Case Study
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Augmenting Subacromial Bursal Stem Cells Mixed with Platelet-rich Plasma in Arthroscopic Rotator Cuff Repair: Technical Note

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Abstract

Background: Rotator cuff tears can be associated with significant shoulder dysfunction and pain. Despite improved surgical techniques and new methods for the rotator cuff reconstruction, there are still problems connected to the coverage of the humeral head caused by the tendon insufficiency due to degeneration or retraction and late/or inadequate tendon-to-bone healing. For that reason, innovative approaches for enhanced tendon healing are required. The potential of the biological treatment enchasing tendon healing has not been sufficiently explored so far. Biological augmentation may be an option to improve the healing process. One of the possibilities for augmentation is the subacromial bursa, easily accessible tissue during rotator cuff repair, highly proliferative rich in mesenchymal stem cells that are capable of differentiating into various cell lines. In this article, we describe the harvesting technique and application of the subacromial bursal stem cells mixed with platelet-rich plasma during the arthroscopic rotator cuff reconstruction, aiming at postoperative pain alleviation, the improvement of the tendon-to-bone and tendon-to-tendon healing. The goal is enhance healing, to reduce recovery process and to increase patient’s satisfaction with the outcome of the rotator cuff reconstruction.

Case: Authors present augmentation technique of the rotator cuff reconstruct using the nearby subacromial bursa tissue rich in stem cells and mixed whit platelet-rich plasma during arthroscopic rotator cuff repair. It is an advanced surgical technique in which we combine the best of proven surgical techniques for the rotator cuff reconstruction with the best of the regenerative medicine-mesenchymal stem cells from the subacromial bursa and platelet reach plasma. The surgical technique is easy to apprehend, it does not extend time of the surgery and, according to our preliminary data, decreases time of recovery.

Results: The use of subacromial bursal stem cells mixed whit platelet-rich plasma in arthroscopic rotator cuff repair seems to be effective in reducing recovery time in the short term follow up

Conclusion: The presented augmenting technique can be used in every procedure, especially in the elderly patients where issues of tendon to tendon and tendon to bone healing may be expected. Further investigation is necessary

Keywords: Rotator cuff tear • Subacromial bursa • Mesenchymal stem cells

Introduction

Pathology of the rotator cuff, mostly its supraspinatus tendon, including injuries to it is an increasing problem nowadays. Gradual onset of pain and restriction of the range of motion is common with aging; it usually appears in the active population and, if not properly treated, can give a way to functional weakness of the arm due to a degenerative supraspinatus tear. Majority of the rotator cuff injuries result from repetitive overhead movements of the upper arm, lifting heavy objects or performing rapid arm working activities such as house painting, construction work, cleaning etc. On the other hand, one third of the shoulder injuries occur during overhead sports (e.g. team handball, water polo, tennis or baseball) [1]. Where a high percentage of the rotator cuff involvement has been noted [2].

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A full thickness supraspinatus tear is the most common single tendon of the rotator cuff with incidence of 36% [3]. Also in multi tendon tears of the rotator cuff, supraspinatus tendon is involved in 84% of tears, infraspinatus tears in 39%, and subscapularis tears in 78% of tears [4-6]. Which means that supraspinatus and subscapularis tears are the most common sites in the rotator cuff injury? Degenerative injuries of the rotator cuff are very common among the senior population. Magnetic resonance imaging in the senior population documents high incidence of the rotator cuff tears (54% of adults over 60 years have a tear) which means its prevalence increases with aging [1]. Nowadays, an arthroscopic rotator cuff repair is a well-established procedure; however, healing problems especially in the cases with the tendon substance loss are still present. Arthroscopic reconstruction is a golden standard in treating the rotator cuff pathology. During a surgery, arthroscopic inspection provides a precise insight into the lesions thus allowing an adequate assessment of coexisting pathologies, like labral tears, lesions of the long head of the biceps and capsular, ligament or specific muscular lesions such as some subscapularis lesions [1].

