Case Report

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Regenerative Medicine

Microfragmented adipose tissue in the treatment of a full-thickness supraspinatus tear: a case report

John L Ferrell*,[1], Alanna Dodson[1] & Joshua Martin[1]

[1]Regenerative Orthopedics and Sports Medicine, Washington DC, 20036, USA

*Author for correspondence: johnferrellmd@rosm.org

A 70-year-old female presented with an 8-month history of right anterior shoulder pain and weakness, unresolved with conservative management. Among other shoulder pathology, the patient was diagnosed with a full-thickness supraspinatus tear and elected to proceed with the microfragmented adipose tissue procedure to treat the injured tendon and nearby relevant structures. Improvements in pain and function were documented along with progressive healing of the supraspinatus on ultrasound and MRI following the procedure. This case demonstrates the efficacy of microfragmented adipose tissue as a relatively novel approach to treating non-retracted, full-thickness rotator cuff tears.

Plain language summary: Fat is an excellent source of stem cells and collagen protein fibers known as a matrix. Mesenchymal stem cells can differentiate into a variety of other cell types. Collagen provides structure and is a major component of muscles and tendons. When transferring stem cells from one's own fat, these cells can support the body's repair process of injured tissue, such as rotator cuff tears of the shoulder. In this case, a patient with a long history of shoulder pain and weakness was diagnosed with a full-thickness tear of one of the four muscles that make up the rotator cuff. Full-thickness tears, compared with partial-thickness tears, are larger, deeper tears that extend across the tendon. This is an injury that has historically been limited to either conservative management (living with the pain) or surgery. The patient underwent a nonsurgical alternative, known as the microfragmented adipose tissue procedure, to repair the injured tendon. Fat was transferred from her hips and injected into the rotator cuff tear of the shoulder. She experienced improvements in pain and function as the tendon healed, documented using ultrasound and MRI. This case supports the benefit of microfragmented adipose tissue, a newer, less invasive approach to treating musculoskeletal injuries, even those as severe as a full-thickness rotator cuff tear.

Tweetable abstract: Microfragmented adipose tissue in the treatment of a non-retracted, full-thickness supraspinatus tear.

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Rotator cuff tears are among the most common musculoskeletal injuries seen in healthcare [1] with potential to greatly impact patients' overall quality of life and wellbeing. An estimated 4.5 million patient visits related to shoulder pain occur annually in the USA [2,3]. There are both direct medical and indirect societal costs related to loss of income and disability, and these costs have been estimated to reach several tens of thousands of dollars per patient depending on age upon injury [3]. A study conducted by Yamamoto *et al.* found the prevalence of rotator cuff tears in subjects between the ages of 22 and 87 to be 20.7%, with 25.6% of subjects in their 60s, 45.8% of subjects in their 70s and 50.0% of subjects in their 80s presenting with rotator cuff tears [4].

Types of rotator cuff pathology & etiology

Rotator cuff lesions are classified by the depth and width of the lesion, as well as degree of muscle retraction. The size of the tear, quality of tissue and preexisting health conditions are considered when determining treatment options and whether patients are good candidates for surgery. The degenerative characteristics associated with rotator cuff lesions in terms of intramuscular fatty infiltration [5,6] and initial and postoperative muscle atrophy [7] are highly

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correlated with retear [5,8] and poor functional outcomes [1,6] following surgical repair. Additionally, larger tear size and age [9] are associated with increased likelihood of retear. It is difficult to estimate postoperative retear rates, as studies have rates ranging from roughly 10 to 90% at follow-up [10–15].

Stem cells for treatment of rotator cuff tears

Autologous mesenchymal stem cell procedures are a viable treatment option for patients with rotator cuff tendinosis and partial-thickness tears, but there is little to no data documenting its use in full-thickness tears without significant retraction (i.e., less than 2 cm). The use of mesenchymal stem cells has gained increasing attention as a treatment option for patients looking to avoid or delay surgery when standard, conservative nonsurgical and pharmacological treatments fail [16]. Trophic signaling, immunomodulatory properties and the differentiation potential of mesenchymal stem cells are implicated as mechanisms by which they facilitate the regenerative process in damaged tendons [16–19].

Adipose tissue is a favorable source of stem cells due to its ease of accessibility by minimally invasive methods, simplicity of preparation for injection and high number of stem cells per unit volume of tissue [16,20]. Adipose-derived stem cells have also been found to proliferate more rapidly in culture and are less susceptible to senescence [20]. The microfragmented adipose tissue (MFAT) procedure utilizes techniques that mechanically fragment adipose tissue, washing away pro-inflammatory oils and blood residue while maintaining its inherent functional structure, including the stem cells necessary to elicit healing [21,22]. Additionally, there are US FDA-compliant devices for obtaining MFAT for autologous use.

