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Case Report

Effect of Stem Cell Injections in an Acute Anterior Cruciate Ligament Injury

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Abstract

Purpose: The purpose of this report is to present the successful treatment of stem cell injections in an acute anterior cruciate ligament (ACL) tear in a competitive tennis player. **Case:** A 55-year-old competitive male tennis player presents with an acute left knee ACL tear. The injury occurred during a competitive tennis match on a hard tennis court. The patient had an MRI that diagnosed an acute ACL tear. The patient underwent physical therapy three times a week for 12 weeks, however, the patient continued to have episodes of instability and was unable to run. After failed conservative treatment, the patient underwent three different stem cell injections of 50 million human umbilical cord mesenchymal stem cells (HUC-MSC) under ultrasound guidance one month apart at an international stem cell medical center. Combined with treatment, the patient continued a home physical therapy program 3-4 times per week that included proprioception and treadmill walking. **Results:** The patient's remarkable recovery is evident in his improved MRI findings and the significant reduction in pain along with an increase in activity levels further underscoring the positive outcomes achieved. **Conclusion:** This case report recognizes the potential role of HUC-MSCs in healing ACL tears. Further exploration of their application in non-surgical approaches is warranted.

Keywords: Anterior Cruciate Ligament; Stem Cells; Ultrasound; Physical Therapy; Tennis; Instability

Introduction

A torn Anterior Cruciate Ligament (ACL) is one of the most common soft tissue injuries that occurs and surgical reconstruction has proven to be highly effective with satisfactory results. While ACL reconstruction surgery is an option for a torn ACL, for acute or partial tears there have been alternative and less invasive treatment options that have shown promise. Platelet-Rich Plasma (PRP) is the most studied treatment; however, the results are not consistent. Other biological techniques studied in clinical trials include remnant-augmented ACLR, bone substitutes, calcium phosphate-hybridized grafts, Extracorporeal Shockwave Therapy (ESWT), and adult autologous non-cultivated stem cells [1].

Recently, the use of therapeutic potential Mesenchymal Cells (MSCs) has been documented in numerous animal and clinical studies for soft tissue, treatment of tendon-bone injury and osteoarthritis of the knee [2–6]. MSCs are stem cells that can differentiate and it has been suggested that they can enable angiogenesis and cell proliferation, reduce inflammation and produce a large number of bioactive molecules that can assist in repairing soft tissue injuries [3,7]. MSCs have been shown to interact with immune cells to help initiate the repairing process at the site of the injury. Human umbilical cord mesenchymal stem cells were chosen for this patient because of their self-renewing and multipotent ability [8]. They exert their therapeutic effects mainly through the extracellular vesicles produced by paracrine actions [9]. This case presentation describes the process of ACL regeneration after stem cell treatment and summarizes the application of stem cells as well as the future perspectives in this field.

Case

A 55-year-old competitive male tennis player presented with left knee pain and instability. The patient had no history of previous injury, surgical treatment, relevant medical history, concomitant medications, or allergies. The injury occurred during a competitive tennis match on a hard court.

Physical Examination

The physical examination was conducted using standard procedures, incorporating key tests such as the Lachman test and anterior drawer test. A positive outcome was determined by increased translation compared to the contralateral side. After the physical examination, anterior-posterior laxity in both knees was quantified using the KT-1000 arthrometer. The KT-1000 is an objective measurement tool employed to assess anterior tibial translation relative to the femur. A 30-pound force was applied to the tibia anteriorly. Physical examination at the time of presentation was notable for a positive Lachman test of the injured knee. Initial KT-1000 measurements revealed a displacement of 1.2 mm in the right knee and 5.5 mm in the left knee.

Imaging

An MRI was performed at the time of injury and one year later. The sensitivity and specificity of MRI for detecting ACL injuries are 95 and 88% respectively [10]. Studies were performed using a 1.5-Tesla clinical imaging system using an 8-channel high-definition knee array. Standard morphologic MRI evaluation was performed using a fast spin-echo sequence in the axial, sagittal, and coronal planes. All MRI evaluation and interpretation was performed by the same independent fellowship-trained radiologist. Initial MRI using a posterior approach showed a full ACL tear site (Figure 1).

Figure 1: Pre-Treatment MRI

Pain Surveys

The Numeric Pain Rating Scale (NRPS; 0 = no pain, 10 = the worst pain), along with condition-specific instruments, including the Knee Injury and Osteoarthritis Outcome Jr. Scale (KOOS Jr; 0 = complete knee disability, 100 = perfect knee health), the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form (0 = extreme problems, 100 = no problems), and the Lysholm Knee Scoring Scale (0 to 100, with higher scores indicating fewer symptoms), were administered [11,12]. The Marx Activity Rating Scale (MARS) was also utilized to assess activity levels [13]. All scales were administered both at the time of injury and one year thereafter.