Case Presentation

Patients

An 82-year-old patient reported 5 months history of the left shoulder pain, which was increasing over time. The standard physical therapy gained no benefits in reducing pain and improving shoulder function. After a careful examination of the patient's history, functional demand, and possible concomitant pathologies, the clinical examination evidenced the supraspinatus tear and the tear of the long head of the biceps tendon. Magnetic resonance imaging confirmed a complete supraspinatus tear measured as massive (>5 cm) and degenerative tear of the LHB (Figure 1).

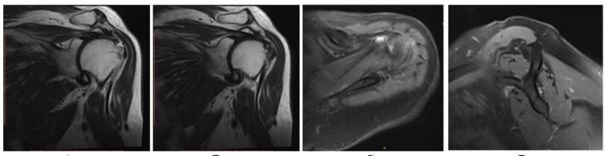

Figure 1. Preoperative magnetic resonance imaging view of the left shoulder. A, B. In the coronal view large rotator cuff tear with an anterosuperior supraspinatus tendon retraction; C. In the axial view, the supraspinatus tendon displays a retracted full-thickness tear; D. In the parasagittal view-supraspinatus muscular atrophy is present.

Methods

Patient positioning and diagnostic arthroscopy: After administration of perioperative antibiotics and while under general anesthesia, the patient was placed in the beach-chair position, 15 mL of venous peripheral whole blood was harvested using 3 Arthrex ACP double syringes prefilled with 1 ml Anticoagulant Citrate Dextrose Solution. The blood was processed using a fully automated 3-sensor technology system based on flow cytometry and light absorption (Angel System; Arthrex) to obtain approximately 2 to 3 mL of platelet-rich plasma (PRP) to be mixed with harvested bursal tissue.

After the surgical preparation and draping, the posterior portal was established and the shoulder was examined. Both, the clinical and MR findings were confirmed. Continuing, the other necessary shoulder portals were established in order to access size, type and localization of the tear and to facilitate instrumentation, anchors insertions and suture management. The long head of the biceps was treated with tenodhesis-we prefer the articular approach fixing tendon at the beginning of the bicipital groove.

Once the intra-articular work has been completed, the scope was transferred in the subacromial space where huge and hypertrophic bursa was identified and harvested with the motorized shaver where Graft Net device was attached. During the inspection, bursal tissue showed no signs of inflammation. After bursectomy/bursal harvest, the "V" shaped anterosuperior supraspinatus tendon tear was detected 3-5 cm in surface, and the strategy for the reconstruction was confirmed. The tendon was mobilized, and the borders were regularized. A further step was addressing the footprint-the footprint was cleaned from the remaining tendon, bursal and scar tissue. Cortical bone on the supraspinatus insertion site was debrided up to the cortical bleeding surface in order to promote healing but leaving enough cortical bone not to decrease an anchor pull out strength. For the repair, one Cork Screw titanium suture anchor was used and the tendon was secured to the bone with the Manson Allen's suture bridge thus restoring complete stability of the supraspinatus tendon over the footprint (Figure 2).

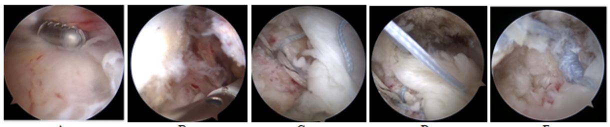

Figure 2. Shoulder arthroscopy intraoperative images. A. View of the subacromial space where the hypertrophic bursa was localized, which was harvested with the motorized shaver with GraftNet attached; B. After bursectomy, "V" shaped anterosuperior supraspinatus tendon tear was identified 3-5 cm wide in the surface area; C. After cleaning the footprint from residual debridement, cortical bone was debrided to create cortical bleeding; finally, one Cork Screw titanium suture anchor was placed into the bone; D. The tendon was reinserted back to the original footprint area using the materas suture; E. The final construct with Manson Allen's suture bridge technique was made, thus restoring complete coverage of the foot print area and stability of the supraspinatus tendon during passive ROM test.