Finally, the thickness and viscosity of MFAT allows it to serve as a matrix to fill in the gaps of rotator cuff tears and remain precisely where it was injected under ultrasound guidance. In practice, persistent adipose injectate is often seen under ultrasound when evaluating healing of tendon lesions weeks to months following the procedure. This is another benefit of adipose-derived mesenchymal stem cells compared with bone marrow-derived mesenchymal stem cells or adipose-derived stromal vascular fraction, for example.

Presentation of case

The patient is a 70-year-old Caucasian female who is right-hand dominant with an 8-month history of right shoulder pain. Onset was gradual and exacerbated by increased activity levels, not improved with physical therapy, activity modifications and NSAIDs.

The patient reported pain ranging between 6 and 10 out of 10, described as sharp and aching with referred pain down the right arm, limiting activities of daily living. Her physical exam was documented, showing 3 out of 5 strength with shoulder abduction, positive empty can test, positive O'Brien's test and 4 out of 5 strength with external rotation, and limited range of motion, with active forward flexion to 90°, active abduction to 65° and active external rotation to 45°.

Her ultrasound exam showed tenosynovitis and subluxation of the biceps tendon, tendinosis of the subscapularis tendon, large partial-thickness tear of the supraspinatus tendon, partial-thickness tear of the infraspinatus tendon and instability of the posterior glenoid labrum.

A magnetic resonance (MR) arthrogram was ordered for further evaluation of the right shoulder. The patient's MR arthrogram from September 2020 showed: 1) full-thickness tear of the anterior supraspinatus tendon, measuring 1.0×0.8 cm; and, 2) low-grade, partial-thickness, articular-sided tear of the posterior supraspinatus–anterior infraspinatus tendons at their footprint (Figure 1). The radiologist noted that the rotator cuff muscle bulk was maintained and without atrophy.

After extensive discussion, reviewing the MRI results and presenting multiple treatment options, the patient opted against surgery and other injections and elected to proceed with the MFAT procedure in October 2020.

Treatment & management

The day of the procedure, risks, benefits and alternative treatment options were discussed once more with the patient before written informed consent from the patient was obtained for the procedure. Pretreatment targets of interest and approximate final volume of adipose tissue required were determined using ultrasound imaging and physical exam evidence and correlated with her previous MRI to ensure comprehensive treatment of shoulder pathology. The approximate volume ratio of lipoaspirate to final MFAT product is 4:1 [16].

The patient was placed in prone position, and the skin overlying the superior buttock region was cleansed with chlorohexidine and draped in the usual sterile fashion. A 27-gauge, 1.25-inch needle was used to superficially

Figure 1. MR arthrogram showing full-thickness tear of supraspinatus before treatment.

infiltrate the skin at the border of the harvest site to inject 5 ml of buffered 1% lidocaine with 8.4% sodium bicarbonate and create a skin wheal. Next, an 11-blade scalpel was used to create a small incision and a 17-gauge, 185 mm Lipogems (MI-IT) blunt tip anesthesia cannula was used with a 60 ml syringe to infiltrate the fat layer with a tumescent solution of 150 ml to each the right and left upper buttock. The tumescent solution made contained 50 ml of 2% lidocaine, 500 ml of normal saline and 1 ml of 1 mg/ml epinephrine. The cannula was advanced medially to laterally to disperse the tumescent anesthesia on each side of the superior buttocks. A total of 15 min was allowed following injection of the tumescent solution prior to harvesting to reduce bleeding.

The fat was then harvested using a 13-gauge, 185 mm Lipogems lipoaspirate cannula attached to a VacLok (UT, USA) 30 ml syringe through a low-pressure vacuum on each side. Care was taken to avoid any air in the syringe, and the lipoaspirate was transferred to a sterile syringe and placed in a sterile container. The harvested lipoaspirate, totaling approximately 120 ml, was then introduced into the Lipogems processing kit for washing, filtering and mechanical fragmentation prior to injection. This technique intraoperatively provides autologous, minimally manipulated MFAT without expansion or enzymatic treatment within 60–90 min. The final product was loaded into 3 ml aliquots for injection. After the shoulder was cleansed with chlorohexidine, a local anesthetic of a 10 ml 1% lidocaine and 8.4% sodium bicarbonate solution was administered using a 27-gauge, 1.25-inch needle. MFAT was then injected using 21-gauge, 2-inch needles under ultrasound guidance to enhance accuracy into the preplanned sites of pathology: 3 ml to the biceps tendon and anterior glenoid labrum, 3 ml to the posterior glenoid labrum, 3 ml to the glenohumeral joint, 3 ml to the supraspinatus tendon and 3 ml to the infraspinatus tendon. The injection sites were cleaned, and adhesive bandages were applied.

