapy, occupational therapy, and regular follow-ups can help improve the patient's quality of life.
- Future research into gene therapies offers hope for potential curative treatments.