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# Stem Cell Therapy as an Alternative to Reconstruction of Complete ACL Tears and Associated Physical Therapy Considerations – A Case Report

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**Stem Cell Therapy as an Alternative to Reconstruction of Complete ACL Tears and Associated Physical Therapy Considerations – A Case Report**

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**Abstract**

**Introduction:** Injury to the anterior cruciate ligament (ACL) is one of the most common injuries in orthopedics and sports medicine. With nearly 200,000 injuries per year in the United States, 100,000 opt for reconstructive surgery. There are a variety of known graft choices including hamstring, patellar tendon, quadriceps tendon, IT band, and allogenous grafts. However, these options do not come without future complications. Regenerative medicine using stem cell therapies is becoming increasingly popular. Thus, the purpose of this case report is to highlight the use of stem cell therapies as an alternative treatment to traditional ACL reconstruction, and to provide insight to its associated physical therapy progression. **Case description:** The rehabilitation of a 26-year-old female with a grade III ACL tear that was less than one cm retracted with goals of returning to an active lifestyle is described. **Outcomes:** MR imaging was assessed at three months which indicated healing of the ACL. Lower Extremity Functional Scale (LEFS) scores increased from 23/80 to 68/80 over the course of 7 months. Other potentially useful outcomes measures are discussed. **Discussion:** Based on the current literature, regenerative medicine using stem cell therapies seems to be a promising alternative to surgical treatment of the ACL. Slight differences exist between rehab of the ACL treated with stem cell therapy vs traditional reconstruction. Although subjective reports of knee pain and function improve over time, more objective measurements to quantify ACL healing are needed. Future research aimed at determining long term effects of stem cell therapies is warranted.

**Keywords:** Anterior cruciate ligament; knee; stem cell; mesenchymal stem cell; sports medicine; orthopedics; physical therapy; rehabilitation

**Introduction**

Injury to the anterior cruciate ligament (ACL) is one of the most common injuries in orthopedics and sports medicine. In the United States, nearly 200,000 injuries occur per year with nearly 100,000 of these individuals opting for ACL reconstructive surgery (ACLR).[1] There are a variety of known techniques to surgically reconstruct this ligament and facilitate return to both recreational and competitive activity. However, the risk of future complications as a result of altered knee biomechanics and inability to return to full activity are relatively high. Following ACL reconstruction, it has been shown to lead to increased anterior position of the tibia and increased internal rotation of the tibia at one-year post ACLR. A result of these altered biomechanics would place more load through the medial compartment, which may be a factor in the increased rate of medial compartment osteoarthritis (OA) after ACLR.[2] The risk of developing future knee OA increases dramatically when the initial injury is paired with a meniscal or chondral lesion.[3] To be considered successful with ACLR, the individual should be able to return to the same level of activity as before the injury occurred. After ACLR, an average of 81% of individuals return to any form of sport, 65% return to pre-injury levels, and only 55% returned to competitive levels.[4,5] This rather low return to play rate may be due to a variety of factors associated with reconstruction of the ACL. An alternative intervention that serves to be less invasive and does not alter the biomechanics of the knee joint is needed.

There are 5 different graft options available to be used in reconstruction of the ACL: hamstring, patellar tendon, quadriceps tendon, IT band, and allogenous cadaveric grafts. Allogenous grafts are less common and will not be discussed. Although all of these options have shown to provide increased stability to the knee joint, they do not come without limitations. Poor proprioceptive awareness, muscular weakness, donor harvest morbidity, inability to restore normal kinematics, and the potential of early onset osteoarthritis are common complications.[6]

*Hamstring autografts* include harvesting from the semitendinosus tendon. When a double-bundle hamstring graft is used, both the semitendinosus and gracilis tendons are harvested. Hamstring complications include strength deficits in knee flexion and internal rotation, and it's been suggested there is a potential for higher re-rupture rates. This may be due to the lack of a bony plug leading to less osteointegration between graft and bone.[7]

*Patellar tendon autografts* include harvesting bone plugs from both the distal aspect of the patella and the tibial tubercle, and 1/3 the width of the patellar tendon. Higher osteointegration rates are seen, likely due to the use of two bone plugs leading to more stability of the graft. Complications include an increased risk of developing anterior knee pain, patellar tendinopathy, and increased subsequent operations for meniscal or chondral lesions, contralateral ACL tears, greater motion loss, and lower clinical outcomes are demonstrated. It is suggested that the prevalence of early onset osteoarthritis is greater with this technique vs the use of a hamstring graft.[8-10]