The patient tolerated the procedure well without any complications or adverse events. After completion of the procedure, the patient was monitored for 15–20 min and stable at discharge. Prior to discharge, the post-procedure instructions were reviewed, and all questions were answered.

Following the MFAT procedure, the patient was instructed to wear a sling for 1 week, avoid NSAIDs for 2 weeks, and resume physical therapy to work on range of motion and strengthening 2 weeks after the procedure. The rotator cuff, glenohumeral joint and glenoid labrum were treated with plasma rich in growth factors 9 weeks later in December 2020, also performed under ultrasound guidance. Following the procedure with plasma rich in growth factors, she was instructed to wear a sling for 1 week, resume physical therapy after 1 week and avoid NSAIDs for 2 weeks. The patient was advised to continue physical therapy two- to three-times per week for a minimum of 6 weeks or longer as the patient saw beneficial until discharged to a home exercise program.

Outcome & implications

In the months following the MFAT procedure, the patient reported gradual but significant improvements in pain and function, and the supraspinatus full-thickness tear showed continued healing with persistent adipose injectate within the lesion on ultrasound. Her progress was monitored using the Disabilities of the Arm, Shoulder and Hand

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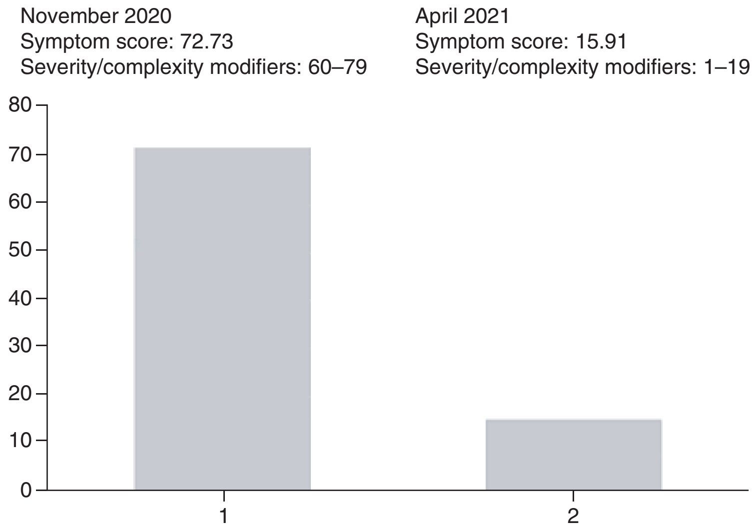

Figure 2. Disabilities of the Arm, Shoulder and Hand (DASH) scores at baseline and at 6 months.

(DASH) questionnaire, measured in November 2020, 1 month after the procedure, and again in April 2021, 6 months after the procedure (Figure 2).

Her physical exam documented in June 2021, 8 months following the procedure, showed 5 out of 5 strength with shoulder abduction, negative empty can test, 5 out of 5 strength with external rotation and nearly full range of motion without pain, with active forward flexion to 170°, active abduction to 170° and active external rotation to 45°. However, her Neer's and Hawkin's tests were still positive and reproduced mild discomfort upon clinical evaluation in June 2021, indicating persistent subacromial impingement.

The patient's follow-up MRI done in August 2021 was read by the radiologist as: 1) status post-rotator cuff repair with scarring and attenuation of the supraspinatus tendon at its footprint related to postsurgical changes with no recurrent full-thickness tear identified; and, 2) tendinosis of the infraspinatus tendon without tear. The radiologist did not comment on rotator cuff muscle bulk on the follow-up MRI. However, there was no atrophy noted per the examining physician's reading.

The patient also reported residual pain localized over the biceps with weightlifting. She opted to proceed with a biceps tenodesis and subacromial decompression in April 2022, which resolved residual pain.

Discussion

To our knowledge, there are no reports documenting outcomes for patients with non-retracted, full-thickness rotator cuff tears treated with MFAT. The patient reported improvements in pain, mobility and overall function and quality of life. Notably, she had plateaued with conservative management, including physical therapy, prior to the MFAT procedure and made significant progress with similar exercises after treatment. These improvements correlated with resolution of the full-thickness supraspinatus tear on MRI and ultrasound (Figures 3–5), with no adverse events reported more than 2 years following the procedure.

