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CASE REPORT

Regeneration of full thickness common extensor tendon tear after percutaneous microfragmented adipose graft

Imran J Siddiqui*[,a], Alyssa Ritner[a], Sanjay Mahadevan[a], Kyle J Dineen[a] and Roosevelt Desronvilles[a]

[a]Regenerative Orthopedics and Sports Medicine, Rockville Pike #300, Rockville, MD 20852, USA

ABSTRACT

Tennis elbow, also commonly known as lateral epicondylitis or common extensor tendinosis, is a common musculoskeletal injury in the adult population. Currently, the standard treatment regimen prescribed for this injury involves a combination of rest, physical therapy, bracing and anti-inflammatory medications. If refractory to these conservative measures, platelet-rich plasma has been shown effective. However, in the case of full thickness tears, surgery has remained the only treatment option until now. We present a case report of a 56-year-old man with a diagnosis of a left large full thickness tear and rupture with retraction of his common extensor tendon (CET) following a corticosteroid injection. The patient was treated with microfragmented adipose transfer. He was re-evaluated around 7 weeks and again at 15 weeks post-treatment and demonstrated ultrasound evidence of complete bridging and remodeling of his prior full thickness CET tear and resolution of retraction. This case presents a promising option for patients with full thickness CET tears who would like to refrain from or are unable to have surgery. Further research and possible randomized controlled trials are needed to further assess the full efficacy of microfragmented adipose transfer in the treatment of full thickness CET tears.

PLAIN LANGUAGE SUMMARY

Adipose cells from a patient's own body fat are one of the best sources of mesenchymal stem cells (MSC) and growth factors that contribute to the generation of collagen protein fibers. MSC's are versatile cells that can differentiate into a variety of cell types, while collagen is an important component of muscles and tendons, as it provides structure. MSC's can be harvested from one's own fat and then used to help supplement the body's natural repair process of a variety of injured tissues. This case presents a patient with a history of persistent elbow pain caused by a large full-thickness tear and rupture of the common extensor tendon (CET) of the elbow. Full thickness tears are large deep tears that extend across the entirety of the tendon. Generally, partial CET tears of varying severities are some of the most common tendon injuries seen in the elbow and are injuries that historically, are treated with conservative management, such as pain medication, cortisone injection, physical therapy, platelet-rich plasma or surgery once/if conservative interventions fail. Full thickness tears, however, usually require surgery for patients to feel better. In this case, the patient underwent a novel regenerative treatment alternative to surgery, known as microfragmented adipose transfer (MFAT), to repair the torn CET. Fat was harvested from his flanks, was washed and cleaned, then injected into the CET tear of the elbow. He experienced significant improvements in function and pain and tendon healing was documented using ultrasound and MRI imaging. This case supports using MFAT for lateral elbow pain caused by full-thickness CET tears as a novel and significantly less invasive method than surgery. Our case illustrates the need for more research and possible clinical trials evaluating MFAT as a treatment option for common musculoskeletal pathologies.

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adipose-derived stem cells; adipose graft; common extensor tendon; mesenchymal stem cells; MFAT; regenerative medicine; tennis elbow; ultrasound guided

1. Introduction

Tennis elbow, otherwise known as lateral epicondylitis or common extensor tendinosis, is the most common painful, non-traumatic condition in the elbow region, affecting roughly 1–3% of adults each year and is thought to be caused by repeated traction of the osteotendinous junction of the structure [1,2]. Full thickness common extensor tendon (CET) tears off the lateral epicondyle of the elbow are less common with only a few documented cases across all databases describing this pathology, all of which were treated surgically [3]. Lateral epicondylitis has a pathophysiology that is degenerative in nature and usually mediated by overuse in the context of repetitive wrist extension activities, forceful gripping or grasping movements, or rotary movements of the arm [4]. Typically, the most common tendon implicated in this process is the extensor carpi radialis brevis (ECRB) tendon that joins into the CET bundle [5]. The consensus is that the ECRB and extensor digitorum communis tendons are adherent but distinguishable in their composition of the 'common