*Quadriceps tendon autograft* harvesting includes a bone plug from the proximal portion of the patella and a graft from the quadriceps tendon to include fibers from vastus lateralis, vastus medialis, vastus intermedius, and rectus femoris. The bone plug allows for greater fixation and when combined with a thick graft has the potential to serve a reliable graft choice without the development of anterior knee pain or decreased strength deficits as in the patellar tendon graft and hamstring grafts, respectively. Complications include quadriceps strength inhibition and strength deficits. This is a relatively new method and continued research is needed.[11]

The *IT band autograft* is a graft choice that is used when there is a need to prevent drilling through unclosed growth plates, such as in pre-pubescent adolescents. This technique is called "extraphyseal" or "physeal-respecting" where the surgeon uses the IT band as the graft and either avoids drilling into the physis completely or compromises only a small physeal area. This procedure has been associated with excellent functional outcomes, low risk of re-rupture rate, and minimal mid-to-long term complications.[12]

There are a variety of techniques and graft choices to use when reconstructing the ACL, however the risk of developing future complications is relatively high. Many of these complications are due to the nature of invasiveness with surgical procedures, or a result of deficits caused by graft harvest. Stem cell therapies may serve as an effective alternative treatment to return integrity to the ACL after partial or complete tears that does not require invasive surgical techniques, such as those used with ACL reconstruction. As a result, they have the potential to not disturb the biomechanics of the knee joint and may decrease the risk of early degenerative changes to surfaces of both the tibiofemoral and patellofemoral joints. The purpose of this case report is to highlight the use of stem cell therapies as an alternative treatment to traditional ACL reconstruction, and to provide insight to its associated physical therapy progression.

**Case Description**

Patient A is a 26-year-old female who presents to an outpatient physical therapy clinic following a stem cell injection of her left knee in an attempt to regenerate a full-thickness ACL tear. The date of injury will be referred to as "day 1." She incurred the ACL tear through a non-contact mechanism when she was skiing and reports there was no fall, she just turned, and her knee felt funny. She had never had a knee injury before, but there was an audible "pop" sensation that she describes as a rubber band snapping and she knew something was wrong. After she heard the "pop", there wasn't much pain involved – something just didn't feel right. She was able to continue skiing for a couple more hours, but the knee kept "giving out" so she decided to be done for the day. Fortunately, a close friend of hers was a physician and she was able to get scheduled for an MRI to take place on the following day. The MRI report showed a grade III full thickness tear of the ACL that was less than one cm retracted. As an active young female, her goals were to return to skiing, trail running, high intensity interval training (HIIT) workouts, swimming, rock climbing, etc. As innovative methods such as regenerative medicine become increasingly feasible and promising as a first line treatment, this warrants the need for physical therapists to be aware of these procedures and their rehabilitation considerations. Although limited, there has been evidence to support success in treating symptomatic patients with grade 1, 2, and 3 tears, as long as the ligament retraction is less than one cm.[13,14]

Patient A had the stem cell procedure on day 7 and followed up her physical therapy evaluation on day 14. To assist with gait, she was using bilateral axillary crutches with orders per the physician to weight bear as tolerated. Her left knee was slightly swollen, graded as 1+ during the time of the initial evaluation. Overall her motion was great – she had full knee flexion and extension, with slight discomfort in the fully extended position which she rated as a 4/10. When assessing strength, her left leg was slightly weaker at 4+/5 globally compared to 5/5 on the right. Due to relationship of muscle inhibition and swelling, neuromuscular re-education exercises were given to facilitate activation of the muscles in the lower extremity which included heel slides, quad sets, and double leg bridging. Towards the end of her evaluation, time was spent educating her on the rationale behind stem cell procedures, relevant anatomy, and a timeline for her return to more vigorous activity. Additional education was given as it relates to stem cell procedures, making sure she did not take anti-inflammatories, blood thinners, or use ice excessively for the first 6 weeks as it may inhibit the inflammatory response needed to maintain an environment that allows the stem cells to remodel the damaged ACL.

