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Intra-articular Adipose-derived Mesenchymal Stem Cell Injection for Rotator Cuff Tear Repair with Concurrent Chondropathy: A Case Report

Guido Bocchino[1,*], Alessandro Singlitico[1], Alessandro El Motassime[1], Daniele Grassa[1], Paolo Satta[2], Vincenzo Campana[2], Riccardo Totti[1,2], Vincenzo De Santis[1,2]

[1]Department of Aging, Neurological, Orthopaedic and Head-Neck Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

[2]Mater Olbia Hospital, Olbia, Italy

[*]**Corresponding Author:** Guido Bocchino, Physician, Department of Aging, Neurological, Orthopedic and Head-Neck Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, Tel.: +393343103404, E-mail: guido.bocchino@hotmail.it

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Abstract

Rotator cuff tears combined with chondropathy pose a significant treatment challenge due to the dual nature of tissue damage. Traditional surgical methods often address one issue at a time, which can lead to less effective outcomes. However, recent advancements in regenerative medicine, particularly with adipose-derived mesenchymal stem cells (AD-MSCs), provide a promising alternative for simultaneously addressing both conditions. Building on the success of orthobiologic treatments in knee joints, this study investigates similar therapies for the glenohumeral joint with reparable cuff tears. This case report details the treatment of a patient with a rotator cuff tear and concurrent chondropathy using intra-articular injections of autologous adipose tissue, emphasizing the procedure, clinical outcomes, and implications for future therapeutic strategies.

Keywords: Adipose-derived Mesenchymal Stem Cells; Rotator cuff repair; Arthroscopy; Chondropathy; Regenerative medicine

Introduction

Rotator cuff tears, which are common musculoskeletal injuries, often occur together with chondropathy, leading to pain, restricted movement, and functional impairment. Non-surgical treatments, such as lifestyle changes, physical exercises, medications, therapeutic physical interventions and intra-articular injections are primary strategies for managing this condition [1]. These methods are cost-effective and carry minimal risk, though surgical treatments become more effective as the disease progresses.

Although a multitude of surgical options exists for management of massive rotator cuff tears, rotator cuff repair for reparable tears and superior capsular reconstruction (SCR) for irreparable tears appears to be the most consistent regarding clinical outcomes [2]. Debridement and biceps tenotomy or tenodesis may be a viable option in the most elderly, low-demand patients with limited functional goals [3].

Debridement procedures of the rotator cuff are usually labeled "salvage procedures" or "limited goals surgery". They are indicated for elderly patients with irreparable tears and limited functional expectation, after failure of nonoperative management. The risk of failure for rotator cuff repair after surgery are increased fatty infiltration of tissue, decreased acromio-humeral distance, smoking, BMI, bone size of the rotator cuff tear and increased tension on the repair [4, 5].

The discovery of the first cytokine produced by adipose tissue with systemic actions, leptin, led to the re-classification of adipose tissue as an endocrine organ [5]. Numerous additional adipokines have been subsequently identified, including adiponectin, omentin, and resistin, all produced by adipocytes. The adipokines play central roles in the regulation of metabolism. Adipose tissue also releases pro-inflammatory mediators, including IL-6, TNF-a, IL-1b, IL-8, and MCP-1, which drive inflammation [6, 7]. It is believed that these cytokines are released by the non-adipocyte cells found in the adipose depot.

Adipose tissue is composed mainly of mature adipocytes, though all adipose depots have considerable cellular heterogeneity. The heterogeneous population of cells includes preadipocytes, pericytes, endothelial cells, smooth muscle cells, fibroblasts, hematopoietic progenitor cells, an array of mature immune cells (B and T-lymphocytes, macrophages, myeloid cells) and ASCs (adipose tissue-derived mesenchymal stem cells). These cells make up a communication network that regulates the activity and function of adipose tissue depots [8].

Like other MSCs, ASCs produce a vast array of soluble mediators and extravascular vesicles (microvesicles) that can alter the biology of cell and tissues and mediate therapeutic effects in vivo. ASCs can influence the biology of target cells through products of the secretion of free macromolecules or the production of extracellular vesicles. The soluble trophic macromolecules produced by ASCs are composed of a broad array of cytokines, chemokines (both pro-inflammatory and anti-inflammatory), adipokines, antioxidative molecules, pro-angiogenic factors, anti-apoptotic factors, growth factors (VEGF, HGF, FGF, IGF-1), brain-derived neurotrophic factor (BDNF), interleukins (IL-1Ra, IL-6, IL-7, IL-8, IL-11). The medium from ASC cultures, denoted as conditioned medium, which contains all of the macromolecules secreted from ASCs (differentiated or not to a specific cell lineage), is considered a cell-free therapy for disease. In addition, several studies have demonstrated that the ASC conditioned media effectively mediates therapeutic benefits [8].ASCs are under investigation as a therapy for a variety of human diseases across the globe. For clinical applications, two strategies are being explored, the infusion of either autologous or allogeneic ASC. Autologous transplantation of ASCs is considered safer; however, the use of allogeneic cells offers the potential for a universal donor approach in which multiple patients with readily available, fully characterized, and optimized ASC are used for treatments [8].