CONTACT Imran J Siddiqui drimran@rosm.org

extensor' origin. A significant cause of ECRB pathology is related to its anatomical position, as it composes the deepest 25–35% of the common origin [6] coupled with the fact that the ECRB portion of the origin tendon attaches in contrasting position to the lateral epicondyle, which allows for it to always remain attached without restriction during movement [7,8]. Of note, the term lateral epicondylitis appears to be a misnomer, as the typical pathogenesis of tennis elbow lacks the requisite inflammation to be characterized as such a disease process. Histologic samples in patients with known tennis elbow symptoms have shown a lack of inflammatory cells, polymorphonuclear leukocytes, lymphocytes and macrophages and rather show a poorly organized collagen fiber matrix of the implicated tendon [9]. These histologic findings are more consistent with the term tendinosis, which is a more degenerative process rather than inflammatory. Thus, we prefer the terms common extensor tendinosis or lateral elbow tendinopathy (LET) [10]. The term tendinopathy is a broader descriptor for all tendon-related pathology, including tendinosis, partial tears and full thickness tears [11].

One of the issues regarding LET is limited clarity of what is an effective standard of care. Generally, relative rest is recommended for low grade tears and tendinopathy, with roughly 89% improvement within 12 months [12]. Bracing is another option to reduce wrist flexion and theoretically allow for improvement in tendinopathy and time for repair. In a sports medicine context, bracing may also be an effective option for offloading tension on the lateral elbow during periods of activity. However, both methods contribute to loss of functional strength of the lateral elbow muscles and risk future reinjury since tendons generally respond poorly to having tension offloaded long term [13]. This is in part caused by the need for mechanical tension and load to prompt repair of injured tenocytes and cause new remodeling at the injury site [14]. While immobilization and rest may provide interval relief of symptoms, it should not be considered an effective long-term solution.

Physical therapy is generally considered a better option for LET as it allows for targeted, progressive strengthening to occur. Many individuals with low grade tendinopathy seem to respond better to this intervention, but healing becomes more difficult with higher grade pathology. Type I collagen fibers typically dominate healthy tendon tissue, but microscopic views of tendinosis tend to reveal an increase in immature type III collagen fibers, with a loss of continuity and a failure to link together that otherwise typically facilitates load bearing [15,16]. As an injury advances from early to later stage tendinopathy, there is increased disruption of collagen fibers, rounding of the tenocytes and degeneration of both vascularization to the tendon and the cellular matrix [17]. Tendons are minimally vascular and only receive blood flow at the osteo/musculoskeletal junctions. Therefore, later stage tendinopathy results in dysfunctional blood vessel formation and inadequate blood flow to the tendon, either due to lack of supply or to collapse of the lumen and other structural degeneration [18]. The result of this process is mechanical inactivation and inhibition of the CET, progressive loss of function and persistent pain, all of which may result in disability. In severe cases, the tendon may rupture under mechanical stress, especially with prior history of repeated corticosteroid injection use [19].

Frequently, corticosteroid injections are used to mitigate the inflammatory response, thereby alleviating pain in the short-term, in patients dealing with lateral epicondylitis or tendinopathy. This approach has come under increasing scrutiny due to the lack of long-term pain relief experienced by patients who receive this treatment. Additionally, some studies suggest that individuals that receive corticosteroid injection are more likely to be symptomatic 26 weeks after injection in comparison to individuals that either had relative rest or physical therapy [20]. Furthermore, studies have demonstrated no physical strength benefits either, as measured by grip strength, in patients who received corticosteroid injections for this pathology [21]. Finally, corticosteroid injections to tendons increase their risk of tearing by up to 7.5-times [22].

Platelet-rich plasma (PRP) has become a more commonly used injection procedure for the treatment of LET. PRP works as an autologous blood product that modulates inflammation and may contribute to repair of injured tendons. After a blood collection draw from a patient, the whole blood product is centrifuged to isolate the plasma and buffy coat containing platelets and leukocytes, which are separated based on the density of the blood components. Once injected, platelet alpha granules release cytokines and platelet derived growth factors to the area of injury [23]. Medical literature has demonstrated that PRP is an effective treatment modality for this pathology [24]. Some of the common issues regarding PRP research continue to be the platelet concentration and dosage used, the amount of volume administered during injection and rehabilitation standards following treatment. Minimally invasive percutaneous tenotomies are also an option for ECRB tendon tears, as there is mild evidence supporting its use [25].

