Autologous Fat Grafting as a Mesenchymal Stem Cell Source and Living Bioscaffold in a Patellar Tendon Tear

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Key Words: fat graft, regenerative medicine, stem cells, bioscaffold, matrix, adipose-derived mesenchymal stem cells, adult mesenchymal stem cells, adipose-derived mesenchymal stromal cells, progenitor cells, stromal vascular fraction

(*Clin J Sport Med* 2011;21:359–361)

INTRODUCTION

The use of regenerative therapies in sports medicine has been increasing with the success of biologics such as platelet-rich plasma (PRP). We present the use of autologous fat grafts and adipose-derived mesenchymal stem cells (AD-MSCs) as a reparative cell source and a living bioscaffold for use in musculoskeletal injuries.

CASE REPORT (INSERTIONAL PATELLAR TENDINOSIS WITH LARGE COMPLEX INTERSTITIAL TEARS)

A 17-year-old basketball player with a tibial tubercle avulsion fracture through the physis was diagnosed with a partial patellar tendon avulsion at the time of surgery. Two large fragment screws were placed for osseous fixation, and #2 FiberWire (Arthrex, Inc, Naples, Florida) was used to attach the tendon to the periosteum.

Six months after the operation, he continued to have pain and was unable to jump or play basketball without considerable pain. Magnetic resonance imaging revealed a thickened patellar tendon insertion. A second surgery was recommended. However, he decided to explore nonsurgical alternatives. Upon initial visit with one of the authors (J.J.A.), diagnostic ultrasound revealed an extremely thickened patellar tendon at the insertion on the tibial tubercle with extensive linear hypoechoic areas, hyperemia, and some calcification (Figure 1). Distension of these hypoechoic areas with local anesthetic confirmed large complex interstitial tears. Two ultrasound-guided injections of 8 to 10 mL of PRP, activated with recombinant thrombin, were administered 5 weeks apart. In each procedure, 1 to 2 mL of 1% lidocaine (plain) was introduced using a 22-gauge needle, which was also used to provide multiple fenestrations in the abnormal areas. At 12 weeks after the initial injection, the patient reported improvement in symptoms such that he could actively scrimmage but had a significant pain afterward. Ultrasound revealed persistent interstitial tears. Retreatment was performed using a combination of bone marrow aspirate, PRP, and autologous fat graft for adipose-derived stem/stromal cells. Lipoaspirated fat graft provided cellular and scaffold (biomatrix) elements and was placed via ultrasound-guided injection to fill the tears at the thickened insertion. Autologous fat harvesting was accomplished according to standard aesthetic surgical technique using a 20-mL Monoject syringe (Covidien Co, Mansfield, Massachusetts) and the Tulip Medical (San Diego, California) closed syringe system (with a 2.1-mm caraway 3-port harvester micro-cannula) and Superluer loc hub. Forty-five milliliters of bone marrow was obtained as per the standard protocol described in the literature and filtered according to the manufacturer's instructions, mixed with 15 mL of whole blood, and centrifuged down to 6 mL. Three milliliters of this mixture was mixed with 3 mL of lipoaspirate and injected into the tears. The remaining 3 mL of the concentrated bone marrow aspirate/PRP was then injected into the surrounding tissue. The Arteriocyte Magellan system was used for all the treatments, both PRP and bone marrow.

He started basketball practice 2.5 weeks after the PRP/fat grafting treatment, and, by 3.5 weeks, started full scrimmage. At 6 weeks, he displayed diminished pain with jumping and was able to play a complete game at a fully competitive level. By 15 weeks, he could play 1.5 hours with minimal discomfort afterward. At 6 months, he played twice per week without pain during and after the activity.