Analysis of the patient's initial IKDC and KOOS Jr. scores provided insight into the considerable pain and mobility limitations he faced pre-treatment. The patient expressed difficulty engaging in activities beyond light tasks such as walking, housework, or yard work, attributing these limitations to constant pain (rated 8 out of 10 on NPRS), knee stiffness, and locking/catching sensations. He experienced challenges with various movements including kneeling, squatting, running straight ahead, jumping, and landing on the involved leg, as well as abrupt stops and starts. The patient reported a Lysholm Knee Scoring Scale score of 25 out of 100.

Treatment

The patient underwent physical therapy three times a week for 12 weeks, however, the patient continued to have episodes of instability and was unable to run.

After failed conservative treatment, the patient underwent three different stem cell injections of 50 million HUC-MSC under ultrasound guidance one month apart at an international stem cell medical center. Administered under ultrasound guidance through a posterior approach using a 22-gauge 3.5 needle, a solution containing 50 million HUC-MSC was injected into the proximal ACL at the site of the tear (Figure 2). After the procedure, the patient was advised to refrain from exercising for two days and to avoid high-impact activities such as running for the following two weeks. Combined with treatment, the patient continued a home physical therapy program 3-4 times per week that included proprioception and treadmill walking. The patient was instructed to perform daily proprioception exercises, including a 30-second single-legged stand with their eyes closed on each leg, followed by walking on a treadmill at a pace of 3.5 for 30 minutes.

Figure 2: Post Treatment MRI

Post-Treatment Outcomes

Upon reassessment one-year post-stem cell intervention, the KT-1000 recorded a displacement of 1.2 mm in the right knee and a notable reduction to 1.8 mm in the left knee, making a 67% decrease in left knee displacement.

An MRI performed one year later revealed 80% ACL reattachment proximally (Figure 2).

After undergoing the stem cell treatment, the patient experienced a significant reduction in pain and a notable improvement in functionality. Post-treatment, the Lysholm score increased to 99 out of 100. He now engages in strenuous activities like jumping or pivoting in sports such as basketball or soccer without significant knee pain, scoring a 0 out of 10 on the NPRS. Morning stiffness, swelling, and incidences of locking or catching are entirely absent. While there remains minimal difficulty in squatting, the patient's ability to perform daily activities has soared from a constrained 50% to unhindered completion. According to the Marx scale, the patient now actively participates in activities involving running, directional changes, and deceleration four or more times a week, along with two to three pivots per week compared to being unable to do any of the activities while he was actively injured (Figure 3,4).

