CASE REPORT
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FUNCTIONAL RECOVERY AFTER WHARTON'S JELLY–DERIVED MESENCHYMAL STEM CELL ADMINISTRATION IN A PATIENT WITH TRAUMATIC SPINAL CORD INJURY: A PILOT STUDY

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ABSTRACT

The use of stem cells in the treatment of traumatic spinal cord injury (SCI) in recent years has provided promising results. Different sources of cells for transplantation have been used, including mesenchymal stem cells [MSCs; e.g., Wharton's jelly-derived (MSCs WJ-MSCs)]. Here, we reported on a 29-year-old man who was treated with WJ-MSCs in the course of therapy for blunt, traumatic SCI due to a work accident. He was operated on within 6 hours of the injury. Three and a half months later, he underwent intrathecal, intramuscular, and intravenous administrations of WJ-MSCs at a target dose of 1x106/kg for each application route (twice a month for 2 months). All the procedures were tolerated well by the patient. In parallel to this, we have not seen any application-related complications so far. After stem cell infusions, progressive improvements were shown in the patient's neurological examination and neurophysiological and neuroradiological findings.

Keywords: Stem cell, transplantation, traumatic spinal cord injury, Wharton's jelly

INTRODUCTION

Spinal cord injury (SCI) is a serious, debilitating condition affecting mostly young individuals. There have been many advances in the early surgical management and rehabilitation of these patients, resulting in improved survival but a lesser degree of functional improvement and independence[1]. The exact pathomechanism of SCI in humans remains blurry because most data about SCI have been acquired from animal models. An extensive interplay between various cells and molecules of the central nervous system (CNS), such as adhesion molecules, immune cells, and scar-forming cells, seems to be involved. It has been suggested that the extents of the astrocytic response and demyelination process are different between the pathomechanisms in humans and animal models; however, the fundamental events are similar[2]. SCI is a bi-phasic assault. In the first phase of SCI, mechanical damage to the spinal cord results in the rupture of neuronal membranes and axonal damage[3]. Decreased blood flow causes hypoxia and diffuse swelling of the cord[4]. The secondary phase causes prolonged and widespread tissue damage resulting from interlinked events like excitotoxicity, ionic imbalance, oxidative stress, and immune and inflammatory responses[5,6]. But setting off of a multitude of vascular, biochemical, cellular, and molecular events exaggerates the inflammatory response and aggravates the lesion[7]. The current treatment for traumatic SCI is surgical decompression of the spinal cord and medical treatment, such as methylprednisolone steroid therapy[8]. Recent advances in neuroscience and regenerative

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treatments, along with an intense focus on cell-based therapy, have yielded promising results. Karaoz et al.[9] suggested that transplantation of rat pancreatic islet-derived stem cell (rPI-MSCs) in the contused spinal cord improved locomotor recovery. Reduction of inflammation factors after rPI-SCs transplantation might be effective for functional outcomes following traumatic injuries to the spinal cord[9].

CASE PRESENTATION

The presented pilot study was a prospective, longitudinal medical experiment. The study was performed at the University of Health Sciences Turkey, Gaziosmanpaşa Training and Research Hospital, İstanbul, Turkey. The MSC trial was approved by the Turkish Ministry of Health (protocol number: 56733164-203-E.2569). The patient was informed of the procedure, and a written informed consent form was obtained per the Helsinki Declaration. The general data collected before the experimental therapy consisted of age, gender, cause of the SCI, length of time since the SCI, previous medical treatment for the SCI, and past medical history.

Medical History

The patient was a 29-year-old male who had fallen from a power pole and was admitted to a private hospital's emergency room in a paraplegic condition. He had been diagnosed with a T5-6 fracture dislocation and blunt, traumatic SCI, which can be stated as a mid-thoracic (T6) American Spinal Injury Association (ASIA) Impairement scale grade-A SCI. He had no motor or sensory function below T6 or in his sacral area. He had undergone operation within 6 hours after the injury and had a T5-7 total laminectomy and T3-11 posterolateral fusion (Figure 1). Postoperatively, his neurological status had not changed. One week after the operation, he reported a crude touch sensation between the T6 and T8 levels, but he was unable to discriminate the examining needle in his detailed neurological examination. No motor recovery or sacral sensory changes were noted. He had been admitted to physical therapy for 3 months, which increased the patient's level of participation in therapy without any improvement in the neurological function (Figure 2A, B; Table 1 and 2). At this stage, the patient was referred to our tertiary level hospital for the MSC trial.