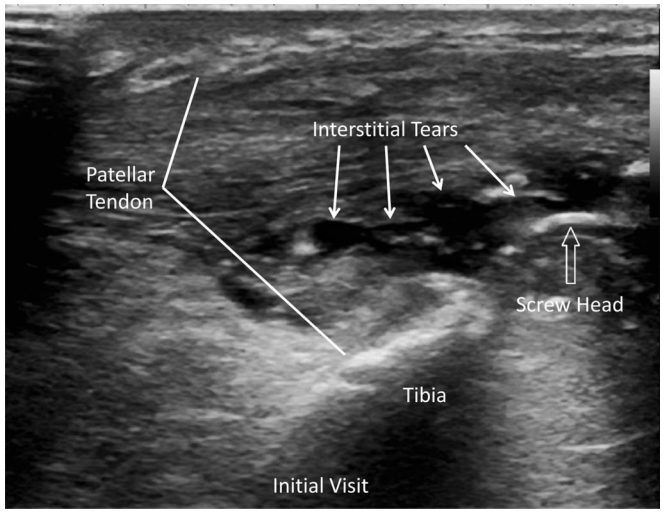

FIGURE 1. Patellar tendon at the tibial insertion on the initial visit. Note the increased tendon thickness and the screw head (open arrow) at the site of the surgical fixation. The arrows show the hypoechoic areas of the interstitial tears.

Submitted for publication September 3, 2010; accepted March 29, 2011.
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The authors report no financial disclosures or conflicts of interest.
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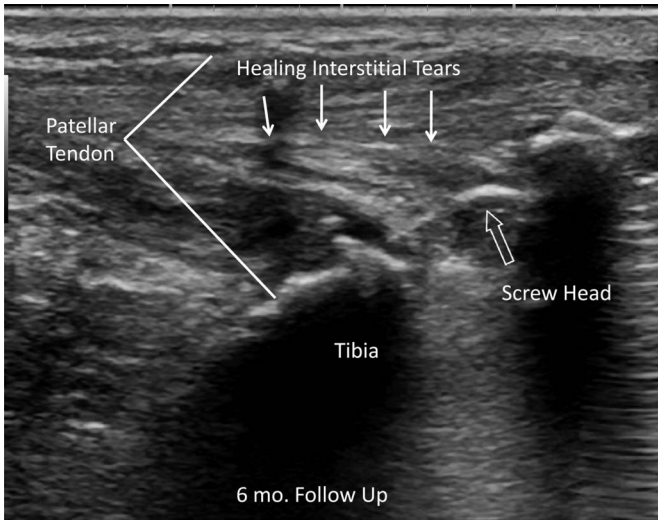

FIGURE 2. Patellar tendon at the tibial insertion on the 6-month follow-up visit. Note the linear hyperechoic areas of the patellar tendon (arrows) representing healing of the tears. The screw head (open arrow) is also visible.

He returned to competition on consecutive days without limitation. Serial ultrasound examinations at each visit showed diminished linear hypoechoic areas. At 6-month follow-up, these hypoechoic areas were still intermixed with hyperechoic areas, indicating the persistence of some fat in these locations (Figure 2).

DISCUSSION

Platelet-rich plasma is one of the most common biologic treatments used in musculoskeletal (MSK) injuries[1,2] and has become more familiar to the general public with treatments of several high-profile athletes. It is increasingly recognized as an effective treatment in various MSK injuries, including tendinosis, partial thickness tears, and interstitial tears. The regenerative potential of pleuripotent progenitor cells (mesenchymal stem cells) in bone marrow and adipose tissue has led to their consideration in MSK applications as well. In animal MSK models[3] and human aesthetic applications,[4–6] the use of these tissues has been demonstrated to be safe and efficacious.

In the preclinical experience, these adult-derived (vs embryonic-derived) progenitor cells provide important advantages, including efficacy, safety, and lack ethical issues.[7] Bone marrow and adipose tissues have become the most studied and accepted sources of adult-derived mesenchymal progenitor cells. Adipose-derived progenitor and stromal cells have the following added benefits when compared with bone marrow: (1) provide a greater concentration of progenitor cells,[4,5] (2) ready availability, (3) ease and rapidity of harvesting, (4) lower morbidity, and (5) diminished cost.[8] In addition, lipoaspirates deliver a natural bioscaffold/matrix accompanying the progenitor cells. Progenitor cells require adhesion to cell membranes, extracellular matrix, and stromal (perivascular) elements to activate and differentiate.