Adipose tissue is a robust source of adipocytes and pericytes, which is due to the highly vascularized nature of adipose tissue. Pericytes are also thought to be high in differentiation potential, which presents obvious advantages in regenerative therapies, while the adipocytes

form a biological scaffold to assist in filling space vacated by ruptured tissue [26]. Adipose derived mesenchymal stromal cells in model organisms injected into Achilles tendon defects have been shown to increase the presence of Type III collagen, which has been associated with tendon healing and remodeling [27,28]. Moreover, there is some literature to suggest that athletes with Achilles tendinopathy returned to sport sooner when treated with adipose-derived stem cells in comparison with PRP [29]. It is important to note that the enzymatic digestion of the adipose tissue to isolate then proliferate stromatic vascular fraction (SVF) and produce adipose-derived stromal cells has been shown as an effective treatment option for LET in other studies [30] and case reports [31] but is currently not an available medical procedure in the USA. This is primarily due to the procedure being considered more than 'minimal manipulation' to the tissue prior to injection [32]. Furthermore, the inability to reliably attribute the cellular mechanism of action of SVF *in vivo* remains a limiting factor in predicting its therapeutic effect, as well as the differential behavior and reaction of adipose-derived stromal cells *in vitro* versus *in vivo* to multiple tumor entities [33,34].

One possible disadvantage of SVF isolation is the removal of the physical adipose connective tissue which may serve as scaffolding for remodeling larger tears, although there is not a consensus on which approach would yield better results. While more recent literature shows promising results for this treatment modality, more Level 1 research evidence is necessary to solidify this treatment as the Gold Standard. Microfragmented adipose tissue (MFAT) has been successfully used to treat full thickness rotator cuff tears in our clinical practice [35], but there is no case to date that has used MFAT to treat a full thickness CET rupture with retraction.

2. Case overview

CB was a 56-year-old Caucasian male who presented with left lateral elbow pain, localized swelling and significant bruising. He underwent prior treatment for his left elbow pain with an outside orthopedic surgeon and received two cortisone injections into the left lateral elbow, the first of which was 5 months prior to initial presentation and the second of which was 2 months prior to initial presentation. It is of note that both corticosteroid injections were delivered without the use of ultrasound guidance. While published evidence on the use of ultrasound guidance for elbow injections is limited [36], it is widely recognized that ultrasound is an important diagnostic tool and important for accurate delivery of an injectate [37–39]. Both injections provided minimal interval improvement in symptoms, with return of pain and limited function. He had also previously undergone a course of physical therapy that did not provide adequate relief of symptoms and prior x-ray imaging of the left elbow which was unremarkable.

He played in a golf tournament 9 days following the second corticosteroid injection. He attempted to offload the lateral elbow with a brace and found significant edema and bruising after prolonged play and his pain and function were significantly diminished from then until he presented to the sports medicine clinic at Regenerative Orthopedics and Sports Medicine 2 months later. A physical exam in the office revealed a positive Cozen's test, which is a highly sensitive test for LET [40]. Furthermore, ultrasonography revealed a full thickness tear with a significant component of retraction of the left CET with surrounding edema and a large radiohumeral joint effusion. This is seen in Figure 1. An MRI completed confirmed a large full-thickness tear and rupture of the CET with retraction of the tendon to the level of the radial head and a few tendinotic fibers remaining posteriorly. A small to moderate elbow joint effusion and intramuscular edema of the ECRB and extensor carpi radialis longus were also noted by the radiologist. These are depicted in Figure 2.

The patient was consulted on treatment options including surgical intervention, conservative care and regenerative treatment using adipose tissue graft transfer. The patient consented to and underwent an MFAT procedure using the Lipogems® system.

The Lipogems® system has received FDA 510 k and CE mark approval for safety and is a sterile, closed-loop, processing system capable of providing minimally manipulated autologous adipose for orthopaedic use [41]. The closed-loop system allows for harvested lipoaspirate to be inserted into the sterile processing device, which washes away patient blood, interstitial fluids and micronizes the raw adipose graft for injection. This device was patented in 2010 and is the primary method of treating pathologies with MFAT in our clinical practice.