Enrollment Criteria

The pilot study included the patient with SCI, with contusions (preserved anatomical integrity of the spinal cord) confirmed by imaging studies [magnetic resonance imaging (MRI), etc.] and neurological examination and neurophysiological findings. Focal CNS lesions (e.g., neoplastic lesions) or chronic diseases (e.g., systemic diseases) that would require long-term pharmacotherapy would be exclusion criteria. Prior to the treatment, the patient was examined by the doctors in the neurosurgery and physical therapy and rehabilitation departments. The Wharton's jelly mesenchymal stem cells (WJ-MSC) implantation procedure was performed when the patient was stable, without contraindications for sedo-/general anesthesia from the viewpoint of internal medicine and without any serious infectious diseases, including sepsis, immediately prior to the procedure.

PROCEDURE

Umbilical cords were obtained from the Good Manufacturing Practice facility of LivMedCell (İstanbul, Turkey). All the umbilical cords were obtained from various donors after informed consent, as approved by an institutional regulatory board (LivMedCell). Postnatal umbilical cords were obtained from donors of full-term pregnancies. Recently, we represented the umbilical cord processing and quality control, characterization of WJ-MSCs by flow cytometry, cell differentiation and karyotyping, pre-transplantation process, and surgical procedure and WJ-MSC transplantation procedure in our previous publications (Table 3)[10,11].

Clinical Evaluation and Statistical Analysis

Pretreatment Neurological Examination

The pretreatment assessment included extensive evaluation by a team of medical and rehabilitation experts (Suppl. Video 1). Detailed neurological and functional evaluation was documented in each step of the procedure (e.g., ASIA). Spasticity

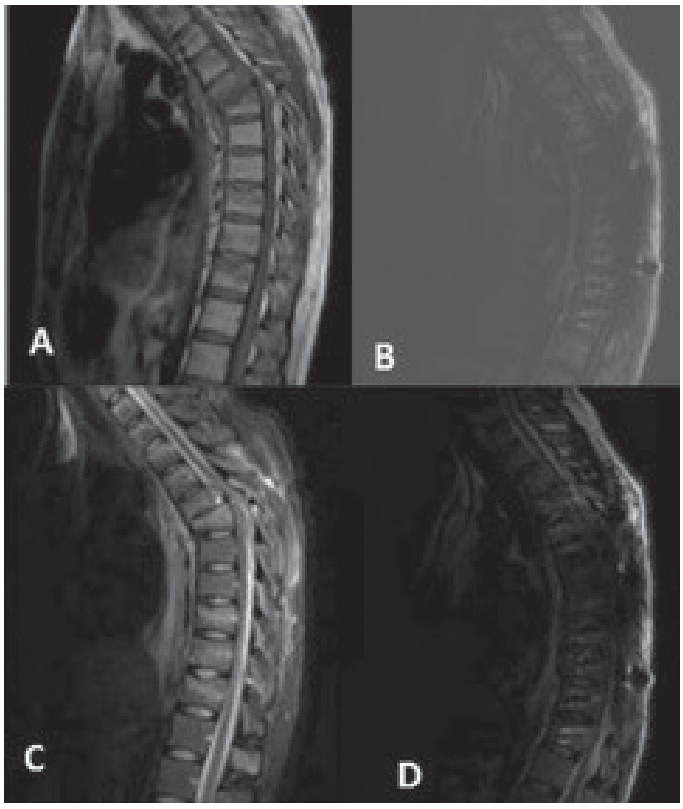

Figure 1. Spinal cord MRI including T1 sequences; (A) postop early, (B) 6 months a.f.i, spinal cord MRI including T2 sequences; (C) post-op early and (D) 6 months a.f.i. showed bilateral myelomalacia

MRI: Magnetic resonance imaging

was assessed using the Modified Ashworth scale, and quality of life was assessed based on parental evaluation according to the Functional Independence Measure (FIM) scale[12].