SVF (stromal vascular fraction) and ASCs have been investigated as an osteoarthritis therapy in several clinical trials [9-11].

While the outcomes from these trials have been mixed, autologous ASCs have been shown to be safe and offer some improvement in disease-associated pain. Many patients have experienced improvements in pain, function, mobility and overall quality of life on various clinical questionnaires after SVF and ASC administration into the affected joints [8].

Building on the success of autologous orthobiologic therapies in knee joints, recent studies have evaluated similar treatments for the glenohumeral joint [12,13]. Orthobiologic therapies, particularly those using adipose-derived mesenchymal stem cells (AD-MSCs), show significant potential due to their promising results [14].

Rotator cuff tear and chondropathy both significantly impair shoulder function and quality of life: the first impacts the tendons and muscles around the shoulder, the second affects the cartilage within the joint causing pain, stiffness and functional limitations. The coexistence of these conditions complicates treatment, often requiring a multifaceted approach [15]. AD-MSCs have emerged as a powerful tool in regenerative medicine due to their ability to differentiate into various cell types, secrete anti-inflammatory factors, and promote tissue repair [16].

As demonstrated by Kim YS et al injection of adipose-derived MSCs loaded in fibrin glue during rotator cuff repair could significantly improve structural outcomes in terms of the re-tear rate. Although still in the early stages of application, MSC augmentation of surgical rotator cuff repair appears useful for providing an adequate biological environment around the repair site [17].

Case Report

A 50-year-old female presented with a six-month history of increasing shoulder pain, restricted range of motion and functional impairment. She had no notable medical history and reported no history of recent trauma. In consideration of a potentially arthroscopic rotator cuff repair questions about her life-style such as BMI, smoking and osteoporosis [18] were made in order to determine the prognostic factors that predict rotator cuff healing after surgical repair and to integrate these factors into a scoring system such as the Rotator Cuff Healing Index (RoHI) [19].

Physical examination revealed tenderness over the greater tuberosity, weakness in shoulder abduction and external rotation, rotator cuff test such as Jobe test for supraspinatus and Neer test for impingement signs were positive, but no signs of biceps tendinitis were found. The shoulder was stable.

Magnetic Resonance Imaging (MRI) confirmed a partial-thickness tear of the supraspinatus tendon (Figure 1) with retraction and moderate chondropathy of the acromioclavicular and glenohumeral joint (Outerbridge grade 2) [20]. An X-ray was performed to initially diagnose glenohumeral arthritis (Kellegren-Lawrence grade 2) [21]. Initially a conservative treatment was considered due to her age, sex, BMI Given the dual pathology, the patient was considered suitable for our novel regenerative approach using AD-MSCs.

Informed consent, including the use of medical and personal data, was obtained from the patient prior to treatment. The study was approved by the Ethics Committee of Mater Olbia Hospital, Italy. The Constant-Murley score (CMS) was used for preoperative and postoperative assessment [22], and shoulder pain intensity was measured using the visual analog scale (VAS) [23].

The patient was positioned supine, and a small incision was made in the abdominal area under general anesthesia. A solution of saline and epinephrine was injected into the subcutaneous fat tissue of the abdomen. Anesthetics were avoided due to their cytotoxic effects on human mesenchymal stem cells [24]. After a 9-minute wait, approximately 60 mL of adipose tissue was manually extracted. The lipoaspirate was processed using the PureGraft system (Figure 2).

The arthroscopic procedure for rotator cuff repair (RCR) was then performed with knotless suture anchors. After completion,

the processed fat was injected into the joint through a posterior-lateral approach with a sterile needle (Figure 3).

The patient's hospitalization lasted for 2 days. No complications were reported. After 2 weeks, the skin suture removal was performed during an outpatient visit. After 4 weeks of sling immobilization, following the standard RCR protocol, shoulder joint mobilization and muscle strengthening exercises were initiated and continued for at least 2 weeks. Gradual return to light activities and sports was allowed based on individual tolerance.