Bursa augmentation and acromioplasty: In this particular case, the subacromial bursa tissue was collected from 2 anatomical sites during the arthroscopic surgery using the GraftNet device connected to the motorized shaver while performing bursectomy through the posterior and lateral portals. The autologous bursal fragments were collected in an easily accessible, sterile filter chamber. The tissue collector was opened and the filter chamber was removed together with the bursal fragments. The harvested tissue was separated from the chamber filter and transferred into a 1-mL syringe with the Luer lock connection. Syringes were filed from behind using plunger to push bursal fragments forward. The next step was mixing bursal fragments with PRP in the ratio 3:1 through a "female to female" adapter. By pushing back and forth several times, a uniform, pasty mass was created and 1-mL syringe was connected to the application cannula and fragments were transferred into the applying cannula. Then fragments were carefully pushed up to the cannula tip using the trocar, until they appeared at the opening. Under the direct arthroscopic visualization through the posterolateral portal the mixture of the bursal tissue and PRP was applied over the reconstruction site.

Before the application of the stem cells, acromioplasty was performed in the standard manner.

A clinical check up in the postoperative period confirmed full ROM and very good strength 3 months after the surgery. An ultrasound exam confirmed complete restoration of the supraspinatus tendon (Figure 3).

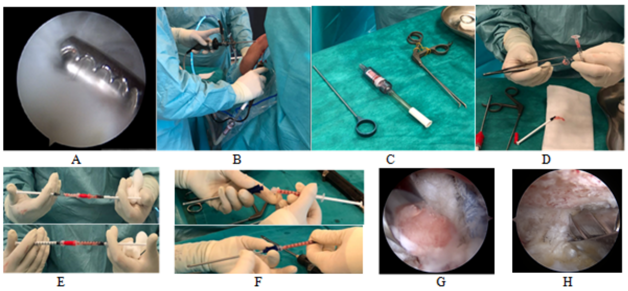

Figure 3. Bursa Augmentation and Acromioplasty, (A) The parietal sheet of the subacromial bursa is mobilized from the lateral sub deltoid region-an arthroscopic intraoperative image; (B) The suction-activated GraftNet device, designed to collect autologous tissue for a multitude of applications; (C) The harvested subacromial bursal tissue was collected in the tissue collector; (D) After separating the tissue collector from the shaver hand piece and tubing system; (E) Mixing bursal fragments with PRP in the ratio 3:1 through a "female to female" adapter by pushing back and forth several times; (F). Then the 1-mL syringe was connected to the application cannula and fragments were transferred into the application device; (G). The cannula was inserted into the arthroscopic port and then tissue mix was carefully applied on the place of lesion; H. Before the application of the stem cells, acromioplasty had been performed in the standard manner.

Postoperative rehabilitation

The postoperative rehabilitation protocol follows general recommendations for the arthroscopic rotator cuff repair. The shoulder should be immobilized in a shoulder sling in neutral physiologic position for 4 weeks. During this period, guided passive mobilization exercises should be performed gradually up to 90 degrees of abduction, 45-50 degrees of forward flexion, extension is forbidden. The sling is discarded gradually during the 5th postoperative week.

Active assisted and active ROM exercises implementation starts from the 5th postoperative week aiming at full ROM that is expected approximately after 10-12 weeks. Strengthening exercises start together with active ROM and submaximal strength is expected 4-6 months after the surgery. A return to shoulder-demanding work or sports is usually possible after 6 months, depending on a patient-specific assessment.

Results

According to our follow-up protocol, the patient was checked clinically 7 and 15 days, then one month and 2 months after the surgery. On the last check up 2 months post-surgery the patient had full abduction and anteflexion of the shoulder; abduction strength with the fully extended arm was 3/5 comparing to the contralateral arm (Figure 4).

Figure 4. Postoperative ROM of patient on two months follow up.