Safety Evaluation Criteria

The safety criteria for the transplantation procedure included the appearance of infection, fever, headache, pain, an increased level of C-reactive protein, increased leukocytosis, allergic reaction/shock, and perioperative complications (anesthesia-and analgesia-related complications, infections of the wound) for 7-14 days after the procedure. The safety criteria for using WJ-MSC included infection, neuropathic pain, cancer development, and deterioration of the neurological state, and they were assessed for a 1-year follow-up period.

Follow-up Assessment of Treatment Success

The follow-up evaluation consisted of a neurological examination evaluating motor function according to the Medical Research Council (MRC) Muscle Strength scale. The progression of the patient's sense was evaluated by detailed sensory examination. Clinical signs of efficacy were observed at 1 week, 1, 2, 3, and 9 months following the injection in both motor and sensory scores based on International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI)[13]. Spasticity was assessed using the Modified Ashworth scale, and quality of life was assessed based on the functional recovery estimated by the FIM scale[14]. In addition, an evaluation of the development of neuropathic pain, secondary infections, urinary tract infections, or pressure ulcers of the skin was performed.

RESULTS

Safety and Adverse Events

The patient tolerated the procedure well and did not experience any severe adverse events related to the injection. Our patient showed only early, transient complications, such as subfebrile fever, mild headache, and muscle pain due to intramuscular (i.m.) injection, which resolved in 24 hours (Table 4). Throughout the 1 year follow-up, no other safety issues or adverse events were reported.

Table 1. Sensory examination

Dermatomes (0: absent, 1: altered, 2: normal)		Time of SCI (06.06.2017)		Post-op. 1st week (13.06.2017)		At discharge (07.09.2017)		After 1st MSC administration (27.09.2017)		After 2nd MSC administration (11.10.2017)		After 3rd MSC administration (25.10.2017)		After 4th MSC administration (29.11.2017)		After 6 months from the final application (08.06.2018)	
		Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
T5	5th Intercostal space	2+C4:R10	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
T6	6th Intercostal space	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2
T7	7th Intercostal space	0	0	1	1	2	2	2	2	2	2	2	2	2	2	2	2
T8	8th Intercostal space	0	0	1	1	1	1	2	2	2	2	2	2	2	2	2	2
T9	Between 8th intercostal space and umbilicus	0	0	0	0	0	0	2	2	2	2	2	2	2	2	2	2
T10	Umbilicus	0	0	0	0	0	0	1	1	2	2	2	2	2	2	2	2
T11	Between umbilicus and inguinal ligament	0	0	0	0	0	0	0	0	1	1	2	2	2	2	2	2
T12	Inguinal ligament	0	0	0	0	0	0	0	0	0	0	2	2	2	2	2	2
L1	Anterosuperior of thigh	0	0	0	0	0	0	0	0	0	0	2	2	2	2	2	2
L2	Anteromedial of thigh	0	0	0	0	0	0	0	0	0	0	2	2	2	2	2	2
L3	Medial condyl of femur	0	0	0	0	0	0	0	0	0	0	1	1	2	2	2	2
L4	Medial malleolus	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2
L5	Dorsal foot at 3rd metatarsophalangeal joint	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1

SCI: Spinal cord injury, MSC: Mesenchymal stem cell

Table 2. Motor and sensory scores according to International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI)