She was then seen 2 times per week for the first month to work on light strengthening and gentle balance training. For additional stability, she used a typical post-operative ACL brace for 4-6 weeks. Since her range of motion was within normal limits and there were no graft harvesting sites, she was able to use the bike and elliptical as tolerated as long as the brace was in place for cardiovascular exercise. It was recommended to jog in the pool using a flotation belt with water up to the chest for 30-45 minutes 3-5x/week to keep the knee moving without much load at the knee joint. She was able to progress the strengthening exercises, and now those included continued quad sets increasing the number of repetitions, heel slides, standing hip abduction, weight shifts, and various core exercises that did not stress the lower extremity. As she progressed over the next 4 weeks, she was able to initiate mini-squats, lateral lunges with conservative distance emphasizing proper mechanics, standing swiss ball terminal knee extension, banded work including side steps, diagonal steps, step downs less than

60 degrees of knee flexion, and bridge progressions. As a general rule, if the activity was more than 2/10 on a pain scale or if there was any instability, then the activity needed to be modified or changed.

She was then seen 4 times over the next 2 months to work on progressing the strengthening and balance exercises. During this period, she no longer needed to wear the brace unless she was attempting hikes with uneven ground. The leg press was utilized to work on double and single leg strength and control, avoiding more than 60 degrees of knee flexion to minimize shear forces on the ACL.[15,16] Progression of banded work to target hip abductor strengthening, single leg exercises, and balance were implemented to work on neuromuscular control. As the patient approached week six, impact progressions such as hops, leaps, and jumps were used to return to sagittal plane jogging. At this time the patient had complaints of “clicking” in the knee, but it was not associated with any pain. The patient returned to straight line jogging at about the 3-month mark. At this time the patient had a scheduled follow-up MRI that demonstrated the ACL was healing, which was required by the physician to move on to the next phase of rehab. Two other benchmarks that were required to progress were single leg balance for 60 seconds (eyes closed, preferably), and 20 repetitions of a single leg squat to 60 degrees of knee flexion.

She was then seen 6 times over the 4 months to work on sport specific exercises and return to full recreational activities. She was instructed to use an ACL brace when initiating cutting exercises and for other recreational activities that including lateral movements. During this time, her main goal was to be able to hike a 14er (a mountain peak higher than 14,000 feet of elevation) without feeling fatigued when going downhill. Impact exercises with an emphasis on eccentric control and soft-landing mechanics were implemented. Exercises including single leg ball drop into squat, single leg drop steps, single leg bosu pistol squats, reactive directional changes, dynamic warmups, etc. were utilized. At 7 months and after 18 physical therapy visits, she was able to fully participate in all desired activities and was discharged.

**Outcomes**

At the local physician’s clinic where the stem cell injections were performed, MRI grey scale measurements were analyzed in order to assess signal intensity of the ACL. Using a software called ImageJ, the physicians were able to obtain quantitative changes where a lower value was indicative of a darker image, correlating with increased ligament density. In this case report, the patient underwent an MRI at 3-months following the stem cell injection. Clearance was given to progress with physical therapy. Although the MRI provided insight, the findings cannot be fully extrapolated to the actual integrity of structures within the knee joint. Yang et al. performed a meta-analysis comparing MRI vs the gold standard of arthroscopy for diagnosing ACL injuries, and found a specificity of .9 and a sensitivity of .87.[17] In other words, a positive test is incorrect in 10% of cases and a negative test is incorrect in 13% of cases. Another method to assess integrity of the ACL is the KT-1000, which objectively measures the anteroposterior displacement of the tibiofemoral joint. Since the healing time frame following stem cell injections are relatively variable and unknown, this assessment may place unwanted loads upon the ACL and may not be an appropriate outcome measure to assess ligament integrity.

Functional outcome measures were used in the physical therapy clinic as well. The Lower Extremity Functional Scale (LEFS) is a questionnaire that is 20 questions regarding the patient’s ability to perform everyday tasks and serves as a tool to measure progress over time. It is a scale from 0-80, 0 indicating greater disability and 80 indicating no disability. At the patient’s initial evaluation, she reported a score of 23. At 5 weeks, she reported a score of 56. At 14 weeks, she reported a score of 65. At 18 weeks, she reported a score of 68. With a score of 68/80, the patient indicated that she was 85% fully functional. The capacity of the LEFS to detect change in lower extremity function is superior when compared with other outcome measures, with the error associated with a given measure on the LEFS at +/- 5 points. The minimal detectable change and minimal clinically important difference are both set at 9 points.[18] Her 45 point change over the 18 visits clearly exceeded both error and minimal change metrics.