Discussion

After surgical repair of the rotator cuff tear, a crucial point for both, the surgeon and the patient, is whether tendon healing has been achieved or not, since tendon healing is the most important condition required to obtain a very good and excellent final clinical outcome [7]. Further, the re-tear rate after the reconstruction of the large and massive tears remains higher than for the smaller tears. Some authors associate large and massive tears with significantly inferior functional outcomes [8]. To promote that healing process, together with the standard technique of the footprint abrasion to the level of the so-called cortical bleeding bone, we introduced the application of the different growth factors, platelet concentrates and mesenchymal stem cells at the end of the arthroscopic reconstruction. The presence of the cortical bone is essential for the anchor stability and pullout strength. Some researches advocate that the pull-out strength of metal screw-type suture anchors is significantly affected by cortical volumetric bone mineral density [9]. In addition, the foot print periosteum has regenerative potential due to pluripotent mesenchymal stem cells having the role of cell mechanosensing and matrix organization, bone microarchitecture and bone strength in the area of the footprint. Activation of the mechanosensing signaling plays a key role in architecture and cell cytoskeletal reorganization under mechanical stress, which is important for healing of tendon to bone footprint [10]. Therefore, it is very important to leave firm cortical bone on the insertion site as one of the prerequisites for the tendon-to-bone healing. To recreate a better biomechanically native footprint insertion, another important issue is tendon-to-bone pressure distribution. Anatomic footprint is an area measuring approximately 1.55 cm2 that should be recreated [11]. The footprint of the supraspinatus has triangular shape, with an average maximum medial-to-lateral width of 6.9 mm and an average maximum anteroposterior length of 12.6 mm. Supraspinatus muscle fibers are divided into superficial and deep layer. Most of the muscle fibers of its superficial layer ran anterolaterally toward the anterior long tendinous portion which always inserts into most anterior area of the greater tuberosity, while the rest of the fibers from the deep layer run laterally toward the medial margin of the highest impression on the greater tuberosity [11,12]. The attachment site between the tendon and the bone is a weak link during the early healing period, and objective evaluation of rotator cuff repairs shows an approximately 30% rate of failure of secure healing between tendon and bone at 3 to 5 years postoperatively [13]. In literature authors describe various repair techniques that can be mainly divided in a single row and a double row reconstruction technique of the foot print area. Biomechanical studies have shown that a double row repair is superior to single-row techniques in terms of fixation strength. Additionally double-row repair restores the footprint closer to its original site [14].Never the less, a single-row arthroscopic rotator cuff repair using double-loaded metal anchors and margin-convergence sutures with concomitant procedures also provides excellent results [1]. Miskulin et al. demonstrated that the single-row arthroscopic rotator cuff reconstruction is a successful repair method in large and massive rotator cuff tears resulting in pain relief and improved mobility, normal muscle strength and overall function [1]. If followed by an adapted rehabilitation protocol, this technique also provides notable patient satisfaction [1].

Investigation has also been dedicated to the biologic side of rotator cuff tendon healing and possible biologic augmentation that may help improve rotator cuff tendon healing. Tendon healing occurs in three overlapping stages: inflammatory, fibroblastic, and remodeling [15]. Various methods of the subacromial infiltrations during rehabilitation process of the conditioned autologous plasma alone or in combination with the collagen have been described with good functional results. Injecting autologous Platelet-rich Plasma (PRP) in sub-acromial space for treatment of a partial supraspinatus tendon tear is comparable to the standard corticosteroid injection but its more favorable clinical results are noticed after 3 months 16. Autologous plated-rich plasma when, properly prepared, has three to seven times higher concentration of plated cells then the regular plasma. Previously platelets were thought only to contribute to hemostasis, but they are now known to initiate wound healing by secreting variation of growth factors and cytokines. In this process of “activation,” platelet alpha granules start to release numerous proteins, including Platelet-derived Growth Factor (PDGF), Transforming Growth Factor (TGF), Vascular Endothelial Growth Factor (VEGF), Insulin-like Growth Factor (IGF), Epidermal Growth Factor (EGF), and Interleukin (IL)-1. Because its ability to stimulate wound healing, to minimize bleeding during surgery and to promote better healing, PRP has found application in many surgical fields [16,17].