	Time of SCI (06.06.2017)	Post-op. 1st week (13.06.2017)	At discharge (07.09.2017)	After 1st MSC administration (27.09.2017)	After 2nd MSC administration (11.10.2017)	After 3rd MSC administration (25.10.2017)	After 4th MSC administration (29.11.2017)	After 6 months from the final application (08.06.2018)
Lower right extremity motor score	0	2	3	8	9	14	16	20
Lower left extremity motor score	0	2	3	7	8	12	14	17
Total lower extremity motor score	**0**	**4**	**6**	**15**	**17**	**26**	**30**	**37**
Right pinprick sensory score	24	27	28	35	36	42	43	45
Left pinprick sensory score	24	27	28	35	36	42	43	45
Total pinprick sensory score	**48**	**54**	**56**	**70**	**72**	**84**	**86**	**90**
Right light touch sensory score	25	28	29	33	35	43	44	47
Left light touch sensory score	25	28	29	33	35	43	44	47
Total light touch sensory score	**50**	**56**	**58**	**66**	**70**	**86**	**88**	**94**

SCI: Spinal cord injury, MSC: Mesenchymal stem cell

Figure 2. A, The total lower extremity motor score at all time points. B, Total pinprick and light touch sensory score at all time points. C, FIM scale scores at all time points.

FIM: Functional independence measurement, ISNCSCI: International Standards for Neurological Classification of Spinal Cord Injury

ASIA Motor Score

The total lower extremity motor score progressively improved from 6 at baseline to 37 at 9 months, with more marked improvement on the right (3 at baseline to 20 at 9 months) with the left side (3 at baseline to 17 at 18 months) (Figure 2A; Table 2).

ASIA Sensory Score

The total pinprick score improved consistently at each time point from 56 at baseline to 90 at 9 months of follow-up. The improvement was similar on both sides, improving from 28 at to 45 at 9 months of follow-up. Similarly, total light touch score also improved on both sides 58 at baseline to 94 at 9 months of follow-up (Figure 2B; Table 2). We also examined the improvement in each dermatomal region. In the lower thoracic level, the improvement was substantially pronounced in the T10 region bilaterally after the first WJ-MSC application and so on. In the lower extremity, the patient experienced improvement in L4, L5 (Table 1).

Table 3. Administration schedule

Date Route WJ-MSC
Round 1
09.20.2017 IT 1x10$_6$/kg in 3 mL 09.20.2017 IV 1x10$_6$/kg in 30 mL 09.20.2017 IM 1x10$_6$/kg in 20 mL
Round 2
10.11.2017 IT 1x10$_6$/kg in 3 mL 10.11.2017 IV 1x10$_6$/kg in 30 mL 10.11.2017 IM 1x10$_6$/kg in 20 mL
Round 3
10.18.2017 IT 1x10$_6$/kg in 3 mL 10.18.2017 IV 1x10$_6$/kg in 30 mL 10.18.2017 IM 1x10$_6$/kg in 20 mL
Round 4
11.22.2017 IT 1x10$_6$/kg in 3 mL 11.22.2017 IV 1x10$_6$/kg in 30 mL 11.22.2017 IM 1x10$_6$/kg in 20 mL

IT: Intratekal, IV: Intravenous, IM: Intramuscular, WJ-MSC:Wharton's jelly-derived mesenchymal stem cell

Table 4. Early and late complications of the proces

Complications	09.20.2017	10.04.2017	10.18.2017	11.22.2017
Early				
Infection	-	-	-	-
Fever	+	+	-	+
Pain	+	-	+	-
Headache	+	+	-	-
Increased level of C-reactive protein	-	-	-	-
Leukocytosis	-	-	-	-
Allergic reaction or shock	-	-	-	-
Perioperative complications	-	-	-	-
Late				
Secondary infections	-	-	-	-
Urinary trackt infections	-	-	-	-
Deterioration of neurologiacal status	-	-	-	-
Carcinogenesis	-	-	-	-

-: Not present, +: Present

Table 5. Quailty-of-life improvement and spasticity evaluated with the use ot the FIM scale, modified ashworth grading and MRC muscle strength scale

Evalualuation periods (Pre and post-transplantation)	FIM scale		Modified ashworth scale						MRC muscle strength scale					
			Hips		Knees		Ankles		Hips		Knees		Ankles	
	Motor	Cognitive	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Pre-transplantation	51	35	2	2	2	2	2	2	0	0	0	0	0	0
After 1st admin.	53	35	2	2	2	2	2	2	0	0	0	0	0	0
After 2nd admin.	56	35	2	2	2	2	2	2	1	1	0	0	0	0
After 3rd admin.	58	35	1+	1+	1+	1+	1+	1+	2	2	1	1	0	0
After 4th admin.	61	35	1+	1+	1+	1+	1+	1+	2	2	1	1	0	0
After 6 months from the final application	65	35	1	1	1	1	1	1	2	2	2	2	1	1