It is believed that use of ultrasound guidance for precision as well as comprehensive treatment of the shoulder (i.e., treatment of the biceps, supraspinatus and infraspinatus tendons, glenohumeral joint, and anterior and posterior glenoid labrum) positively contributed to the long-term benefits observed.

MFAT is an orthobiologic intervention with evidence to facilitate healing of damaged tissue by positively modulating the inflammatory cascade to a more anabolic pathway. Research suggests that it is paracrine signaling via cytokine and growth factor release that stimulates healing [23], promoting neovascularization, collagen synthesis and increased inflammatory cell recruitment necessary for tissue regeneration [18].

This case demonstrates the efficacy of MFAT to treat full-thickness rotator cuff tears without significant retraction. Although MFAT is not the gold standard treatment for rotator cuff tears, these findings support MFAT as an effective alternative for patients who are poor surgical candidates or who are looking to avoid or delay surgery. The faster recovery period and decreased invasiveness of the procedure are reasons why some patients may consider MFAT for treatment. It is estimated that full functional recovery following arthroscopic rotator cuff repair takes approximately 6 months, considering age, the size of the tear and other shoulder pathology [24]. Full functional recovery following

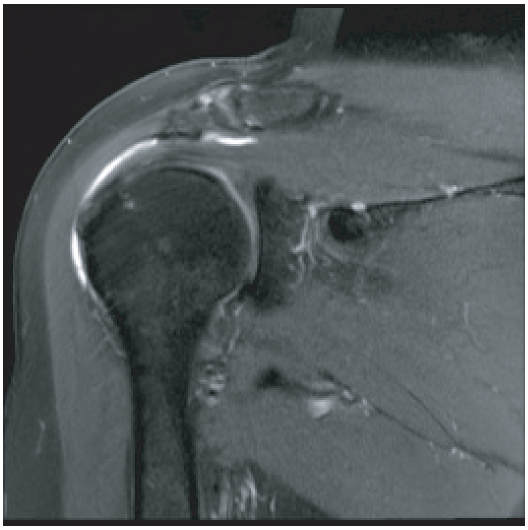

Figure 3. MRI 10 months after MFAT procedure showing resolution of full-thickness tear.

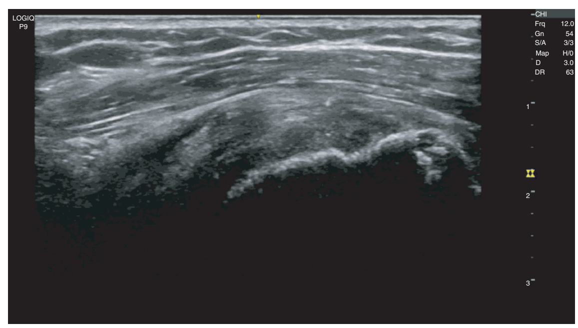

Figure 4. Ultrasound image showing large supraspinatus tear before procedure.

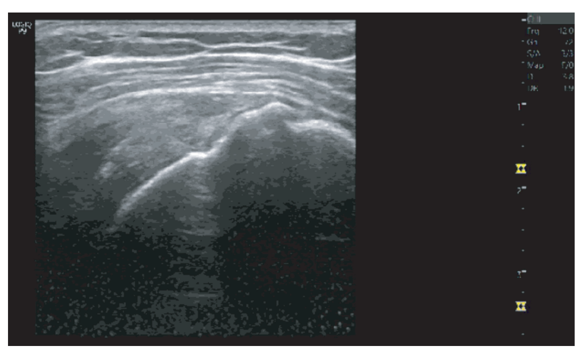

Figure 5. Ultrasound image 10 months after MFAT treatment showing new tissue in the supraspinatus where there was a full-thickness tear previously.

the MFAT procedure generally ranges between 3 and 6 months. However, it is important to note that this MFAT data generally references treatment of rotator cuff tendinosis and partial-thickness tears.

One notable finding was that the patient's follow-up MRI done 9 months after the procedure was interpreted as 'status post-rotator cuff repair' with 'no recurrent full-thickness rotator cuff tear' identified by the same radiologist who interpreted her initial MRI and who was unaware of the treatment the patient had undergone. This supports the remarkable capacity of MFAT as a relatively novel treatment option to yield results comparable to successful surgical intervention. It is important to note, however, that the initial MRI was an MR arthrogram, while the second MRI was completed without contrast. This is considered a limitation of this study. MR arthrograms have slightly higher sensitivity and specificity regarding detection of rotator cuff tears compared with MRIs without contrast. Nonetheless, both have sensitivity and specificity above 90% [25–27]. The use of MRIs without contrast is supported in clinical practice, especially when correlated with healing on ultrasound imaging and patient reports of improved function and decreased pain.