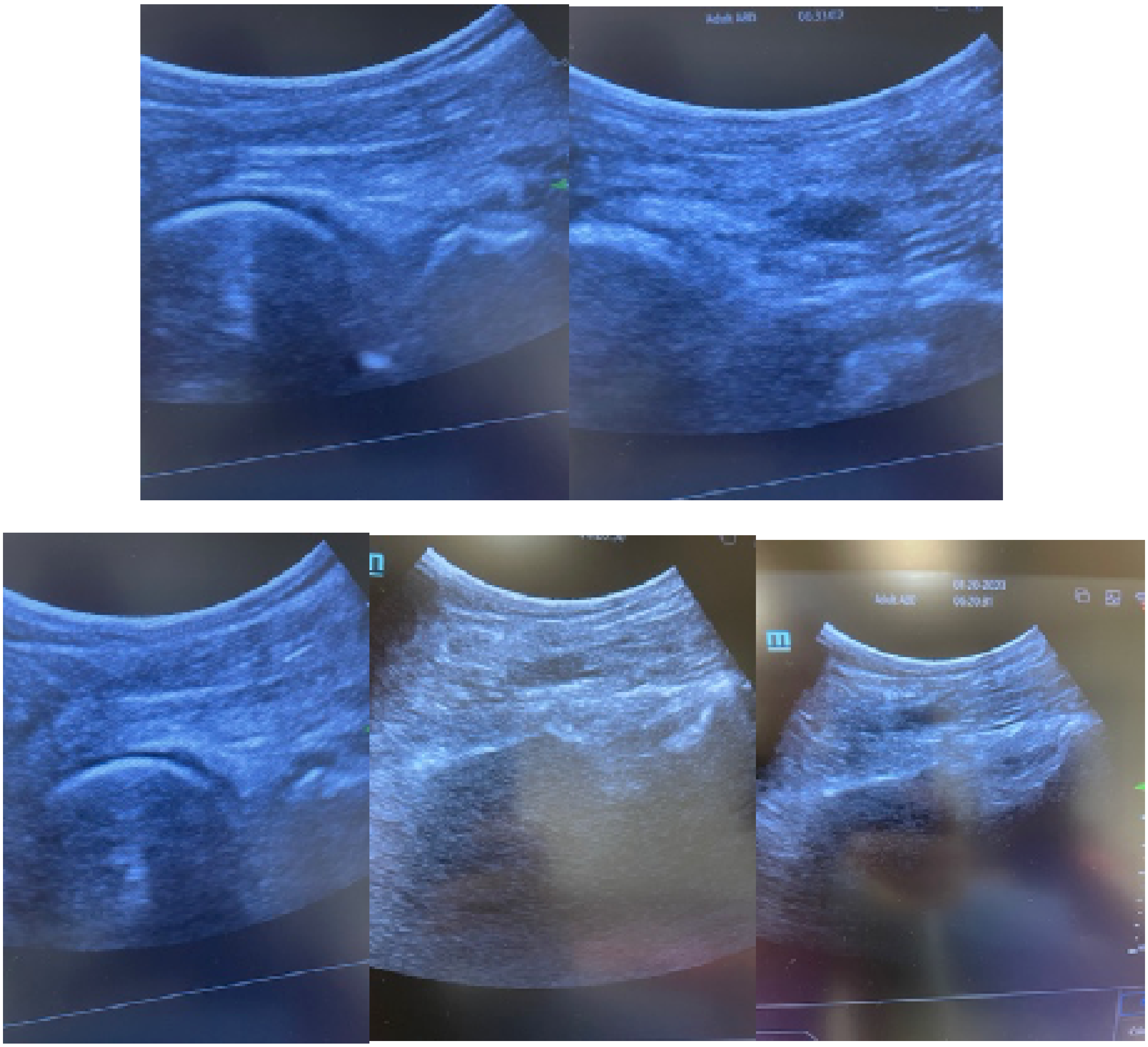

Figure 3: Ultrasound images of proximal ACL injection via posterior approach

Figure 4: Knee model image of the needle reaching the proximal ACL via posterior approach

Discussion

The notable recovery of a 55-year-old male competitive tennis player after an ACL tear through stem cell therapy in tandem with physical therapy underscores its emerging and effective role in the field. The patient did not have any surgical interventions done. When injured, ligaments do not heal well on their own due to their avascular nature, rendering primary ACL repair largely impractical, given its high clinical failure rate. Arthroscopic ACL reconstruction is an alternative surgery that produces favorable outcomes. Although arthroscopic ACL reconstruction has gained popularity with modern techniques, the procedure is intricate and time-consuming, often resulting in the formation of fibrous scar tissue that influences patient prognosis [13].

In response to these challenges, scientists are exploring the potential of stem cells to heal and restore ligaments. Recent literature has shown promising outcomes for ligament reconstruction with stem cells in animal models, emphasizing improved tendon-bone regeneration and healing through fibrocartilage formation [14]. This case utilizes HUC-MSCs due to their continuous self-renewal and easy differentiation into various cell types, particularly osteoblasts and chondrocytes, compared to other mesenchymal cells [8]. In clinical trials using stem cells therapy for ACL graft regeneration, four relevant completed human trials have been reported, while five relevant trials are still in progress. The completed trials currently include Bone Marrow- Derived Mesenchymal Stem Cells (BMSCs), Adipose-Derived Stem Cells (ADSCs), and Human Umbilical Cord Blood-Derived Mesenchymal Stem Cells (hUCB-MSCs) as cell resources. Notably, only one of two trials using BMSCs showed positive outcomes. Despite BMSCs high proliferation, they pose disadvantages such as low content, donor pain and infection, and less homogeneity [15]. BMSCs have been the most widely used MSCs in cell therapy until recently. However, HUC-MSCs and BMSCs demonstrate similar immunosuppressive effects through distinct mechanisms, suggesting potential substitution in cell therapy in the future [16]. While hUCB-MSCs were considered, the trial revealed that the stem cells were safe to use but had no clinical advantage [14].

Our study found an improvement in clinical outcomes and in the MRI result. This trial is different than other trials because this patient lacked any ACL reconstruction prior to the introduction of stem cells. Treating the patient conservatively is often risky because patients treated non-operatively after isolated ACL tears are at a significantly higher risk of secondary meniscal tears, arthritis, and TKA when compared to age and sex-matched subjects without ACL tears [17]. However, in an older patient or a patient who no longer wants to partake in highly competitive sports, stem cell therapy may be the better option for recovery than surgery. As the long-term effect of a patient treated for an ACL tear with stem cells alone has not been studied yet, it will be interesting to follow this patient's recovery and outcomes. It is necessary to acknowledge that our findings are based on a single patient, and factors like the patient's initial health and specific type of stem cell used could have influenced the recovery. Nevertheless, these promising results warrant further exploration and consideration in future research.

Conclusion

Our approach demonstrated positive outcomes in both imaging and patient surveys using HUC-MSCs alone after an ACL tear, underscoring the potential to eliminate the need for surgical interventions.

Acknowledgments

Ethical Guidelines: This retrospective review was approved by ANTIGUA HEALTH AUTHORITY.

Conflict of Interest: There are no potential conflicts of interest reported by any author related to this case report.

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