Admin: Administration, FIM: Functional independence measurement, MRC: Medical research council

Table 6. Quality of life improvement evaluated with the use of the FIM scale

Measurement	Pre-transplantation	After 1st administration	After 2nd administration	After 3rd administration	After 4th administration	After 6 months from the final application
Self care						
Eating	7	7	7	7	7	7
Grooming	7	7	7	7	7	7
Bathing	6	6	7	7	7	7
Dressing-upper body	6	6	7	7	7	7
Dressing-lower body	6	6	6	6	7	7
Toileting						
Sphincter control						
Bladder management	1	1	1	1	1	1
Bowel management	1	1	1	1	3	4
Transfer						
Bed, chair, wheelchair	5	5	5	5	5	7
Toilet	5	5	6	6	6	7
Tub, shower	5	5	5	6	6	6
Locomotion						
Walk/wheelchair	1	2	2	3	3	4
Starrs	1	1	1	1	1	1
Motor subtotal score	**51**	**52**	**56**	**58**	**61**	**65**
Communication						
Comprehension	7	7	7	7	7	7
Expressionr	7	7	7	7	7	7
Social cognition						
Social interaction	7	7	7	7	7	7
Problem solving	7	7	7	7	7	7
Memory	7	7	7	7	7	7
Cognitive subtotal score	**35**	**35**	**35**	**35**	**35**	**35**
Total FIM score	**86**	**88**	**91**	**93**	**96**	**100**

FIM: Functional independence measurement, FIM scale in detail; 7 Points: Complete independence, 6 Points: Modified independence, 5 Points: Supervision, 4 points: Minimal assistance, 3 Points: Moderate assistance, 2 Points: Maximal assistance and 1 Point: Total Assistance or not testable. Total motor score: 91 points, total cognitive score: 35, and total FIM score is 126

FIM Scale Score

Substantial improvement in quality of life was observed, as assessed using the FIM scale 6 main questionnaire including motor and cognitive scores. The total FIM Scale score improved from 86/126 at baseline to 100/126 at 9 months. The total motor score improved consistently at each time point from 51 at baseline to 65 at 9 months of follow-up. The total cognitive score was 35 and remained stable at 9 months of follow-up (Figure 2C; Table 5, 6).

Modified Ashworth and MRC Muscle Strength Scale

The Modified Ashworth Scale score was similar on both sides, improving from 2 at baseline to 1 at 9 months of follow-up. Similarly, MRC Muscle Strength scale score also improved on both sides from 0 at baseline to 2 in his knees and hips at 9

Table 7. Summary of the neuroradiological and neurophysiological findings using MRI and EMG before and after treatment

	Date	MRI appearance of cord
MRI	Pre-t.p.	Ischemia (T2 hyperintensity)
	Post-t.p.	Bilateral myelomalacia
	Date	**EMG findings**
EMG	Pre-t.p.	Upper motor neuron involvement
	Post-t.p.	Not present

MRI: Magnetic resonance imaging, EMG: Electomyography, t.p.: transplantation

months of follow-up. On the other hand, MRC Muscle Strength scale score improved on both sides from 0 at baseline to 1 in his ankles at 9 months of follow-up (Table 5).

Neuroradiological and Neurophysiological Findings

In the early postoperative spinal cord MRI, there was ischemia (T2 hyperintensity) in the injured thoracic spinal cord (T6). On repeating spinal cord MRI at 3 months after the first interventation (a.f.i.), there was bilateral myelomalacia in the injured thoracic spinal cord (T6). In the electromyographic (EMG) a.i.f readings showed normal motor and sensory transmission without firing of motor unit potentials, revealing an upper motor neuron lesion in accordance with the original spinal cord lesion at T6. Post-transplantation EMG wasn't presented due to clinical improvement of the patient (Data not shown) (Figure 1; Table 7).

