

CASE REPORT

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EFFECT OF STRUCTURED EXERCISE REGIMEN ON QUALITY OF LIFE, BALANCE AND STRENGTH ON A PATIENT WITH MIYOSHI MYOPATHY – A CASE REPORT

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ABSTRACT

Background: Dysferlinopathy is an autosomal recessive disease seen in adolescence or young adulthood. Miyoshi Myopathy is characterized by weakness and wasting of posterior compartment leg muscles rather than the anterior compartment and distal upper limb muscles. Still, the intrinsic muscles of the foot and hands are spared. There are several undiagnosed cases in India and also around the world with dysferlinopathy. Diagnosis for the same requires advanced biological laboratories along with high economic funding for diagnostic purposes.

Case Summary: This case report presents a 22-year-old male diagnosed with Miyoshi myopathy/LGMD2b (dysferlinopathy). The subject complained about a loss of balance, strength, and difficulty in performing activities of daily living. The patient was given Aquatic Therapy along with conventional physical therapy for a duration of 6 weeks, which included three days of supervised therapy along with 3 days home protocol and a rest day kept at the end of every week.

Outcome Measures: Standardized scales like the Barthel Index and the Berg Balance Scale were used for the assessment of pre and post the progress of the subject for Quality of Life and Balance, respectively. Manual Muscle testing was used for assessments for pre and post muscle strength of the subject.

Conclusion: The timely diagnosis of a rare condition before the advancement of the disorder and thus the use of appropriate intervention of physiotherapy, which consisted of progressive muscle-strengthening exercises along with balance training proved to be promising in preventing falls, muscle atrophy and thus making the patient independent for doing daily activities.

Keywords: Limb-girdle muscular dystrophy(LGMD), Miyoshi Myopathy, Dysferlinopathy, Quality of life, Structured exercise regimen, Aquatic therapy.

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INTRODUCTION

Miyoshi myopathy was first reported in 1986 by K. Miyoshi in Japan [1]. Dysferlinopathy is an autosomal recessive disease seen in adolescence or young adulthood [2]. In this type of dystrophy, some mutations lead to an absence of muscle protein dysferlin [3]. The mutation for Dysferlinopathy occurs at chromosome 2p13 [2]. It is categorized as one of the rare diseases, and its prevalence is still not known [4,5]. Dysferlin, a protein composed of 2080 amino-acids, is located mainly at the muscle membrane in adult muscle and the T-tubule system in early development. Dysferlin is widely expressed in skeletal muscles as well as cardiomyocytes, and also in non-myofibres such as monocytes. Dysferlin is a sarcolemmal protein that also takes part in the repair of Sarcolemma. Dysferlin-containing vesicles fuse to form a “membrane patch.” The patch would then be added to the membrane disruption site for resealing. Dysferlin may also play a role in the central nervous system, notably at the blood-brain barrier level. However, Detailed interactions of Dysferlin with other proteins are still under investigation. Dysferlin and its proteins are associated with its functions in calcium-mediated membrane repair [3]. It is also associated with Vesicle trafficking and membrane remodeling [6]. The types of Dysferlinopathy are Miyoshi Myopathy and LGMD2B phenotype, both of which were observed in different individuals of the same family [7].

1. Miyoshi Myopathy- It is characterized by Marked weakness and wasting of posterior compartment leg muscles rather than the anterior compartment and distal upper limb muscles. Still, the intrinsic muscles of foot and hands are often spared.
2. LGMD2b -It is characterized by weak proximal muscles of the hip and shoulder [2].
3. Distal Myopathy with Onset in Tibialis Anterior-The anterior tibialis muscles are first involved, then the posterior muscles are affected by muscle weakness [7].

The diagnostic tests for Dysferlinopathy are as follows:

1. Serum CK concentration: Levels are increased up to 20-150times [2,3].
2. Electromyography (EMG) studies: The test is useful in the diagnoses of DMAT [8].
3. Muscle histology: Necrotizing process is found in muscles in patients with dysferlinopathy; however, at an early level, dystrophic changes may be minimum with easy split muscle fiber, centrally placed nuclei, and restricted degeneration of muscle fibers. Muscle biopsy still matters because the lesions are best observed in the affected muscles [8].
4. DNA Studies: DNA analysis remains the most reliable way to confirm the diagnosis of primary dysferlinopathy. It is seldom expensive, though [8].