For this patient, we chose this device due to its 510k status and ability to provide a suitable graft to fill the retracted component of the tear. The Lipogems system is able to wash out toxins, oils and fibrous tissue found in unprocessed adipose that would be counterproductive to the healing process, yet still maintain the structural integrity of the adipose clusters, which are important to create a tissue scaffold needed to repair a full thickness tear [42]. More research is needed to determine the impact of fat cluster size and the role of minimal manipulation on the efficacy of MFAT as a treatment, as the mechanism is not entirely understood.

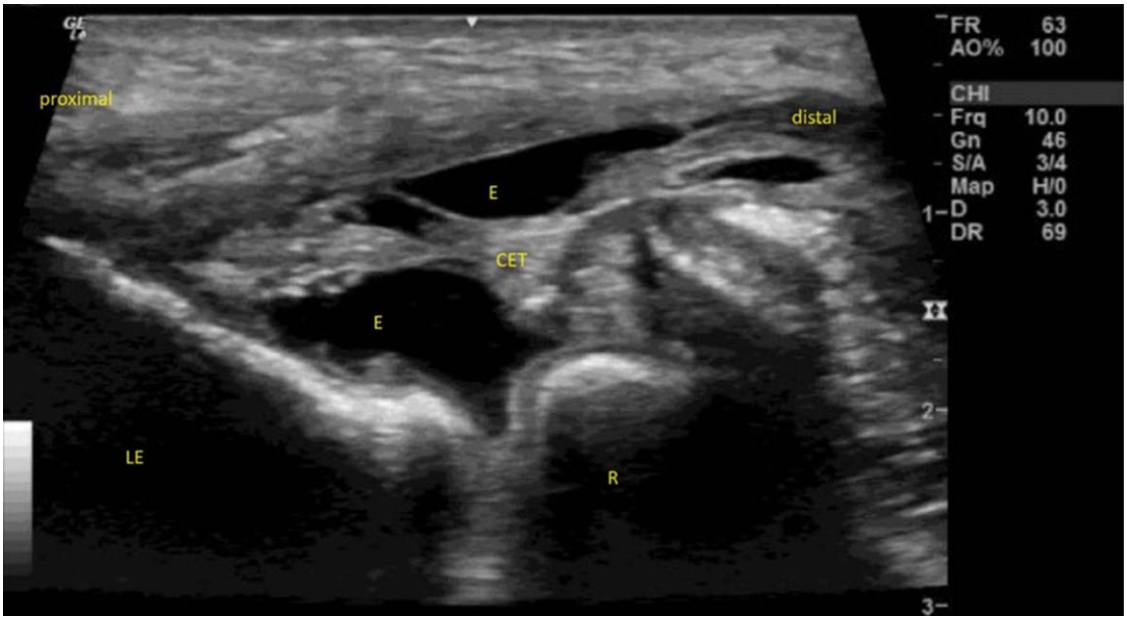

Figure 1. Ultrasound imaging of the patient's left elbow showing CET rupture with retraction to the level of the radial head (R) at origin, the LE and significant E at multiple locations. The radiohumeral joint is widened with significant effusion and RCL sprain.
CET: Common extensor tendon; E: Edema; LE: Lateral epicondyle; RCL: Radial collateral ligament.

2.1. Procedure details

After anesthetizing the skin, 240 ml of tumescent (500 ml normal saline, 1 ml of 1:1000 epinephrine, 50 ml of 2% lidocaine) was infiltrated into the flank, via a 17G 185 mm blunt tip anesthesia cannula. The cannula was advanced medially to laterally to disperse the tumescent anesthesia to the bilateral flank.

After waiting 15 min, a 13G 185 mm lipoaspirate cannula attached to a low-pressure vacuum syringe was used to extract 60 cc of un-decanted lipoaspirate. The lipoaspirate was then transferred to the device for washing and mechanical fragmentation which generated 10 cc of final microfragmented adipose product. The harvest site was then cleansed and the puncture site dressed with a sterile 4 × 4 gauze, which was then covered by Tegaderm. An All Cotton Elastic wrap was placed along the harvest site to minimize swelling, bruising and postprocedure pain.