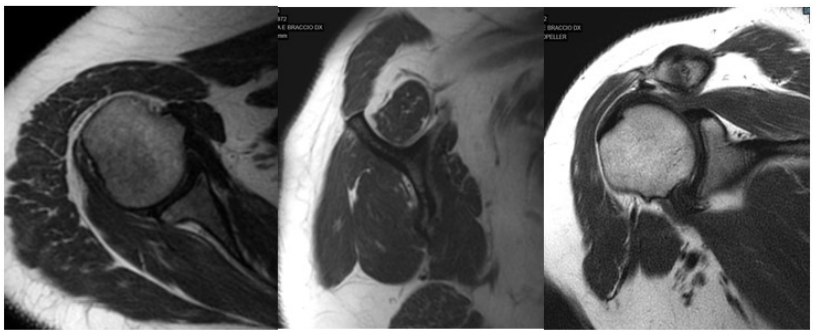

Figure 1: Cuff tear on MRI

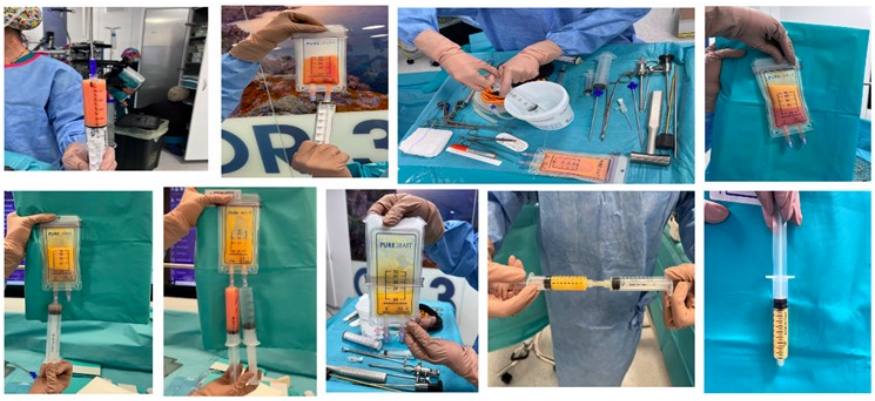

Figure 2: Intraoperative fat harvesting

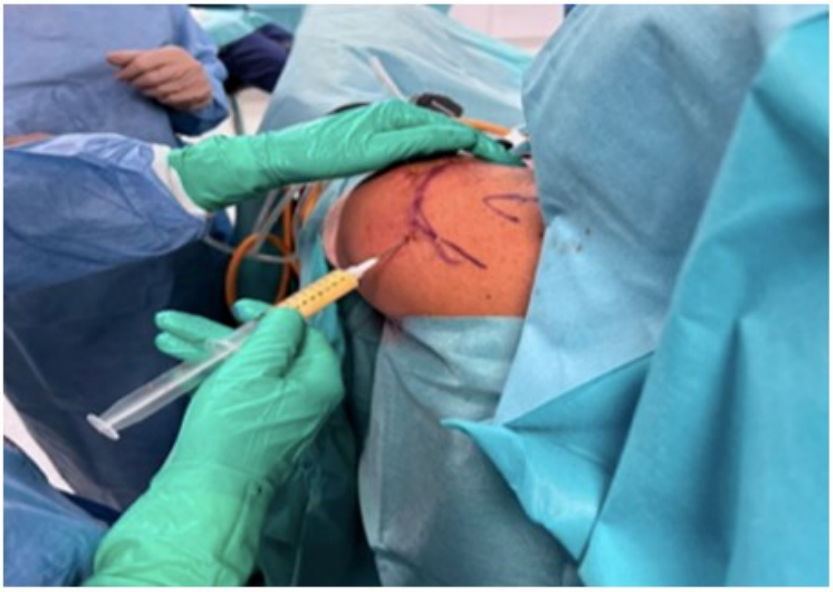

Figure 3: Intraoperative ADMSCs injection

Results

The patient was assessed at 1, 3 and 12 months post-injection in our orthopedic outpatient clinic. At month 1, we just checked the clinical condition and the pain level.

Significant improvements were observed in pain levels (Visual Analog Scale), shoulder function (Constant-Murley Score) and range of motion at month 3. By the 12-month mark, the patient reported significant enhancement in daily activities and was able to resume light occupational duties without discomfort. We reported CMS, VAS and ROM on tables 1, 2 and 3. Shoulder abduction showed the most significant improvement, as anticipated. No adverse events were noted, suggesting the safety and feasibility of AD-MSC therapy.