Symptoms of Dysferlinopathy include the following: In the early phase patient has difficulties in standing for a long time, running, walking for long distances and stair climbing. As the disease progress, it becomes difficult for patients to

perform activities that require upper limb mobilization for a prolonged duration. There is also muscle dystrophy seen as the disease progress further. There are possibilities that one side may be more affected than others [9]. Available medical treatment shows that Glucocorticoids can be used for patients suffering from Dysferlinopathy. There are also beneficial effects of prednisone for sustaining the strength of the muscles observed ¹⁰. There isn't any established curative remedy for Dysferlinopathy, including gene therapy, and immunosuppressive therapy is not suggested for this condition [10, 11]. Conservative management with physiotherapy has been proven to benefit patients with Limb-girdle muscular dystrophies in terms of functional improvement. However, there is no specific structured exercise plan that targets a specific type of limb-girdle muscular dystrophy (e.g., Miyoshi Myopathy). Following the case report is one such study wherein the authors developed a structured exercise regimen for a specific case of Miyoshi Myopathy.

PATIENT INFORMATION

The subject was a 22-year-old male with no previous medical history. In 2016 by the end of the year, he noticed difficulty while walking, with no treatment for a year. As his symptoms aggravated, he started taking Ayurvedic treatment. As there was no potential benefit from the treatment, he then switched for homeopathic management. During this treatment, he noticed that there was some relief in his condition. Later on, he consulted a Neuro physician who then suggested for investigations like CPK (Creatine Phosphokinase) TEST along with EMG/NCV study. Reports revealed a significant rise in the CPK level. EMG/NCV reports concluded that both the lower limbs are consistent with primary Myopathic illness. He then consulted a neuro physician in Mumbai, where he was suggested for Focused Exome Sequencing. The results showed that he had Muscular dystrophy, limb-girdle, type2B. Currently, the patient is on medications and physical therapy care. His functional limitations include gait and recreational activities. Written consent was taken from the patient for this study after explaining everything in detail.

PHYSICAL EXAMINATION

Subject reported with deficits in muscle strength, history of recurrent falls, and dependency in activities of daily living. The subject's pre-assessments for strength, balance, and quality of life reflected reduced strength of the key muscles of the lower limb. Limb girth was also reduced. Balance assessments placed the patient in high-risk Category according to the POMA scale and low fall risk in the Berg Balance Scale. The quality of life of the patient was assessed by the Barthel Index Scale, which placed him in moderate dependency. All the assessments about the pre, mid treatment, and post-treatments were noted down (table 2,3,4 and 5).

Table 2: Manual Muscle Testing

JOINT	MOVEMENT	RIGHT			LEFT		
		PRE	3 rd week	6 th week	PRE	3 rd week	6 th week
HIP	FLEXION	2-	2+	3	2+	2+	3
	EXTENSION	2+	3+	4	2+	3+	4
	ABDUCTION	3	4	4	3+	4	4
	ADDUCTION	3+	4	4	4	4	4
	INT. ROT	2-	4	4	2-	4	4
	EXT. ROT	2+	4	4	2+	4	4
KNEE	FLEXION	3+	4	4	4	4	4
	EXTENSION	2-	2+	2+	2+	2+	2+
ANKLE	DORSIFLEXION	4	4	4	4	4	4
	PLANTAR-FLEXION	3	4	4	3	4	4
	INVERSION	4	4	4	4	4	4
	EVERSION	4	4	4	4	4	4

NOTE: Manual Muscle Testing (MMT) 5-point grading scales are as follows

Grade 0: Nil muscle contraction, Grade 1: Negligible Muscle Contraction, Grade 2: Full Active Range of Motion (AROM) in gravity eliminated position, Grade 3: Full AROM against gravity without any external resistance. 4: Full AROM against gravity, able to hold against moderate resistance 5: Full AROM against maximal resistance [16].