Patient reported improvements in function are arguably the most important aspect of patient care. Measures such as the International Knee Documentation Committee (IKDC) questionnaire and the Numeric Pain Scale (NPS) would have been useful in this case study in order to obtain more subjective information regarding how the patient felt they were progressing over time. In patients who had partial and full thickness tears of the ACL, Centeno et al. demonstrated improvements with the IKDC at all time points (1 month to 36 months) and improvements in the NPS at nearly all time points (1-24 months) in patients who were treated with stem cell therapies.[14] This is represented in **Table 1.**

**Table 1**. Subjective outcome measures monitored over 36 months in patients with ACL stem cell injections. First number indicates the average score reported and the second is the number of subjects who responded, indicated by parenthesis. This table is adapted from Centeno et. Al. (2018)

| | **Baseline** | **1** | **3** | **6** | **12** | **18** | **24** | **36** |
|---|---|---|---|---|---|---|---|---|
| **Modified SANE** | | 25.0 (14) | 65.3 (19) | 75.5 (19) | 66.7 (21) | 78.8 (16) | 82.6 (17) | 88.8 (8) |
| **NPS** | 2.5 (25) | 1.9 (15) | 1.8 (20) | 1.0 (19) | 1.4 (19) | 1.1 (16 | .8 (18) | 1.0 (8) |
| **LEFS** | 51.1 (23) | 61.4 (14) | 65.7 (19) | 72.0 (19) | 72.2 (19) | 74.1 (16) | 75.9 (17) | 72.6 (8) |
| **IKDC** | 53.4 (20) | 67.6 (14) | 72.9 (18) | 82.4 (18) | 83.7 (16) | 83.7 (16) | 87.0 (18) | 87.9 (8) |

SANE: Single Assessment Numeric Evaluation; NPS: Numeric Pain Scale; LEFS: Lower Extremity Functional Scale; IKDC: International Knee Documentation Committee

## Discussion

The purpose of this case report was to highlight the use of stem cell therapies as an alternative treatment to traditional ACL reconstruction, and to provide insight to its associated physical therapy progression. As previously stated, there is evidence to support success in treating grade 1, 2 and 3 tears with less than 1 cm retraction.[13,14] Although protocols vary by physician, typically the first step in the injection protocol is to administer a pre-injection of a hypertonic dextrose solution into the ACL 2-5 days prior to the injection of the bone marrow concentration (BMC). The purpose of this pre-injection is to provide a chemical irritant to the ACL with aims to promote a brief inflammatory response. This is why it's important to avoid anti-inflammatories for 6 weeks and excessive icing during the first 7 days. The next step is to harvest bone marrow from the patient and isolate the mesenchymal stem cells. Using fluoroscopic guidance, the bone marrow is extracted from the patient's iliac crest. Once completed, venous blood is drawn and used to isolate a platelet rich plasma (PRP) and platelet lysate (PL). After the harvest, the reinjected solution consists of equal parts of BMC, PRP, and PL and is injected directly into the ligament. When withdrawing from the ligament and still within the joint capsule, the remaining BMC, PRP, and PL is injected.[13]

There are three different types of stem cells: embryonic, induced pluripotent, and mesenchymal. These are summarized in **Table 2**. Embryonic and induced pluripotent stem cells are both considered pluripotent stem cells. As a result, they have the capacity to differentiate into all three germ layers: ectoderm, endoderm, and mesoderm. The ectoderm gives rise to the different skin layers and the central nervous system. The endoderm gives rives to the inner organ systems including the digestive and respiratory tubes. The mesoderm gives rise to cells that form bone, cartilage, muscle, adipose and synovial tissue.[19] Mesenchymal stem cells (MSC) are considered multipotent, resulting in a more limited differentiation capacity as they are farther down the lineage. These stem cells only have the capacity to differentiate into cells of mesodermal origin which include bone, cartilage, and muscle, and adipose. Due to the high differentiation capacity (i.e. ability to turn into all three germ layers) of both embryonic and induced pluripotent stem cells, these are considered oncogenic as there is a significantly higher risk of these cells developing into cancerous cells.[20] When taking these factors and the ease of harvest into consideration, this is why mesenchymal stem cells have become the preferred stem cell choice in the treatment of musculoskeletal conditions.