Table 1: CMS at T0, T1, T2

Baseline	T1 (3 months)	T2 (12 months)
48	71	86

Table 2: VAS at T0, T1, T2

Baseline	**T1 (3 months)**	**T2 (12 months)**
53	13	4

Table 3: ROM at T0, T1, T2

Baseline	**T1 (3 months)**	**T2 (12 months)**
Abd 100°, Flex 105°, IR 65°, ER 40°	Abd 110°, Flex 120°, IR 70°, ER 45°	Abd 155°, Flex 160°, IR 75°, ER 60°

Discussion

The initial findings from this case report offer valuable insights into the potential benefits of adjunctive adipose cell therapy for managing rotator cuff tears. The notable reduction in pain scores and improved range of motion are consistent with previous research emphasizing the regenerative potential of adipose-derived cells in tissue repair. Due to their high proliferation rate, multipotency, and relative ease of isolation from various tissues, AD-MSCs are highly promising for promoting the healing of the tendon-bone junction [25]. The proposed mechanisms of action for AD-MSCs include their ability to differentiate into cartilage and bone and their immunomodulatory properties [26].

Limitations of the study

Adipose tissue depots are complex physiologic environments central to cellular activities, including energy metabolism, endocrinology, and immunity. Adipose tissue is a heterogeneous population of cells. Research indicates that both the heterogeneous SVF and the more homogeneous culture-expanded ASCs have therapeutic potential in regenerative medicine and possibly applications in tissue engineering. While the biologic properties of ASCs are still being understood, the cells are under clinical investigation in human trials for an array of diseases. However, a deeper understanding of the therapeutic potential of SVF or ASC-derived subpopulations, the secretome produced by the cells and the immunomodulatory capabilities may permit the isolation of application-specific ASCs. However, investigators must address several considerations regarding ASCs, including developing standardized methods for cell isolation, culture conditions, proliferation, differentiation and characterization methodology, and ensure safety and efficacy. Donor-to-donor variation significantly impacts the biologic and therapeutic potential of both SVF and ASCs regarding their differentiation, growth, and therapeutic effectiveness. More research into the im-

pact of donor characteristics such as age, BMI, health status, environmental factors, ethnicity, and gender will allow for a deeper understanding of the therapeutic potential of ASCs.

This case report describes the application of AD-MSCs in a patient with a rotator cuff tear and chondropathy, highlighting the potential of this treatment approach over a 12-month follow-up period.

Conclusions

The use of intra-articular AD-MSCs offers a promising therapeutic option for patients with rotator cuff tears and concurrent chondropathy. This case report demonstrates the feasibility, safety, and potential efficacy of this treatment, paving the way for further research and clinical applications in regenerative orthopedic medicine.

Further prospective studies with larger sample sizes are needed to validate these findings and explore the long-term benefits of this combined approach in managing rotator cuff tears. Based on these positive outcomes, we are conducting an additional case-control study at the same institute involving 61 patients. This study aims to further evaluate the effects of AD-MSCs on rotator cuff tears and chondropathy, using a more extensive patient cohort and a comprehensive assessment protocol. The ongoing research will provide valuable insights into the long-term benefits, safety, and overall efficacy of AD-MSC therapy, contributing to the optimization of treatment strategies for these challenging conditions. Future research should address these limitations through larger prospective studies with longer follow-up periods and rigorous methodologies to provide more robust evidence on the comparative effectiveness of these treatment approaches.

References

1. Park HS, Choi KH, Lee HJ, Kim YS (2020) Rotator cuff tear with joint stiffness: a review of current treatment and rehabilitation. Clin Shoulder Elb, 23: 109-17.

2. Collin P, Matsumura N, Leadermann A, Denard PJ, Walch G (2014) Relationship between massive chronic rotator cuff tear pattern and loss of active shoulder range of motion. *J Shoulder Elbow Surg,* 23: 1195–202.

3. Bedi A, Dines J, Warren RF, Dines DM (2010) Massive tears of the rotator cuff. *J Bone Joint Surg Am,* 92: 1894–908.

4. Chung SW, Kim JY, Kim MH, Kim SH, Oh JH (2013) Arthroscopic repair of massive rotator cuff tears: outcome and analysis of factors associated with healing failure or poor postoperative function. *Am J Sports Med,* 41: 167483.

5. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L et al. (1994) Positional Cloning of the Mouse Obese Gene and its Human Homologue. *Nature,* 372: 425-32.

6. Caër C, Christine Rouault C, Le Roy T, Christine Poitou C, Aron-Wisnewsky J et al. (2017) Immune Cell-Derived Cytokines Contribute to Obesity-Related Inflammation, Fibrogenesis and Metabolic Deregulation in Human Adipose Tissue. *Sci. Rep,* 7: 3000.