Recently, several studies have reported subacromial bursa as a potential source of mesenchymal stem cells [18]. The subacromial bursa is an easily available tissue, rich in mesenchymal stem cells that enable and accelerate tissue regeneration possessing having a high capacity for self-renewal, as well as an exceptional potential for differentiation into different tissue types. Scientific researchers have pointed to the facts that, due to all their characteristics, mesenchymal stem cells play an essential role, not only in all stages of the human body development, but also during the healing process. Because of their unlimited potential for proliferation and self-renewal, they are considered immortal. It has been demonstrated that the natural intrinsic healing mechanism of the rotator cuff starts from the bursal side epitenon: “The vascularized connective tissue covering the area of tear and the proliferating cells in the fragmented tendons reflected more of the features of repair than of degeneration and necrosis; The main source of this fibrovascular tissue was the well of the Page 4 of 5subacromial bursa” [19]. Other researchers demonstrated in an experimental rat model the migration of autogenous host stem cells in tendon grafts mainly from the bursal side of the tendon stumps [20]. Furthermore, the bursa, like the peritoneum, possesses the function of rapidly forming protective adhesions, to confine inflammation, to enable fibrovascular tissue migration and to incorporate (absorb) into the place of the tear restoring function of entire or part of the tendon to enable mobility of affected tissue [21]. Comparing proliferation of bursal stem cells with bone marrow stem cells, the mesenchymal differentiation including chondrogenesis, osteogenesis, and adipogenesis, significantly superior capacity was seen in differentiation of bursal steam cells [22].

Another important issue is the muscles atrophy of the rotator cuff tendons, predominately the infraspinatus tendon, often observed in patients with the supraspinatus tear. Most probably the reason of atrophy is a retraction on the suprascapular nerve following rotator cuff tears [11]. Warner reported that seven of twenty-six patients with a massive rotator cuff tear and fatty degeneration/ replacement of the muscle fibers showed dysfunction of the suprascapular nerve [23]. High levels of neurotrophic factors found in bursal stem cells compared with bone marrow cells might also be useful for the restoration of the neuromuscular unit and the neurogenic control of cell turnover of the soft tissues, which can possibly enable better healing, strength, and range of motion of the shoulder in the postoperative rehabilitation [24].

We found out that bursal tissue is not always present in the same volume; consistency of the bursal tissue is very variable in thickness and volume, and in some cases, being insufficient, may not be an option for the augmentation of the repair. In cases where subacromial bursa is thick and voluminous we started to use the Graft Net device (Arthrex) to collect as much of the bursal tissue as possible in order to obtain as much of the stem cells with extracellular matrix for the application to where is most needed. The collected bursal tissue is mixed with Platelet Rich Plasma (PRP), rich with growth factors that modulate the inflammatory pathway and encourage healing of tendons, ligaments, muscles, and bone [25,26]. There are researches suggesting that application of PRP significantly decreased rates of incomplete tendon healing in small to medium tears and medium to large tears. Application of PRP has significant result also in pain reduction 30 days post-operatively [27].

If the bursal tissue in the subacromial space is not present or its volume is inadequate, we continue to use PRP infiltration during the postoperative rehabilitation process, in either one highly concentrated application or 5 weekly infiltrations.

Conclusion

Recently, a huge body of scientific evidence is available of stem cell’s clinical efficacy and safety in almost every field of medicine. It is certainly a new frontier in orthopedics too. This paper presents a case report on the successful application of the stem cells mixed with PRP in the augmentation of the supraspinatus tendon repair. Further studies are required to investigate the mechanisms of action and proper application of autologous blood-derived PRP and subacromial mesenchymal stem cells in order to establish better protocols of treatment of the rotator cuff tears combining surgical, mechanical repair with the orthobiological augmentation, which, we hope, will improve functional outcomes for patients.

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