**Table 2**: Overview of the different types of stem cells with source, advantages, and disadvantages. Note: table adapted from Saltzman et al.

| Stem cell type | Source | Advantages | Disadvantages |
|---|---|---|---|
| *Embryonic stem cells* | Embryonic tissue | Pluripotent to all three germ layers: mesoderm, endoderm, ectoderm | Oncogenic potential, allogenic rejection, ethical and legal constraints |
| *Induced pluripotent stem cells* | Adult somatic tissue transfected with embryonic transcription factors | Pluripotent, decreased ethical concerns due to adult source, no allogenic rejection | Oncogenic potential, modest induction yield |
| *Mesenchymal stem cells* | Multiple fetal and adult tissue such as bone marrow, adipose, synovium, periosteum | Can differentiate into tissues of interest: bone, cartilage, and tendon; immunosuppressive allowing for allo- and xeno-transplantation | Limited differentiation capacity, modest yield from host tissue. |

Mesenchymal stem cells can be isolated from a number of different tissue sources including bone marrow, synovium, periosteum, muscle, and adipose.[19] This is summarized in **Table 3.** Although there are several tissue sources to obtain the mesenchymal stem cells, each tissue sources leads to MSC with varying characteristics and differing proliferation capabilities. For example, the synovium and bone marrow have the highest proliferation potential, meaning they are able to proliferate for the longest period of time resulting in the most cells. When evaluating chondrogenesis, bone marrow, synovium, and periosteum led to the largest increase in chondrocyte pellet size and increases in extracellular matrix composition. Furthermore, adipocytes had the lowest proliferation potential. Due to the nature of different tissue sources leading to different characteristics, mesenchymal stem cells derived from bone marrow have become the preferred choice due to the relative ease of harvest and more optimal outcomes.[19]

Often times, stem cells are used in adjunct with platelet rich plasma (PRP) and platelet lysate (PL) injections. Although PRP and PL are outside the scope of this case report, they are discussed briefly for completeness. After obtaining a blood draw, a centrifuge machine is used to obtain a concentration very rich in platelets. These platelets produce a very large number of biologic factors including growth factors (PDGF, TGF-B, IGF-1, VEGF), cytokines, proteins, and extracellular components. PL is formed via “freeze-thaw” method, where the concentration rich in platelets is cooled down to -20C, and when they begin to thaw, they release the abundant biologic factors. PRP releases these components over the course of a week and PL is more of an immediate release, however both of these adjuncts are used to augment the effect of the mesenchymal stem cells. The reported effects are increased proliferation of mesenchymal stem cells, increased ability to maintain differentiation capacity into osteoblasts, chondrocytes, etc., and increased immunosuppressive properties. [21,22]

**Table 3.** Summary of mesenchymal stem cell sources. Note: table adapted from Saltzman et al. (2016)

| MSC Source | Differentiation potential | Advantages |
|---|---|---|
| *Bone Marrow* | Chondrocyte, muscle, osteoblast, cardiocyte, mesangial cell, hepatocyte | Highest differentiation potential |
| *Adipose* | Chondrocyte, muscle, osteoblast, stromal cell | Easily accessible, higher colony formation compared to bone marrow derived cells |
| *Synovium* | Adipocyte, chondrocyte, muscle, osteoblast | Applicable for cartilage and tendon healing |
| *Periosteum* | Chondrocyte, osteoblast | Applicable to fracture nonunion healing |

Although still limited, there is slightly more literature involving partially torn ACLs. In animal studies, partially torn ACLs applied with intra-articular BM-MSC demonstrated repaired tissue whereas the group with no injection demonstrated further retraction and no repair. Another study found that when the medial halves of the ACLs were transected and applied with BM-MSC that histological and biochemical outcomes were almost the same as normal uninjured ACLs at 4 weeks.[23,24] This case report progression is consistent with other studies of the same intervention. Centeno et al. found that 77% of patients treated with BMC into the ACL demonstrated improvements in ACL integrity at 8.8 months and improvement in LEFS scores at all time points compared to baseline.[14]

Stem cell therapies have also been used as an adjunct in ACLR and used to treat other orthopedic conditions such as knee osteoarthritis, rotator cuff (RTC) tears, and discogenic low back pain. Recently, Chen et. al. demonstrated that when BMC was injected at the time of ACLR there was an increase in the amount of a myofibroblast termed smooth muscle actin positive (SMA+). This myofibroblast increases the number of growth factors and proteins in the ECM, helps form sharpey's fibers, and promotes a denser formation of collagen in the ligament. Sharpey's fibers are a sign of osteointegration, which is a hallmark of healing between soft tissue and bone. Not only was the collagen denser, but it had a more orderly arrangement that ultimately led to increased ligamentization and higher stiffness in the ligament. Additionally, there was decreased bone tunnel areas and increased bone volume in both the femur and tibia, which leads to better graft fixation.[25] For knee OA, MSC have demonstrated potent anti-inflammatory properties, improved cartilage, and improved quality of life outcomes at one year post-injection. The process of allocating stem cells is called "homing." This is followed by differentiation and proliferation, regeneration of the damaged tissue, and then healing of the intraarticular cascade.[26] Additionally, stem cells influence natural killer cells, macrophages, and lymphocytes and act to inhibit their proliferation, chemiotaxis, and promote cytotoxic action of immune cells.[26] When MSC are used for the treatment of RTC tears, they've been shown to decrease the amount of fatty infiltrate, create a more elastic bone repair at the bone-tendon interface, and decrease inflammation.[26] Lastly, there are three major mechanisms by which MSC act to ameliorate discogenic low back pain. First, they act to slow or reverse the catabolic process by secreting anabolic growth factors. Second, they aim to restore the disk tissue by promoting the synthesis of type II collagen and proteoglycans. Thirdly, they act to decrease the primary nociceptive disk pain by restoring the mechanical support and stopping the inflammatory milieu that lead to increased nerve growth in the first place.[26]

