Case Report

Stem cell therapy in a child with Duchene Muscular Dystrophy (DMD) at Bangladesh Shishu Hospital and Institute, Dhaka

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Introduction

Duchenne muscular dystrophy (DMD) is the most common and severe form of muscular dystrophy, predominantly affecting males.[1,2] It is an X-linked, progressive, degenerative myopathy, with approximately two-thirds of cases inherited maternally and one-third arising from de novo mutations.[1] DMD occurs in approximately 1 in 3,500 male births and results from mutations in the dystrophin gene located at Xp21.2.[3] Among the causative mutations, approximately 65% are intragenic deletions, 6–10% are intragenic duplications, and 30–35% are point mutations or other sequence variants.[3]

DMD is an early-onset, debilitating disorder characterized by progressive muscle weakness that typically manifests around 4 years of age and advances rapidly.[4] The disease is caused by the absence of dystrophin or the production of a nonfunctional dystrophin protein, a key component of the dystrophin–glycoprotein complex (DGC), which provides structural stability by linking the cytoskeleton to the extracellular matrix in skeletal and cardiac muscle.[5] Loss of dystrophin leads to muscle fiber degeneration, progressive muscle wasting, and weakness, ultimately resulting in loss of ambulation during puberty.

A characteristic clinical feature of DMD is a positive Gowers' sign.[6] Pseudohypertrophy of the calves, tongue, buttocks, and shoulder muscles, typically observed between 4 and 5 years of age, is another hallmark finding.[7] Muscle weakness initially affects the lower limbs and predominantly involves proximal rather than distal muscle groups. Most affected individuals become wheelchair-dependent by approximately 12 years of age. Premature death commonly occurs in the mid-to-late twenties due to respiratory failure, cardiomyopathy, or a combination of both, with an estimated life expectancy of 25–26 years.[8,9] Becker muscular dystrophy (BMD), a milder variant of muscular dystrophy, is distinguished by later onset, slower disease progression, delayed loss of ambulation and longer survival. Diagnostic confirmation of DMD requires markedly elevated serum creatine kinase (CK) levels, electromyography, muscle biopsy, and positive genetic testing. Additional serum enzymes, including alanine aminotransferase, aspartate aminotransferase, aldolase, and lactate dehydrogenase, are also typically elevated. [10,11]

Yet there is no curative treatment is available for DMD. Corticosteroid therapy and physiotherapy remain the mainstay of management and have been shown to slow disease progression. [12]However, recent advances in the management of Duchenne muscular dystrophy (DMD) include disease-modifying approaches such as exon-skipping therapies, gene therapy, and stem cell–based interventions aimed at altering the disease process and slowing disease progression.[13] Autologous stem cell therapy represents one such strategy, wherein stem cells are harvested from the patient with DMD, genetically modified in vitro to restore dystrophin expression, and subsequently reintroduced into the same individual.[14]

In this report, we describe the clinical course of a 5-year-old boy diagnosed with DMD, highlighting his distinctive clinical features, diagnostic findings, and treatment with autologous stem cell therapy. To the best of our knowledge, this is the first reported case in Bangladesh in which autologous stem cell therapy has been administered for the treatment of DMD.

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Case report

A 5-year-old boy of a non-consanguineous parents presented to the Department of Neuroscience at Bangladesh Shishu Hospital and Institute, Dhaka, with a 1-year history of progressive difficulty in walking, characterized by frequent falls, easy fatigability, muscle weakness, and inability to climb stairs. Over the preceding 6 months, he had also developed difficulty in rising from a sitting position. There was no history of muscle pain or cranial nerve involvement. His intelligence quotient was reported to be within the normal range. Family history was notable for two siblings affected by a similar illness, and one maternal cousin who had died at a young age due to the same illness.

On general physical examination, the child was alert and cooperative but demonstrated difficulty in standing, walking, rising from a sitting position, and climbing stairs. Neuromuscular examination revealed predominant proximal muscle weakness, calf pseudohypertrophy, and a positive Gowers' sign. There was no evidence of muscle wasting, fasciculations, or abnormal muscle tone. Cranial nerve examination was unremarkable.