Physical Therapy

We also observed considerable improvement in physical therapy at follow-up. Starting from the first transplantation, the patient underwent intensive neurorehabilitation that included physiotherapy as a part of the treatment program. The patient was placed on a personalized exercise program that emphasized techniques for facilitating mobility and the multiplication of the injected stem cells, thereby giving enhanced results. The personalized program comprised one session (50 min.) per day, 5 times a week, including posture, balance, range of motion and strength and stretch exercises. On the stem cell application days, the exercise program was interrupted. After 1 week following the initial administration of MSCs, the patient mentioned that he had gained some sensation back in previously numb areas (T6-10 dermatomes). Two weeks later, a 2nd administration of MSC resulted in improved sensation between the T6 and T11 dermatomes, just below the umbilicus. A 3rd MSC administration resulted in sensory extension down to the L2-3 dermatomes (Table 1; Suppl. Video 2). After the 4th MSC administration, the patient began to show marked improvements. His trunk balance and control improved; the patient could walk with bilateral push knee splints and elbow crutches (Suppl. Video 3). The patient has been followed up every 6 months thereafter to further assess his progress. He was walking with a walker and his motor functions improved in this time frame. According to the ASIA scale assessment, he had changed from ASIA A to ASIA C during a 1 year period (Suppl. Video 4).

DISCUSSION

SCI is a severe, debilitating injury, not just because of the loss of neurological function but also the psychological and social burdens the patients, families, and society as a whole have to face. Previously, it was thought that the CNS was unable to regenerate; however, several studies have suggested that alterations to the local environment of the injury site may aid the regeneration of nerve cells[15]. These alterations include transplantation of fetal spinal cord tissue, peripheral nerves, Schwann cells, and fibroblasts, as well as removal of nerve growth inhibitory factors[16-18].

Aras et al.[19] suggested that the transplantation of MSCs derived from different tissues improved the locomotor recovery following SCI, and the capacity of rat adipose tissue-derived (rAT)-MSCs to differentiate into the oligodendrocyte lineage improved the functional recovery. An important point of this study was the determination of the ideal transplantation time: The results revealed that the local conditions at the time of the transplantation were important for the cell behavior[19]. Moreover, Kabatas et al.[20] suggested that the MSCs can be isolated from the dental pulp and cultured and passaged *in vitro*. After transplantation of the passaged MSCs into rats with SCI, the isolated MSCs can survive in rat bodies without any immune rejection. The implanted MSCs can differentiate into nerve cells, and they are involved in the recovery of the damaged spinal cord. This improves the scores of motion behavior and promotes the recovery of motor function after SCI[20]. All these results provide a theoretical and experimental basis for MSC transplantation applied in the treatment of SCI. Previously, we reported on the safety and feasibility of both the triple route and multiple WJ-MSC implantations, using this treatment strategy in a patient with hypoxic-ischemic encephalopathy[10]. As the studies have been further improved and deepened, it is now possible to apply WJ-MSC transplantation to the clinical treatment of SCI. In this article, we present a patient with a blunt, traumatic SCI who was treated with WJ-MSC therapy. MSCs, also known as mesenchymal progenitor cells, are self-renewing, multipotent progenitor cells that can differentiate into different mesodermal tissues ranging from bone and cartilage to cardiac muscle[21]. They have been advocated as a promising novel treatment strategy for patients with SCI[22]. Previously, bone marrow (BM) was considered a good candidate as a source of MSCs. However, since BM aspiration is an invasive procedure and the proliferation and differentiation capacity of cells decreases with donor age, alternative sources of stem cells were pursued. Fetal-derived MSCs, which are more primitive and have less immune reactivity, have recently been suggested as better alternatives for BM-MSCs.

