CASE REPORT

Role of Platelet-Rich Plasma and Adipose-Derived Stem Cells in the Treatment of Spinal Cord Injury: A Case Report

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ABSTRACT

Autologous platelet-rich plasma (PRP) and adipose tissues have proven beneficial in treating diabetic ulcer, eye infections, cataracts, and dermatologic conditions. We treated a patient with spinal cord injury with two consecutive platelet-rich plasma and stem cell therapies with an interval of 15 days. We assessed the patient's gait, posture, and deep tendon reflexes before and after the therapy. Before the treatment patient exhibited hyperreflexia, was unable to stand without support, and could not maintain an upright posture. No improvement was observed after the initial treatment. However, after the second therapy, the patient reported marked control of his lower limbs and the ability to stand upright without support. Subsequently, his condition further improved and he began to walk without support. Our observation suggests that the use of platelet-rich plasma and adipose-derived stem cell (ADSC) in cervical spine injuries is beneficial and should be further tested in randomized trials.

Keywords: Adipose-Derived Mesenchymal Stem Cells; Platelet-Rich Plasma; Spinal Cord Injury.

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https://doi.org/10.36283/PJMD10-2/018

INTRODUCTION

Several studies have shown the facilitation of tissue repair and accelerated response to injury by platelet-rich plasma (PRP) [1]. Spinal injury may result in total loss of sensation, pain, numbness, muscle spasticity, paralysis, and incontinence[2]. In recent years, there has been substantial research on the regenerative properties of mesenchymal stem cells (MSCs). They have been found to stimulate progenitor cell mitosis and inhibit apoptotic pathways. Adipose-derived stem cells (ADSCs) are one of MSCs which have shown effective cartilage regenerating properties. The simple procedure of isolation of ADSC, as well as its abundance, has made it a promising procedure in regenerative medicine. Similarly, Platelets have certain growth-enhancing as well as inflammatory properties. Angiogenesis and mitoses by platelets make them preferred regenerative agents[1]. Platelet-rich plasma (PRP) could help the regeneration of an injured spinal cord. PRP is a biological product obtained by centrifugation of plasma which results in an increased amount of autologous platelets[3,4]. Treatment of spinal injuries with autologous ADSCs is promising as these cells can be differentiated into specific lineages[5].

CASE REPORT

A 35-year-old previously healthy man with a history of road accident in 2006, suffered from a cervical spine injury. Magnetic resonance imaging (MRI) was performed which showed loss of disc space between C6 and C7 vertebra, corresponding with cervical spine damage with motor injury and hemiparesis on left-hand side. Transiently, physiotherapy helped with the recovery of sensations and motor control of limbs. Later on, his condition deteriorated, he needed assistance for

maintaining an upright position and walking. Symptoms of upper motor neuron lesions including spastic paralysis and involuntary jerks were more pronounced on his left side. The patient did not have any compounding comorbidities.

His first visit to Musavvir Stem cell clinic, Karachi, Pakistan was in March 2017. MRI was performed. We explained the detailed treatment procedure and possible adverse effects to the patient. After his written consent, the treatment was started. This was first case from this region, which showed the possibility of ADSCs and Stromal Vascular Fraction (SVF) in regenerating spinal injury in Spinal Cord Injury (SCI) patients. The study was performed according to the Helsinki Declaration and was approved by ethical review committee of Musavvir Stem Cell Clinic granted the approval.

Adipose Stromal vascular fraction (SVF) was obtained by liposuction. A few small incisions were made in the patient's thigh. Approximately 100 g of adipose tissue was removed. Lipoaspirate was then washed with 0.9% normal saline. Afterwards, the stem cells within the matrix of the adipose tissue were centrifuged and the pellet, including the bottom portion of the centrifuge, was considered to be SVF.

Initially, 20 cc of blood was drawn from the patient and transferred to the PRP kit (BCT, REGEN Labs, and Switzerland). The blood sample was centrifuged at 2500 rpm for 5 minutes to separate. The PRP tube was locked and then centrifuged for 8 minutes at 3000 rpm. The platelet-rich plasma (PRP) was collected with the help of spiral needle in a sterilized falcon tube. SVF obtained was then added to the PRP preparation. The final panel was then placed in AdiLight-2 for 20 minutes. AdiLight-2 (AdiLight-2, AdiStem Ltd, Hong Kong) is a Plasma/cell Activation Device, which provides selected monochromatic frequencies in the colored light spectrum. Cells were photo activated for 20 minutes at 3 laser diodes for 3 frequencies each in the red, green, and yellow.