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Another limitation of this study is the inability to distinguish to what extent improvement in pain scores was due to treatment of shoulder osteoarthritis versus treatment of the rotator cuff tears. The DASH questionnaire generally evaluates patients' self-reported abilities to perform certain activities of daily living involving the upper extremities. Although the decreased symptom scores observed are generally positive, we are unable to specify to which degree the treatment of the patient's full-thickness rotator cuff tear with MFAT contributed to improvements in her overall pain and function. This also highlights the clinical utility of physical exam tests for tracking patients' progress from baseline to after treatment, as her abduction and external rotation strength and empty can tests used to evaluate supraspinatus integrity also improved.

Other directions to explore include the use of autologous mesenchymal stem cells as an adjunct to shoulder surgery, either intra- or postoperatively to potentially augment healing. Currently, the benefit of the use of stem cells in conjunction with arthroscopic rotator cuff repair surgery is being investigated in the randomized trial by Cole *et al.* at Rush University Medical Center [28].

Conclusion

In conclusion, MFAT should be considered as a novel approach to treating non-retracted, full-thickness rotator cuff tears. This case study demonstrates MFAT's efficacy as a treatment option, especially when done in a comprehensive manner. Because this procedure is much less invasive compared with surgery, MFAT represents an alternative option for patients who have not had success with conservative treatments but are not yet ready to undergo the invasiveness and recovery time associated with surgical rotator cuff repair. In addition to MFAT's use for patients looking to avoid or delay surgery, intra- and postoperative application of stem cells to potentially enhance or expedite healing should be explored further. Although literature demonstrating MFAT's utility for these cases is limited, these findings suggest that future research is warranted for MFAT's use in full-thickness and partial-thickness rotator cuff tears, tendinosis and more complex musculoskeletal injury cases.

Future perspective

In the next 5–10 years, we anticipate seeing more data supporting the use of regenerative medicine as a disease-modifying treatment for orthopedic conditions. We hope to therefore begin using these treatments as preventative medicine to slow degeneration that naturally occurs with aging. As an example, we will be able to screen patients for mild-to-moderate osteoarthritis, treat them earlier in the degenerative process and hopefully see increased success in patient outcomes in terms of less pain and better overall function. In the context of the case presented here, we hope to be able to screen patients for rotator cuff tendinosis and partial-thickness tears and treat them to prevent progression to larger partial-thickness or full-thickness rotator cuff tears.

We also anticipate using these treatments in conjunction with surgical procedures to optimize healing, especially for procedures that do not have great outcomes with surgery alone. Examples include subacromial decompression in the setting of labral instability or partial-thickness rotator cuff tears and knee arthroscopy or meniscal debridement in the setting of knee osteoarthritis. We believe that using MFAT as an adjunct to surgery, either intra- or postoperatively, will improve patient outcomes and prevent or delay the need for more invasive and extensive surgical procedures.

Executive summary

- Rotator cuff tears occur at higher frequency with aging.
- Currently, good treatment options for partial-thickness rotator cuff tears are limited.
- Full-thickness rotator cuff tears can be repaired surgically but require significant downtime and rehab. Surgery and conservative management are generally thought to be the only options for full-thickness rotator cuff tears.
- The microfragmented adipose tissue (MFAT) procedure may be a viable treatment option for patients with full-thickness rotator cuff tears without significant retraction (non-retracted or less than 2 cm) and who are poor surgical candidates or opt to avoid surgery.
- Treating the shoulder in a comprehensive manner (i.e., biceps and rotator cuff tendons, glenohumeral joint and glenoid labrum as opposed to the torn tendon alone) may help to optimize treatment.
- To our knowledge, this is the first case to show healing of a full-thickness supraspinatus tear with MFAT.
- MFAT may be an option to optimize outcomes for certain surgical procedures as well.

Author contributions

JL Ferrell, A Dodson and J Martin made substantial contributions to the conception and design of the work and acquisition, analysis and interpretation of data for the work; made substantial contributions to the drafting and revision of the work critically for important intellectual content; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human experimental investigations.

The authors state that they have obtained verbal and written informed consent from the patient for the inclusion of their medical and treatment history within this case report.

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