However, positive outcomes have been recorded following rehabilitation of ACL-deficient knees as well.[14,27] It is difficult to determine whether the success of this case report was due to the stem cell injections regenerating the ACL, or whether these outcomes would have been recorded if she would have chosen no intervention other than conservative rehabilitation alone. It is also not clear whether the injected MSCs are directly participating in repairing the tissue by biochemical synthesis, or whether they are activating a cascade of events that eventually leads to the repair by modulating tissue through fostering an ideal environment. Additionally, cell-based therapies are typically applied by percutaneous intra-articular injections of autologous BMC, which will have additional components other than the MSC. Thus, it is difficult to say what precisely is the key ingredient. When looking at objective tests, the majority of studies in humans are using MR imaging to extrapolate density of the ligament. There are a variety of factors that go into determining signal intensity of MRIs when comparing pre and post, and discrepancies in this process may bias results. The lack of objective anterior laxity measurements of studies in the current literature make it difficult to determine that even if the ligament has undergone a remodeling process, that this process leads to protection of excessive anterior translation of the tibia. The literature is growing and the use of stem cells for treatment of orthopedic conditions becomes an increasingly favorable alternative. However, due to the nature of small sample sizes and limited randomized controlled trials, the research of stem cell injections specific to the regeneration of the ACL must be interpreted with caution as publication bias may be present.[20] Although it is a great place to start, most of the data at this time is from uncontrolled registry studies or case series published by the physicians who injected the BMC, and as a result the data must be interpreted with caution. Another factor to consider is the age of the patient – this case report focused on a 26-year-old female who was overall very healthy and had no limiting psychosocial factors. The differentiation capacity of stem cells may not be same with increasing age, and thus patient selection for these types of operations may be very important. Lastly, the financial cost associated with stem cell therapy is very high. At this stage, insurance does not cover these procedures. In order to get stem cell therapy, you must meet the inclusion criteria to be involved with a research study or you must pay out of pocket, with current estimates ranging from $5,000-$12,000. As a result, most of the data comes from studies who have strict inclusion criteria (healthy, no other knee injuries, etc.) and so this data should not be extrapolated to the general population.

Future research geared towards post injection biochemical analyses of both intra-articular environment changes as well as intra-ligament environment changes may help provide insight to the mechanisms by which stem cell therapy acts for musculoskeletal conditions and may help determine the appropriate subset of individuals where this is most advantageous. Mid to long term follow up studies monitoring overall health and function are needed as they may provide insight to potential negative consequences of MSC injections (i.e., cancer) or if this more conservative alternative mitigates the risk of developing early onset osteoarthritis. As the use of stem cell therapies increases this will provide further insight to appropriate timelines of ligamentization, which will allow physical therapists to get a better understanding of appropriate progressions for ACL rehabilitation.

Overall, MSC injections seem to be a promising alternative treatment to regain integrity to the ACL without undergoing surgical interventions. This may potentially decrease the risk of future complications such as strength imbalances and early onset osteoarthritis, as knee biomechanics are preserved. The limited research regarding ACL regeneration using stem cell therapies need to be interpreted with caution as it is not well controlled and sample sizes are small. As stem cell therapies for orthopedic conditions become more common, this case report serves as an example of rehabilitation time frames for an individual treated with MSC for a full thickness ACL tear that was less than one cm retracted. Time frames presented in this case report are very similar to guidelines for other ACL reconstruction methods, with special attention being paid to anti-inflammatories, ice, and excessive shear forces during the early stages as there is no graft fixation and tensile load capacity is unknown.

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