Stem cells were injected via multiple intrathecal and IV infusions. After the initial panel, no improvement was recorded. The patient was called for second phase of treatment after two weeks. However, after two days of the second panel of treatment, the patient reported that he was able to stand for 2 minutes 30 seconds. Gradually, marked control of lower limbs and the ability to stand upright without any support was achieved. Later on, he was able to walk for 3 minutes 30 seconds without support, as evidenced by a supporting video of the patient. After 5 panels, MRI was performed which showed hyper intense signals within the spinal cord at level C5 and C6 vertebra, representing post-intervention changes. These findings were compared with the previous MRI images.

DISCUSSION

The advent of stem cell therapy, especially in the treatment of spinal cord injury, has shown miraculous results. Mesenchymal stem cell (MSC) therapy has been gaining popularity in tissue regeneration after traumatic injury and has been applied in various disease treatments[6]. In cases of accidental damage to spinal cord, loss of sensation and motor control is lost below the site of the injury is evident. Despite the dramatic progress in the fields of medicine and surgery, there was not much hope for these patients.

In the current case, we observed that PRP had positive effects on nerve regeneration and healing. Kucuk et al. utilized PRP in an experiment of sciatic nerve cut model and reported the positive effects of PRP on the nerve regeneration process. They concluded that in comparison to the control group, the tissue regenerative response in the PRP group was significantly accelerated[7]. Tissue regeneration by PRP therapy largely depends on growth factor concentration especially those involved in mitosis and angiogenesis[1].

In the current study, we evaluated the efficacy of the PRP and ADSCs injected into the patient with upper motor neuron syndrome. The utilization of adipose tissue in the regenerating process is attributable to the fact that they have increased concentration of mesenchymal stem cells (MSC) in comparison to bone marrow (BM) [3]. Furthermore, the efficacy of PRP depends on a large number of growth factors and cytokines found in the platelets. These factors are involved in the processes of angiogenesis, cellular proliferation, stem cell migration as well as inflammation[4]. PRP serves as a signalling molecule. When the platelets in PRP are activated and degranulated, they release multiple growth factors including fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF), hepatocyte growth factor (HGF), and Insulin-like growth factor (IGF). Together they contribute to modifying the microenvironment of cells[1,2].

The result of our treatment showed improvement in motor control. Furthermore, hyperreflexia, jerky movements, balance, and postural control during walking and standing showed marked improvement in this patient, when compared to pre-treatment state. Treatment with stem cell therapy has brought revolutionary results. The inference derived from experiments in animal models revealed successful outcomes in spinal cord injury treatment[5]. Our findings are strengthened by a study from Hu et al.; they experimented with human

umbilical mesenchymal cells' effectiveness in the regeneration of post-traumatic spinal cord. Their study emphasized the utilization of embryo-derived tissues such as the umbilical cord since it is a safe and non-invasive procedure. However, the process has limitations due to ethical issues concerning the human embryo. They further believe that human umbilical cord stem cells have much greater proliferative and lower immunogenic potential. Moreover, they can conveniently be transformed into various tissues of the body including adipose tissue, skeletal muscle, cardiac myocyte, cartilage, bone, endothelium, as well as neural tissue. In comparison, stem cells derived from bone marrow and adipocytes may show limited differentiation and proliferative capacities. Furthermore, umbilical cord stem cells not only activate neurogenic stem cells but also promote the production of cytokines, inhibit immune response and inflammation[8].

The primary objective of surgery in cases of nerve injury is to restore the structural integrity of nerves. Recent researches on nerve repair have shown a positive response to PRP therapy. However, some researchers concluded that PRP therapy shows much-improved outcome when combined with surgical nerve repair. Furthermore, it has also been reported that histological, clinical, and electro graphical results, all indicate an increase in the total number of axons in such cases[7].