Table 3: Limb Girth

Above knee	Right			Left		
	Pre	3 rd week	6 th week	Pre	3 rd week	6 th week
5cms above	37	37	37	39	39	39
10cms above	39	40	40	42	42	42
15cms above	43.8	44	44	45	45	45
At calf (bulkiest part)	29	29.5	29.5	29	30	30

Table 4: Balance Parameter

	Pre	3 rd week	6 th week post
BERG BALANCE SCALE	45/56 Low fall risk	47/56 Low fall risk	48/56 Low fall risk
POMA	17/28 High fall risk	19/28 Medium fall risk	25/28 Low fall risk

Table 5: Quality of Life: Moderate Dependency

BARTHEL INDEX SCALE	Pre	3 rd week	6 th week post
	75/100	80/100	90/100

INTERVENTION

The patient was given both supervised training and home protocol for six weeks (3 sessions of supervised and three sessions of the unsupervised home protocol) along with one day as rest. The section included stretching, warm-up, Main exercise regime followed by a cool down. The warm-up period was of 5-10mins. Exercise included were ankle pumps, heel slides, Brisk walking, and free movements of other joints. Stretching: - Hamstrings, Quadriceps, Tendon

Achilles, Piriformis, and Adductors with 30secs hold for three sets. Exercise: - Exercise protocols ranged from low-intensity exercises to moderate-intensity exercises. Details of the protocol with progression are given in table 1.

Exercises

Active Straight leg raise with 10 seconds hold. Progression was done by providing resistance with a Thera band of different colors. Dynamic quads (Gravity eliminated plane) along with dynamic quads in water, followed by isometric hold against gravity for a brief period followed by light resistance band exercises. Hip musculature exercises were performed with light resistance by elastic bands against gravity. Stationary cycling was performed at the end of 10 minutes.

Aquatic therapy

Aquatic therapy was given (Figure 1) followed by ground exercises with variation in the level of water ranging from deep water (till manubrium sterni), moderate water (till xiphoid process), and mild water (till anterior superior iliac spine) which included the following exercises. i.e., Squatting, Lunges, Dynamic quads, Jogging, and Running.

Figure 1: Aquatic therapy



Figure 2: Tandem Standing



Balance Training

Additionally, balance training was given in the following order. Tandem standing along with catching a ball. Tandem walking with upper limbs elevated. One leg standing with eyes closed. The specific interventions have been explained in table 1.