The microfragmented adipose was transferred into 3 cc syringes for injection with a 21-gauge, 1.5-inch needle. After anesthetizing the skin, 5 cc of microfragmented adipose was injected into the full thickness CET tear under direct ultrasound guidance.

The patient tolerated the procedure well without any adverse effects. After completion of the procedure, the patient was monitored for 15–20 min and stable at discharge. Prior to discharge, the patient was provided the postprocedure instructions, which were reviewed in person.

3. Postprocedure information & results

The patient was discharged without complications and was prescribed oxycodone (5 mg) for pain management. He was advised to avoid anti-inflammatory medications for 2 weeks and have relative rest for 2 weeks prior to restarting physical therapy. The patient underwent follow-up at 8 weeks post-MFAT. The physical exam revealed a mildly positive Cozen's test, but with marked improvement in strength with additional mild lateral tenderness of the epicondyle, but also improved from prior to the treatment. Ultrasonography revealed complete bridging of prior full thickness CET retracted rupture with improved echotexture and echogenicity along with a reduced radiohumeral effusion but revealed that a small partial tear of the radial collateral ligament (RCL) remained. These changes are seen on Figure 3. The patient continued conservative care and physical therapy and underwent a follow-up PRP treatment to the left CET and RCL at 16 weeks post-MFAT. At 24 weeks post-MFAT, he reported overall marked improvement in symptoms with minimal residual stiffness and weakness in grip strength but had no activity limitations on golf and weight training. At that visit, an ultrasound showed normal appearance of his CET and RCL. At 30 months post-MFAT, the patient continued to maintain full activity without pain. He underwent a follow-up MRI that revealed significant interval healing of the prior high-grade CET tear, which appears grossly intact without evidence of tear. On the MRI, which is shown in Figure 4, the tendon

Figure 2. Pre-treatment MRI imaging of the patient's left elbow showing a large, full-thickness rupture of the CET with retraction to the level of the radial head (R), intrasubstance E and the LE.
CET: Common extensor tendon; E: Edema; LE: Lateral epicondyle.

appeared thickened and the radiologist attributed this to reflecting post-traumatic and post-treatment changes. The RCL remained intact and without pathology.

4. Conclusion

This case represents the first documented use of MFAT as a treatment option for CET rupture in the upper extremity. Since most large studies conducted using MFAT are in weight bearing joints, use of MFAT in an upper extremity represents a novel treatment option. As previously discussed in this work, traditional conservative care for CET pathology includes a combination of bracing, physical therapy, corticosteroid injection and eventual surgical consideration. The patient in this case had failed all prior conservative care means with acute exacerbation of a chronic injury – resulting in a rupture with retraction. Use of MFAT as a treatment for this indication may provide another interventional approach short of surgery with the capacity to affect pathologies of this degree. This is the key finding of the case and prompts further need to rigorously study MFAT for treatment of upper extremity pathologies. In short, MFAT application to this pathology should be explored in a controlled trial.

Currently, there is a lack of formal criterion to assess regeneration of ruptured connective tissues using orthobiologics such as MFAT. However, both MRI and ultrasound imaging determined the large, edematous components of the rupture to be resolved following MFAT treatment to the CET, which coincided with the symptomatic improvement of this patient. With ultrasound visualization, shown in Figure 3, there is distinct improvement in the echotexture and echogenicity of the tendon