In support of our results, Sánchez and colleagues, in an extensive review, reported multiple case reports and series showing positive results in various nerve injuries. The outcome of studies on animal models revealed that the application of PRP resulted in axonal regeneration and functional recovery. Improvement in muscle atrophy was also noted. Furthermore, it was also observed that scarring associated with nerve repair was minimized. These beneficial effects were thought to be mediated by insulin-like growth factor 1. Similarly, functional recovery in patients with peripheral nerve injury was reported if PRP therapy was applied within three years of traumatic injury. A significant improvement in patients of Pudendal neuralgia and pain alleviation in patients with Carpal tunnel syndrome was also reported. These patients were given intraneural or perineural ultrasound-guided injections of PRP[9].

Adipose-derived stem cells have shown the potential of improvement in cavernous nerve injury, ischemic stroke as well as wound healing. Following peripheral nerve injury, the death of Schwann cells occurs, which is a critical step in determining the survival and repair of nerves post-trauma. ADSC also have the capability to inhibit the apoptotic process of Schwann cells in peripheral nerves and induce their proliferation. These experiments were performed in rat models. Results from human experiments are still awaited[10]. This case report aimed to observe the outcome of PRP and ADSC in the treatment of traumatic spinal injury. The patient showed marked improvement in muscle strength and eventually regained control of his lower limbs.

CONCLUSION

We reported the very first case from our region of a patient with traumatic spinal injury showing an enormous clinical improvement after treatment with PRP and ADSCs. After a few treatment sessions, the patient regained control of his lower limbs was able to stand upright and walk. MRI findings were also in agreement with clinical improvement.

ACKNOWLEDGEMENTS

We would like to acknowledge the staff of Musavvir Stem Cell Clinic for their immense contribution.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this case report was presented.

ETHICS APPROVAL

The study was performed according to the Helsinki Declaration and approved by the Ethical Review Board (ERB) of Musavvir Stem Cell Clinic, Pathological and Molecular laboratories, Karachi, Pakistan.

PATIENT CONSENT

A written informed consent was obtained from the patient.

AUTHORS' CONTRIBUTION

RG conceived the idea and treated the patient. NJ wrote the manuscript while SFA helped in the procedure and recording the treatment response. UN critically reviewed the case report.

REFERENCES

1. Wasterlain AS, Braun HJ, Dragoo JL. Contents and formulations of platelet rich plasma. Platelet Rich Plasma in Musculoskeletal Practice; Springer, London 2016. pp. 1-29.
2. Rivers CS, Fallah N, Noonan VK, Whitehurst DG, Schwartz CE, Finkelstein JA, *et al*. Health conditions: Effect on function, health-related quality of life, and life satisfaction after traumatic spinal cord injury. A prospective observational registry cohort study. Arch Phys Med Rehabil. 2018; 99(3):443-451.
3. Panni AS, Vasso M, Braile A, Toro G, De Cicco A, Viggiano D, *et al*. Preliminary results of autologous adipose-derived stem cells in early knee osteoarthritis:

identification of a subpopulation with greater response. Int Orthop. 2019;43(1):7-13.
4. Alves R, Grimalt R. A review of platelet-rich plasma: history, biology, mechanism of action, and classification. Skin Appendage Disord. 2018;4(1):18-24.
5. Sahni V, Kessler JA. Stem cell therapies for spinal cord injury. Nat Rev Neurol. 2010;6(7):363-372.
6. Shuai Y, Liao L, Su X, Yu Y, Shao B, Jing H, *et al*. Melatonin treatment improves mesenchymal stem cells therapy by preserving stemness during long-term *in vitro* expansion. Theranostics. 2016;6(11):1899-1917.
7. Kucuk L, Gunay H, Erbas O, Kucuk U, Atamaz F, Coskunol E. Effects of platelet rich plasma on nerve regeneration in a rat model. Acta Orthop Traumatol Turc. 2014;48(4):449-454.
8. Hu SL, Luo HS, Li JT, Xia YZ, Li L, Zhang LJ, *et al*. Functional recovery in acute traumatic spinal cord injury after transplantation of human umbilical cord mesenchymal stem cells. Crit Care Med. 2010;38(11):2181-2189.
9. Sánchez M, Garate A, Delgado D, Padilla S. Platelet-rich plasma, an adjuvant biological therapy to assist peripheral nerve repair. Neural Regen Res. 2017;12(1):47-52.
10. Liu CY, Yin G, Sun YD, Lin YF, Xie Z, English AW, *et al*. Effect of exosomes from adipose-derived stem cells on the apoptosis of Schwann cells in peripheral nerve injury. CNS Neurosci Ther. 2020;26(2):189-196.