Table 1: Structured Exercise Regimen

WEEK1	WEEK2	WEEK3	WEEK4	WEEK5	WEEK6
<p>1.Warm-up:- 5-10 minutes</p> <p>2.Stretching 3sets with 30seconds hold.</p> <p>3.Exercises:- 1. Static abdominals, static back withholds, 2. Straight leg raises active assisted (gravity eliminated), Abductions against gravity, hip extension (gravity eliminated plane.) 3. Dynamic quads (gravity eliminated plane) and active-assisted, knee flexion against the elastic band.4.Dorsiflexion and plantar flexion resistance exercises.10reps x 3sets. 5. Stationary cycling forward and backward 10 minutes</p> <p>4. Aquatic exercises: - 1.Mild water hamstring curls, Dynamic quads, 2.Underwatersquatting, Underwater lunges. 3sets x10reps. 3.Under-water toe standing, walking, underwater spot marching, 15mins each</p> <p>5.Balance training:- 1.Tandem walking, Tandem standing eyes closed (Figure 2), 2.Ball catching with a narrow base of support.</p>	<p>1.Warm-up:- 5-10 minutes</p> <p>2.Stretching 3sets with 30seconds hold.</p> <p>3.Exercises:- 1. Static abdominals and static back withholds, 2. Straight leg raises active assisted (gravity eliminated). 3.Abductions (against gravity), hip extension in gravity eliminated plane. 4. Dynamic quads in gravity eliminated plane, knee flexion against the elastic band. 5.Dorsiflexion and plantar flexion resistance exercises.10reps x 3sets. 6.Stationary cycling forward and backward 10 minutes</p> <p>4. Aquatic exercises:- 1.Mild water hamstring curls, Dynamic quads, 2. Underwater squatting, toe standing, Underwater lunges. 3sets x10reps. 3. Underwater walking, underwater spot marching, 15mins each</p> <p>5.Balance training:- 1.Tandem walking, Tandem standing with perturbations, 2. Ball catching with a narrow base of support</p>	<p>1.Warm-up:- 5-10 minutes</p> <p>2.Stretching 3sets with 30seconds hold.</p> <p>3.Exercises: -1.Abdominals curls, pelvic bridging 2. Straight leg raises (against gravity- active-assisted) 3.Abduction against elastic resistance, 4.Hip extension against gravity. 5. Dynamic quads against gravity active assisted. Knee flexion against elastic bands. 6.Dorsiflexion and plantar flexion against resistance.10reps x 3sets. 7.Stationary cycling forward and backward 10 minutes against resistance.</p> <p>4. Aquatic exercises:- 1.Mild water walking, jogging, 10mins steps climbing 5mins. 2. Deepwater jumping, toe standing 3sets 10reps. 3. Mild water squatting, lunges 3sets x10 reps.</p> <p>5. Balance training:- 1.Tandem walking with upper limbs in different positions. 2.One leg standing with perturbations. 3.Ball catching with tandem position. 4.Tandem standing with eyes closed with perturbations</p>	<p>1.Warm-up:- 5-10 minutes</p> <p>2.Stretching 3sets with 30seconds hold.</p> <p>3.Exercises:- 1. Abdominal side curls, pelvic bridging. 2. Straight leg raises (against gravity- active-assisted). 3.Abduction against elastic band against advanced color coding. 4.Hip extensions. 5.VMO strengthening. Ball kicking activities. 3sets x10 reps. 6.Stationary cycling forward and backward 10 minutes against resistance.</p> <p>4.Aquatic exercises:- 1.Mild water jogging, running, forward, and backward walking for 10mins. 2. Step climbing for three minutes. 3. Mild water squatting and lunges. 3setsx 10 reps</p> <p>5. Balance training:- 1.2Tandem walking with upper limbs in different positions. 2.One leg standing with weights. 3.Tandem standing with eyes closed with perturbations. Ball catching activities</p>	<p>1.Warm-up:- 5-10 minutes</p> <p>2.Stretching 3sets with 30seconds hold.</p> <p>3.Exercises: - 1. Abdominal curls, pelvic bridging withholds 2. Straight leg raises (against gravity). 3.Abduction against elastic band against progressive resistance levels. 4.Hip extension with holds. Ball kicking activities. 3sets 10 reps. 5.Stationary cycling forward and backward 10 minutes against resistance.</p> <p>4. Aquatic exercises:- 1.Mild water jogging, spot marching, forward and backward walking for 10 minutes. 2. Steps climbing x Three mins 3.Mild water squatting and lunges 3 sets x 10 reps</p> <p>5.Balance training:- 1.Tandem walking with weights. 2.Tandem standing with eyes closed with perturbations. Ball catching 3. Activities with a narrow base of support</p>	<p>1.Warm-up:- 5-10 minutes</p> <p>2.Stretching 3sets with 30seconds hold.</p> <p>3.Exercises:- 1.Resistance training with elastic bands for hip abduction. 2. Pelvic bridging withholds, Hip extensions withholds, 5secs hold 10 reps. 3. Straight leg raises. 4.Abdominal curls 3sets x10 reps, ball kicking, 3sets x 10 reps 5.Cycling forward and backward 10 minutes</p> <p>4. Aquatic exercises:- 1.Mild water jumping, spot marching, jogging, steps climbing, forward and backward walking, 15 minutes With resistance. 2.Low water squatting. 3sets x10 reps</p> <p>5. Balance training: - 1.Tandem walking with weights, One leg standing with weights, eyes closed and tandem standing perturbations, 2. Ball catching activities with a narrow base of support.</p>

Termination criteria for exercises of Miyoshi Myopathy:

1. Angina (moderate to severe).
2. A rise in neural symptoms like ataxia or syncope.
3. Indications of poor perfusion like cyanosis or pallor.
4. If the subject request to stop the exercises.
5. Exercise-induced fatigue [12].