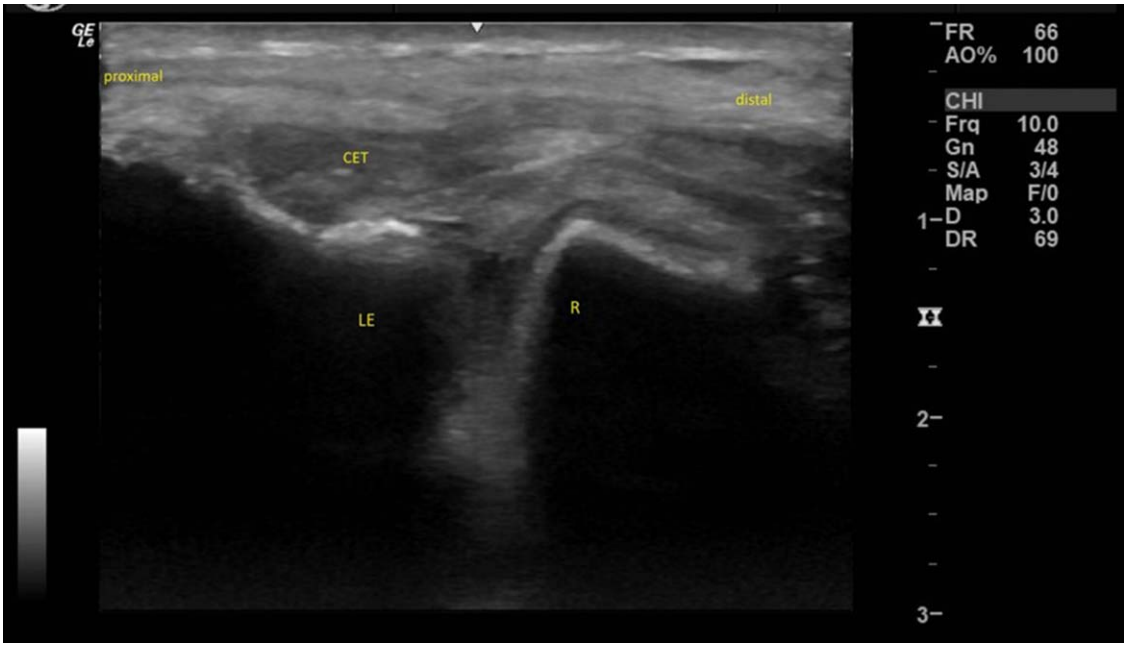

Figure 3. Ultrasound imaging of the patient's left elbow after MFAT treatment, showing bridging of the prior CET rupture with small residual RCL tear, the R and the LE. Intrasubstance edema is resolved with improved echogenicity and echotexture of the CET.
CET: Common extensor tendon; LE: Lateral epicondyle; MFAT: Microfragmented adipose transfer; R: Radial head; RCL: Radial collateral ligament.

before and after treatment with resolution in edema. As seen on Figure 3, there are marked improvements in the appearance of the MFAT graft and granulation tissue in previously retracted aspect of the rupture at 8-week follow-up. The MRI at 30-month follow-up also confirms that the sites of the rupture were adequately filled with the MFAT graft and the tendon fibers were intact with normal parallel orientation. In this sense, we may deduce that the bioactive factors associated with MFAT and the scaffolding provided by the adipose graft, may have contributed to significant interval improvements in both the anatomical and symptomatic improvements found in this case.

Our case highlights the role orthobiologics may have in the treatment of occult soft-tissue injury. MFAT may have use in larger tendon tears or in tears with a notable component of retraction within the rupture due through a healing graft that serves as new architecture for the body to leverage while remodeling injured tissue. The significant anatomical improvement from this case also highlights the mechanistic changes injured tissues may undergo after exposure to MFAT. While not understood, pathological and degenerative tenocytes responded well to the insertion of the graft which resulted in an improved fiber radiographic appearance on MRI at 30 months. While prior literature has shown PRP to be a suitable treatment option for CET pathology, it has not been used with MFAT or in a tear of this degree. The role of PRP may have been improved due to the placement of the graft within the area of retracted rupture; although, this is also theoretical and must be explored with future studies. We are also unsure of the fiber type changes associated with the remodeled tissue, which should be explored in future studies, but it appears that the new fibers represented healthy tissue on MRI and ultrasound imaging.

Our case also advances previously established findings for orthobiologic treatment of CET pathologies. PRP is seen as a suitable option for treating CET tears and its use is well published for small tears. However, there is minimal prior work showing orthobiologics for ruptured tears with retraction in the field of regenerative medicine. Our findings provide new, novel insights into the application of MFAT to larger CET ruptured tears and offer new considerations for providers and patients in the management of such injuries.