7. Coppack SW (2001) Pro-Inflammatory Cytokines and Adipose Tissue. *Proc. Nutr. Soc,* 60: 349-56.

8. Bunnell BA (2021) Adipose Tissue-Derived Mesenchymal Stem Cells. Cells, 10: 3433.

9. Bui KHT, Duong TD, Nguyen NT, Thanh Duc Nguyen TD et al. (2014) Symptomatic knee osteoarthritis treatment using au-

tologous adipose derived stem cells and platelet-rich plasma: A clinical study. *Biomed. Res. Ther,* 1: 2–8.

10. Comparative clinical observation of arthroscopic microfracture in the presence and absence of a stromal vascular fraction injection for osteoarthritis (2017) *Stem Cells Transl. Med,* 6: 187–95.

11. Clinical results and second-look arthroscopic findings after treatment with adipose-derived stem cells for knee osteoarthritis. *Knee Surg. Sports Traumatol. Arthros (*2015), 23: 1308–16.

12. Holzbauer M, Priglinger E, Kølle ST, Prantl L, Stadler C et al. (2024) Intra-Articular Application of Autologous, Fat-Derived Orthobiologics in the Treatment of Knee Osteoarthritis: A Systematic Review. Cells, 13: 750.

13. Agarwal N, Mak C, Bojanic C, To K, Khan W (2021) Meta-Analysis of Adipose Tissue Derived Cell-Based Therapy for the Treatment of Knee Osteoarthritis. Cells, 10: 1365.

14. Francis SL, Duchi S, Onofrillo C, Di Bella C, Choong PFM (2018) Adipose-Derived Mesenchymal Stem Cells in the Use of Cartilage Tissue Engineering: The Need for a Rapid Isolation Procedure. Stem Cells Int. 2018.

15. Feeney MS, O'dowd J, Kay EW, Colville J (2003) Glenohumeral articular cartilage changes in rotator cuff disease. J Shoulder Elbow Surg, 12: 20-3.

16. Eshima K, Ohzono H, Gotoh M, Abe R, Nakamura H (2024) Effects of adipose-derived cell supplementation on tendon-bone healing in a rat model of chronic rotator cuff tear with suprascapular nerve injury. J Int Med Res, 52: 3000605241232550.

17. Kim YS, Sung CH, Chung SH, Kwak SJ, Koh YG (2017) Does an Injection of Adipose-Derived Mesenchymal Stem Cells Loaded in Fibrin Glue Influence Rotator Cuff Repair Outcomes? A Clinical and Magnetic Resonance Imaging Study. Am J Sports Med, 45: 2010-8.

18. Hong JP, Huang SW, Lee CH, Chen HC, Charoenpong P, Lin HW (2022) Osteoporosis increases the risk of rotator cuff tears: a population-based cohort study. J Bone Miner Metab, 40: 348-56.

19. Kwon J, Kim SH, Lee YH, Kim TI, Oh JH (2019) The Rotator Cuff Healing Index: A New Scoring System to Predict Rotator Cuff Healing After Surgical Repair. Am J Sports Med, 47: 173-80.

20. Slattery C, Kweon CY (2018) Classifications in Brief: Outerbridge Classification of Chondral Lesions. Clin Orthop Relat Res, 476: 2101-4.

21. Schumaier A, Abboud J, Grawe B, Horneff JG, Getz C et al. (2019) Evaluating Glenohumeral Osteoarthritis: The Relative Impact of Patient Age, Activity Level, Symptoms, and Kellgren-Lawrence Grade on Treatment. Arch Bone Jt Surg, 7: 151-60.

22. Constant C, Murley A (1987) A Clinical Method of Functional Assessment of the Shoulder. Clin. Orthop. Relat. Res, 214: 160–4.

23. Langley GB, Sheppeard H (1985) The Visual Analogue Scale: Its Use in Pain Measurement. Rheumatol. Int, 5: 145-8.

24. Jacob B, Zippelius T, Kloss N, Benad K, Schwerdt C et al. (2019) Local Anesthetics' Toxicity toward Human Cultured Chondrocytes: A Comparative Study between Lidocaine, Bupivacaine, and Ropivacaine. Cartilage, 10: 364-9.

25. Yang S, Sun Y, Yan C (2024) Recent advances in the use of extracellular vesicles from adipose-derived stem cells for regenerative medical therapeutics. J Nanobiotechnology, 22: 316.

26. Kunze KN, Burnett RA, Wright-Chisem J, Frank RM, Chahla J (2020) Adipose-Derived Mesenchymal Stem Cell Treatments and Available Formulations. Curr Rev Musculoskelet Med.