Laboratory investigations revealed a markedly elevated serum creatine kinase (CK) level of 20,200 U/L, lactate dehydrogenase of 595 µg/dL, and alanine aminotransferase of 124 U/L. Ultrasonography of the calf muscles demonstrated increased echogenicity and thickness of the gastrocnemius muscle, consistent with fatty infiltration of muscle tissue (Figure/Photo 1). Genetic analysis (Figure 1) confirmed the diagnosis of Duchenne muscular dystrophy.

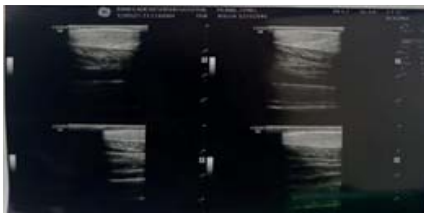

Photo-1: USG of calf muscle

gastrocnemius muscle shows higher echogenicity & increased thickness of muscle due to fat accumulation within the muscle layer

FINDINGS RELATED TO PHENOTYPE

Gene&Transcript	Variant	Location	Zygosity	In silico Parameters**	Disorder(OMIM)	Inheritance	Variant Classification
DMD NM_004006.3	c.8399T>A p.Leu2800*	Exon 57	Hemizygous	CADD: 40	MUSCULAR DYSTROPHY, DUCHENNE TYPE; DMD:310200	X-linked Recessive	Likely Pathogenic

* Genomic Position based on Assembly GRCh37, **Number of applied in silico programs predicting the effect of the variant on the protein outcome (CADD: Combined Annotation Dependent Depletion (v1.6), SIFT, PolyPhen-2, MT: Mutation Taster), N/A: Not Applicable, ***Minor Allele Frequency as described in GnomAD (Controls), ****based on ACMG Guidelines. het-heterozygous, hom-homozygous, hemi-hemizygous.

Figure 1: Genetic analysis report

Taken together, the clinical presentation, markedly elevated muscle enzymes, imaging findings, and positive genetic analysis confirmed the diagnosis of Duchenne muscular dystrophy. Current management of Duchenne muscular dystrophy (DMD) in Bangladesh primarily consists of corticosteroid therapy and physiotherapy, which may delay loss of ambulation by approximately 1–3 years but do not provide a cure. Following confirmation of the diagnosis, the patient was treated with deflazacort for 6 months; however, no significant clinical improvement was observed. During this period, the child developed unclear speech and learning difficulties, resulting in irregular school attendance for approximately 6 months.

Long-term corticosteroid therapy is associated with significant adverse effects, including weight gain, reduced bone mineral density, Cushingoid features, and behavioral disturbances etc. In view of the lack of clinical response and the potential for steroid-related complications, alternative therapeutic options were considered. As no curative treatment for DMD currently available and most emerging therapies remain investigational within the field of regenerative medicine, autologous stem cell therapy has been proposed as a potential disease-modifying approach. This strategy aims to restore dystrophin expression in affected muscle fibers through transplantation of modified stem cells capable of fusing with existing myofibers. Accordingly, the decision was made to treat this patient with autologous stem cell therapy at Bangladesh Shishu Hospital and Institute, in compliance with the "Guidelines for Regulatory Approvals of Stem Cell and Cell-Based Products (SCCPs)" issued by the Directorate General of Drug Administration, Ministry of Health and Family Welfare, Government of the People's Republic of Bangladesh.

After appropriate counseling and obtaining informed consent, the patient was admitted to the Department of Neuroscience at Bangladesh Shishu Hospital and Institute for treatment with autologous stem cell therapy. Autologous stem cells were harvested from the patient's bone marrow under strict aseptic conditions and mild sedation in a modular operation theater.

A total of 25 mL of bone marrow aspirate was obtained and processed using a cell separator by centrifugation. Within 30 minutes of collection, the bone marrow aspirate concentrate (BMAC) was administered to the patient via multiple routes: intrathecal (5 mL), intravenous (5 mL), and intramuscular (5 mL) injections.