This case has notable limitations. While this patient reported significant interval improvements in symptoms, with similar improvements seen on ultrasound imaging, we cannot directly attribute these to either the MFAT or PRP procedures. It is likely that the most notable improvements were seen following MFAT injection and placement of the graft into the retracted rupture site, but having both treatments completed within a narrow timeframe makes a distinct analysis challenging. Theoretically, MFAT has higher concentrations of mesenchymal cells and bioactive factors than PRP and should contribute

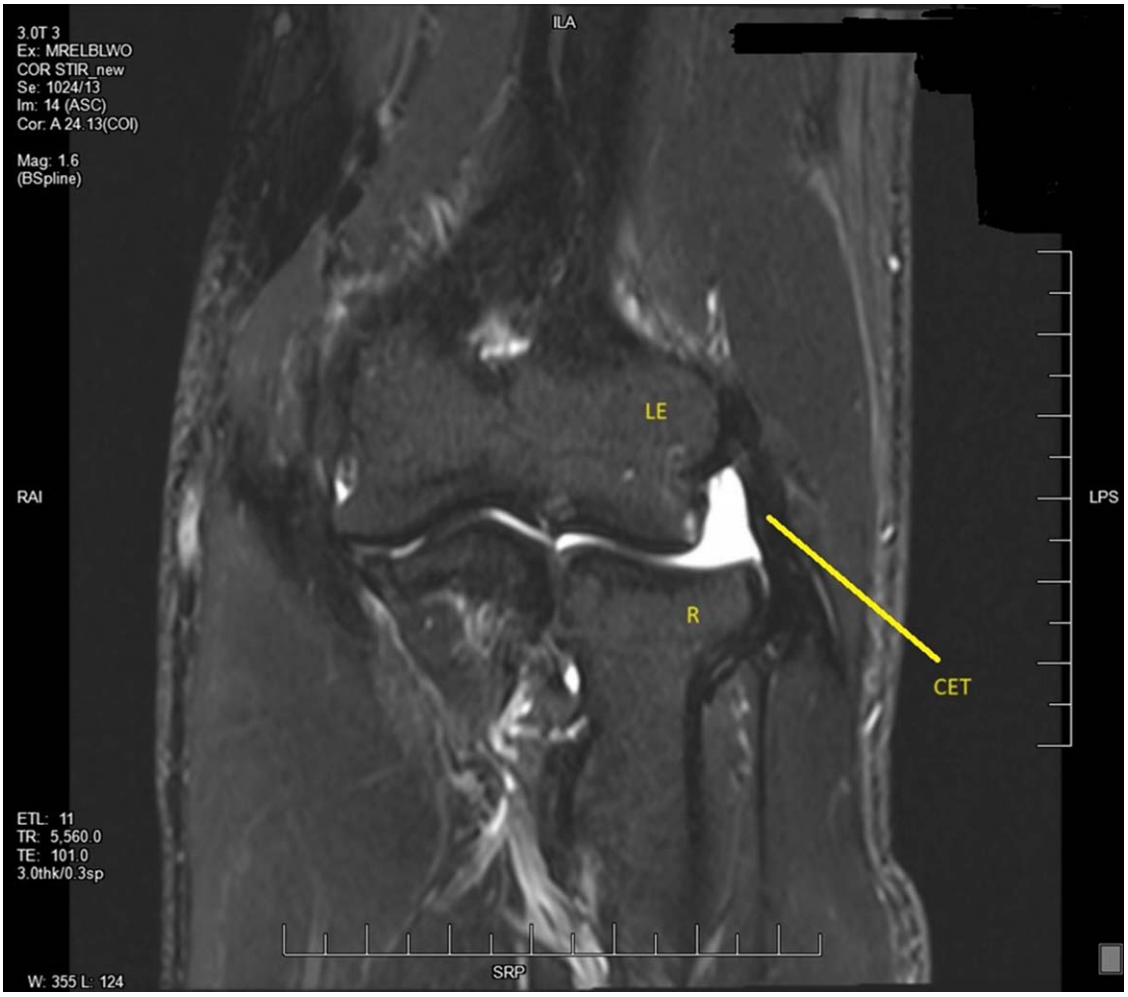

Figure 4. Post-treatment MRI imaging of the patient's left elbow showing significant interval healing and remodeling of the prior full-thickness CET rupture, which appears grossly intact without evidence of tear, R, the LE and an intact RCL. There is resolution of intrasubstance edema and the retracted component of the tear is marked as resolved with post-procedural changes.
CET: Common extensor tendon; LE: Lateral epicondyle; R: Radial head; RCL: Radial collateral ligament.