Effective use of nonmanipulated progenitor cells derived from the adipose tissue in both animal and human models has been well documented. Reports from equine[9] and canine[3] models of cartilaginous, tendon, and bone injuries show excellent safety and efficacy, including large, randomized, double-blinded, multicenter controlled trials. In humans, a variety of tissues and injuries have begun to be treated with adipose-derived progenitor cells, including structural fat grafting, tenoligamentous tissue repair, cranial bone repair, articular cartilage, cardiac wall, functional repair of myocardial infarct, functional improvement after stroke, and sciatic nerve after primary repair.[10–14] Nonmanipulated autologous grafting with lipoaspirates and centrifuged fat has been used for more than 2 decades in aesthetic applications. With these human uses and the many animal studies, including those noted above, there has been no reported evidence of neoplastic alterations.

Over the past 2 years, we have used closed-syringe lipoaspirants and PRP concentrates using guidance via ultrasonography for precise placement of a therapeutic triad of tissue components. We are among the first to describe this novel triad for clinical use in MSK conditions. This triad has been termed "Autologous Regenerative Matrix" (ARM) (Crane Clinic, oral communication, April 2010).

This ARM is composed of (1) platelet concentrates (PRP), which provide active cytokines and growth factors for wound healing and activation of progenitor cells; (2) progenitor cells derived from lipoaspirants or, alternatively, bone marrow; and (3) a living bioscaffold provided by adipocytes and matrix derived from extracellular matrix and stromal vascular elements. This ARM is then transferred in the form of an injectable autologous graft.[5]

The bioscaffolding is considered an important component in MSK tissue regeneration because the progenitor cells must have adherence to proliferate, differentiate, and begin migration within the microenvironment (niche).[15] This is especially true for larger MSK defects when a larger matrix volume is indicated. Both paracrine and autocrine signaling systems are enhanced by cellular progenitor cell activities and platelet releasates within the microenvironment of tissue injury.[12] Fresh, low-pressure, lipoaspirated, autologous adipose tissue serves an integral function by providing cellular contact via adipocytes and stromal vascular fraction, which is essential to deliver viable AD-MSCs to the injured tissue. The combination of fat with PRP has been reported to enhance the tissue acceptance of autologous grafts in thousands of cases in the aesthetic literature.[12] It is the authors' belief that this is also true when using the ARM protocol for MSK conditions.

Autologous fat harvest by closed syringe lipoaspiration contributes to all the 3 elements of the ARM protocol. Considering the direct secretion of growth factors (and its autocrine amplification system) and signal proteins (cytokines) by AD-MSCs themselves, autologous fat contributes directly to all the 3 key components of the therapeutic protocol.[5]

The use of ARM and autologous fat grafts in the MSK field is in the preclinical phase but offers a novel application of a safe and potentially effective therapy.[16] Autologous fat grafts are now being studied in several controlled clinical trials.[10] Numerous conditions can benefit from this grafting technique, including tendinoses, partial to full thickness tendon tears, interstitial tendon tears, ligament tears, muscle strains/fibrosis,

osteoarthritis, obsessive-compulsive disorder, and disc damage.[14,16] The benefits may include healing of a cell-depleted injury site, accelerated healing, and a less invasive option with lower cost when compared with surgical alternatives. Further clinical evaluation of autologous fat grafting using the ARM protocol is warranted in MSK conditions.

ACKNOWLEDGMENTS

The authors acknowledge the Bluetail Regenerative Therapeutics for introducing the protocol and nomenclature of the Autologous Regenerative Matrix.

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