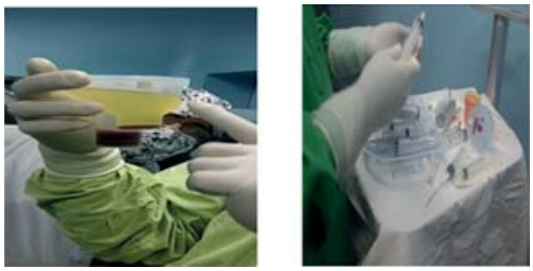

Fig. Separation of BMAC after collection

Autologous stem cell therapy is generally considered safer than allogeneic blood transfusion, as the risk of immunologic transfusion reactions is minimal. In this case, the patient received autologous stem cell therapy at 3-month intervals for a total of three treatment cycles. Follow-up evaluations were conducted one month after each treatment session.

Follow-up and Outcome

At each follow-up visit, clinical assessment was performed using the North Star Ambulatory Assessment (NSAA) scale,[15] and serum creatine phosphokinase (CPK) levels were measured to monitor biochemical response.

Table I: Outcome after giving stem cell therapy

	10 meters walking	6 min walking test	Time to climb 4 stairs	Time taken to stand >30 sec
1st Follow up	>12 sec	<325 meter	>8 sec	>30sec
2nd Follow up	>12 sec	<325 meter	>8 sec	>30 sec
3rd Follow up	>12 sec	<325 meter	>8 sec	>30 sec

Table II: Investigation before and after stem cell therapy

	Before therapy	After 3rd follow up
Serum CPK	20,200 u/ml	1000u/ml

Serial NSAA evaluations demonstrated that the patient's clinical condition remained static over the follow-up period. Biochemically, a reduction in serum CPK levels was observed following stem cell therapy. Clinically, improvement in speech was noted, with clearer phonation. The child resumed school attendance; however, academic performance showed minimal improvement. Further assessment of social, emotional, and adaptive functioning using standardized psychometric tools is planned after completion of 1 year of therapy.

Discussion

Stem cell therapy represents one of the most promising investigational approaches for the treatment of muscular dystrophies. Stem cells are characterized by their capacity for long-term self-renewal and their ability to differentiate into multiple cell lineages.[16] They play a critical role in tissue development, repair, and maintenance.[17] Experimental studies have demonstrated that stem cells may differentiate beyond their tissue of origin; for example, transplanted bone marrow cells and enriched hematopoietic stem cells (HSCs) have been reported to give rise to mesodermal,[18] endodermal,[19] and ectodermal lineages.[20] These discoveries have led to the emergence of the fields of stem cell medicine and regenerative medicine.

Stem cell–based therapeutic strategies for Duchenne muscular dystrophy (DMD) broadly follow two approaches. The first involves autologous stem cell transplantation, in which cells derived from the patient are genetically modified in vitro to restore dystrophin expression and subsequently reintroduced into the patient. [21] The second approach is allogeneic stem cell transplantation, in which cells obtained from a donor with functional dystrophin are transplanted into the dystrophic patient. [22]

Bone marrow–derived autologous stem cells are inherently non-immunogenic, thereby minimizing the risk of immune rejection. In the present case, autologous stem cell therapy was administered at 3-month intervals. During follow-up, the patient's clinical condition remained static, with no further deterioration in motor function. Additionally, improvement in speech clarity and school attendance suggested a positive impact on cognitive or functional domains.

Although the absence of extensive investigational support and limited duration of therapy may have restricted the extent of observable clinical improvement, the patient's preserved mobility and ability to perform activities of daily living suggest a potential therapeutic benefit of stem cell therapy. The patient continues to receive adjunctive physiotherapy, as well as cognitive and behavioral interventions. Ongoing long-term follow-up is essential to evaluate sustained efficacy, functional outcomes, and safety of stem cell therapy. At present, cautious interpretation of outcomes is warranted, and further studies are needed before definitive conclusions regarding the role of stem cell therapy for DMD in Bangladesh can be drawn.

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