The primitive connective tissue of the umbilical cord between the umbilical vessels and amniotic membrane is known as "Wharton's jelly," and it protects fetal umbilical vessels from compression and torsion. During embryogenesis, hematopoietic and mesenchymal cells migrate through the WJ, and some of them become trapped, making this tissue a good source of MSCs[23-25]. Stem cell therapy (SCT) for SCI involves acquiring endogenous stem cells *in vivo*, harvesting or altering them *ex vivo* and transplanting them into the injured site, thereby promoting neuronal regeneration and the secretion of neurotrophic molecules[26]. Harvesting protocols and isolation methods may vary among different institutes. Animal studies using transplanted human umbilical MSC-derived neurospheres

on transected SCI rat models have shown recovery of hindlimb motor function at 5 weeks compared with control groups without MSC therapy[27].

Various studies have demonstrated that MSCs display their therapeutic benefits via paracrine regulation with growth factors and cytokines[28]. In a previous study, we suggested that, after performing SCI, the injection of rPI-SCs is likely to prevent immune cell activation, and especially, to reduce the secretion of proinflammatory cytokines (e.g., interleukin-6) as possible direct markers of spinal cord inflammation. Inhibition of these inflammation factors positively affects the SCI healing process[9]. In addition, Németh et al.[29] demonstrated that anti-inflammatory mediators (e.g., IL-1ra) increased after MSC treatment. We also demonstrated that rPI-SC administration was found to be effective for increasing the intensity of IL-1ra in the injured area of the spinal cord, suggesting an anti-inflammatory role for these cells[9,29]. Our patient had four cycles of intrathecal (i.t.), intravenous (i.v.) and i.m. MSC injections at 2 week intervals starting 3 and a half months after SCI from a fall. With SCT and intensive neurorehabilitation, he showed moderate improvements in bowel control. His physical examination revealed gradual improvement in sensation down to 11 levels (9 levels a.f.i) below the level of his lesion, and his motor function improved in stages. On the other hand, treatment involving SCT combined with physiotherapy (as a supportive therapy) offers a tremendous opportunity for patients with neurological disorders, e.g., after SCI. The rehabilitation itself could prevent the process of muscle atrophy and joint stifness, but it cannot repair the damaged nerve function[30]. This improvement is thought to be related to the migration of MSCs to the injury site and promotion of neuroregenerative mechanisms there. On the other hand, it is important in such cases to distinguish gains attributable to therapy from spontaneous recovery following the injury[31]. In the current report, we have presented both subjective (physical therapy reports) and objective (ISNCSCI, FIM, Modified Ashworth and MRC Muscle Strength Scales' scores) measures to demonstrate that the patient, after reaching a plateau of spontaneous improvement at 3 and a half months postinjury, experienced improvement in neurological and functional status.

CONCLUSION

Therapeutic administration of stem cells has a theoretical role in the treatment of SCI, and this is supported by many preliminary clinical studies in the literature; no serious adverse effects of this therapy have been documented to date. Although promising results from many publications have been reported, there is still no consensus on which cellular therapy should be administered to which patient at what time after SCI. There seems to be a need for a tremendous amount of work to elucidate the underlying mechanisms of how MSCs interact with damaged host tissues and how this interaction results in a cascade of events that lead to some functional neuronal recovery. These findings suggest that quality of the cells, optimization of the cell dose, standardization of the cell processing, the timing, route of administration and patient selection as well as the role of clinical experience of the physcisian are critical to the success of SCT in SCI patients.

Ethics

Ethics Committee Approval: Ethical approval to report this case was obtained from the IRB of Turkish Ministry of Health, Department of Organ, Tissue Transplant and Dialysis Services' Scientific Committee (protocol number: 56733164-203-E.2569), Ankara, Turkey.

Informed Consent: The patient was informed of the procedure, and a written informed consent form was obtained per the Helsinki Declaration.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: S.K., E.K., Design: S.K., E.K., Data Collection or Processing: S.K., E.C., E.C.S., N.K., E.Ç., F.D., O.B., G.G., Analysis or Interpretation: S.K., E.C., E.C.S., N.K., E.Ç., F.D., O.B., G.G., Literature Search: S.K., E.C., E.K., Writing: S.K., E.C., E.C.S., N.K.

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Video 1.
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