Follow-up and Outcomes

The pre and post-intervention assessment of the subject was documented. Post manual muscle testing grading showed an improvement in strength from 2 to 4 in most of the muscles. Barthel index scale also showed an increase in the ADLs from 75/100 to 90/100. Performance-Oriented Mobility Scale (POMA) was taken pre and post, which concluded that the patient improved from prior high-risk fall with a scoring of 17/28 to the low fall risk with a scoring of 25/28. In the Berg Balance Scale, the subject was placed in low fall risk with a reading from 45/56 to 48/56. The limb girth measurements (Table no. 3) also showed an increase in muscle mass, thus preventing further muscle atrophy and maintenance of muscle mass. The subject also reported that there was no decrease in strength and history of falls for six months after the treatment.

DISCUSSION

Many forms of muscular dystrophies are being identified in our country due to the advancement of genetic analysis. Modern muscle biopsy, histochemistry, and advancement in gene testing have made it possible to diagnose different forms of limb-girdle muscular dystrophies. The ultimate goal of the genetic analysis is to provide an accurate diagnosis of the type of myopathy and to rule out the cardiac, pulmonary, along with musculoskeletal problems. Based on the genetic diagnosis, neurological involvement can be ruled out, and early physiotherapy interventions can help to enhance career routes.

In the present report, an appropriate diagnosis of the condition was done due to which it was easy to rule out the primarily affected muscles, thus enhancing the treatment to be focused on a specific muscle group. Before the treatment was initiated, the patient was self-ambulatory and had a moderate dependency due to which the set treatment protocol was followed that included warm-up, stretching, progressive resisted exercises, hydrotherapy, and cool-down. Animee K et al. in 2017 used a combined approach of both aquatic and land-based physiotherapy resulting in the improvement in functional mobility and

quality of life. The patient indicated less tiredness and greater confidence in bed mobility and ambulation [13]. Takashi K et al. in 2019 carried research on dysferlinopathy in which he stated that Glucocorticoids are the best known pharmacological management for dysferlinopathy while the use of deflazacort (Steroid used against inflammation) can lead to the worsening of the muscle strength [10]. Monica S et al. in 2019, stated that the patients with dysferlinopathy had a different type of unique gait, and waddling is just a component of their gait [14]. Another research by Satish K in 2017 stated that the genetic identification of both myopathies coincides have the same genetic defect, so they are named together as dysferlinopathy [15]. Olivier B, in their study in 2013, mentions that concentric/isometric exercises training and refraining from any eccentric load will improve the muscle strength without causing membrane damage. Based on this exercise training statement, the above treatment was formulated, which resulted in better muscle strength and preservation of the muscle mass. In 2017 Patel NJ, in her study, explained that at present, there is no curative treatment for muscular dystrophy, gene therapy will have a future role, and Immunosuppressive drugs are not advisable. Thus only available mainstay for the treatment is physiotherapy with the help of graded strengthening protocol [11]. There was a significant improvement in the muscle strength as well, balance, and quality of life of the patient. The treatment protocol was formulated on the statement given by Olivier B, which majorly included isometric/concentric exercises avoiding eccentric exercises leading to an increase in muscle strength. Equally, the balance assessments also showed positive effects resulting in the placement of the patient in low fall risk on the POMA scale. There was also an increase in the quality of life of the patient because of the significant increase in strength and balance, leading to the ease of carrying out daily activities.

The study had several limitations. Firstly, the exercises were of short duration. Secondly, the study did not address the changes at the cellular level due to a lack of funding. The exercise regimen included combined land-based and aquatic treatments. Therefore, the benefits of isolated interventions remain unclear.

This is not a generalized protocol for dysferlinopathy like Miyoshi Myopathy, LGMD2b, or a combination of both. But the present case study is suggestive that with the help of a structured exercise regimen and exercises performed daily, there can be a significant rise in muscle strength reducing the chances of injury due to falls.

CONCLUSION

The presented case report showed that the appropriate use of advanced genetic analysis leads to an early diagnosis of LGMD. This leads to a timely diagnosis of a rare condition before the advancement of the disorder and, thus, the use of appropriate intervention of physiotherapy. The physiotherapy approach should be focused on making the patient independent and maintaining long term mobility. There should be awareness of LGMDs and early referral for

physiotherapy management before the disorder advances, thus making the patient independent to enhance their career route.

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Conflict of Interest: NONE

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