to more effective remodeling, but this is still unproven and this purported claim lacks the basic science *in vivo* studies to strongly support it. Additionally, MFAT's action mechanism and the bioactive factors associated with tissue remodeling are not clearly understood. We did not conduct a cellular analysis of the concentration of bioactive factors and cells in this patient's adipose, or analysis to clarify which components contributed to cellular changes. Lastly, this patient did not complete patient reported outcome measures to effectively track changes from baseline across the follow-up intervals. While they anecdotally report significant improvements, future cases and studies should include such measures to track symptomatic improvement over time.

Within the next decade, we anticipate observing an increasing amount of documented evidence and data supporting the use of orthobiologics as a disease-modifying agent for common musculoskeletal pathologies and potentially the inclusion of culture expansion procedures (such as SVF) in the USA. Therefore, we believe the most logical next step is to begin researching the efficacy of these treatments as interventions to assist in remodeling both the progressive deterioration of musculoskeletal pathology and age-related degeneration. By screening patients and treating them in the early stages of various degenerative processes, we hope to see significantly improved outcomes regarding increased functionality and decreased pain. This case reflects relatively early intervention of orthobiologics preventing escalation of invasive care for a chronic injury. Regarding this case report, we anticipate future consideration of MFAT treatment for full-thickness tendon tears or higher-grade ruptures as an interventional option in lieu of surgery in our clinical practice and for a wider clinical audience. Additionally, we anticipate these findings may provide disease modifying effects for patients with early-

stage CET pathologies; but this also warrants further research.

Finally, we also anticipate utilizing regenerative treatments such as MFAT, as an adjuvant treatment to surgical procedures, either intra- or postoperatively, to optimize the repair process. This will be especially advantageous for surgical procedures that do not typically produce satisfactory outcomes or have slowed post-surgical remodeling in patients. For example, MFAT could be used intra-operatively during a CET origin repair, in lieu of sutures when repairing and reattaching the tendon [43]. The potential for orthobiologics as both a preventative and adjunct intervention is vast and warrants additional research.In conclusion, this case represents the first novel, documented use of MFAT as a successful treatment modality for full-thickness CET rupture with retraction. In our opinion, this case warrants scientific reproduction of higher rigor with many outstanding questions remaining. MFAT treatment for CET pathology may represent a viable alternative treatment to surgery as it has a quicker recovery time and lower risk profile. These findings demonstrate that further research and formal study is warranted for the use of MFAT for full thickness tendon tears, but our results appear quite promising.

Article highlights

- Lateral epicondylitis, or more aptly named common extensor tendinosis, is the most common elbow pathology
- Common extensor tendinosis can typically be managed by conservative measures such as physiotherapy, but for full thickness common extensor tendon (CET) tears, surgery is often the only viable option
- Microfragmented adipose transfer (MFAT) procedure may be a viable alternative to surgery for patients with full thickness CET/common extensor ruptures with minor retraction who are not good surgical candidates or prefer to avoid surgery
- MFAT is viable alternative to surgery as it has faster recovery time and reduced risk profile in comparison to surgery
- 56-year-old man with a large full thickness tear and rupture of his CET was treated with MFAT, along with a follow-up treatment of platelet-rich plasma 15 weeks later. Post-treatment MRI and ultrasound imaging demonstrated evidence of complete bridging of his prior full thickness CET tear at 30 months
- This case represents a novel documented use of MFAT as a successful treatment modality for full-thickness CET tears
- Further research is warranted on the efficacy of MFAT for full thickness tendon tears.

Author contributions

IJ Siddiqui, A Ritner, S Mahadevan, KJ Dineen and R Desronvilles 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.

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The authors have no 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.

Competing interests disclosure

The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, stock ownership or options and expert testimony.

Writing disclosure

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

Ethical conduct of research

The authors state that they 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. As this a case report, this does not meet the federal DHHS requirements for human subjects research and thus, IRB approval is not required for this case.

ORCID

Imran J Siddiqui https://orcid.org/0000-0003-0813-951X
Sanjay Mahadevan https://orcid.org/0009-0007-2475-1019

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