

CASE REPORT

Secretome Therapy, Potential Treatment for Rotator Cuff Tear: A Case Study

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ABSTRACT

Introduction: Rotator cuff tears (RCTs) are the most frequent pathologies within the shoulder girdle, and this injury is the most commonly diseased tendons in the human body. RCTs can cause pain and weakness in the shoulder. A 42-year-old woman has been experiencing right shoulder pain and arm-lifting problems for almost a year. Ultrasonography revealed a full-thickness Supraspinatus tear. The patient underwent an Ultrasound-guided supraspinatus tendon injection of 2 ml umbilical cord Mesenchymal Stem Cell (MSC) secretome.

Methods: This is a case report analyzing the role of secretome therapy in rotator cuff tear potential treatment. The study was conducted at RSCM Hospital.

Results: During the one-week follow-up, the patient's Shoulder Pain and Disability Index (SPADI) score decreased from 56.9% to 48.5%, her pain scale reduced from 8 to 6, and her shoulder Active Range of Motion (AROM) improved. After a month, there was an improvement in her shoulder AROM. However, the ultrasound shows no significant improvement in the supraspinatus tear structure after the secretome injection.

Conclusion: Secretome has a potential effect on reducing pain and improving functional outcomes in rotator cuff tears in this patient. These findings raise the prospect of secretome as a potential regenerative therapy for rotator cuff tears.

Keywords: mesenchymal stem cells conditioned-medium, rotator cuff tear, secretome, supraspinatus tear.

ABSTRAK

Pendahuluan: Robekan pada tendon *rotator cuff* merupakan gangguan yang paling sering terjadi pada sendi bahu, serta merupakan gangguan tendon paling sering terjadi pada tubuh manusia. Robekan pada tendon *rotator cuff* dapat menyebabkan nyeri dan kelemahan pada area bahu. Seorang Wanita 42 tahun mengeluhkan nyeri bahu kanan dan kesulitan mengangkat lengan selama kurang lebih satu tahun. Pemeriksaan ultrasonografi menunjukkan robekan total pada tendon supraspinatus. Pasien mendapatkan suntikan 2 ml MSC sekretom tali pusat pada tendon supraspinatus dengan panduan ultrasonografi.

Metode: Laporan kasus ini menganalisis peran dari terapi sekretom pada robekan tendon *rotator cuff* di RS dr. Cipto Mangunkusumo.

Hasil: Pada pemeriksaan minggu pertama, skor *Shoulder Pain and Disability Index* (SPADI) pasien berkurang dari 56,9% menjadi 48,5%, skala nyeri berkurang dari 8 ke 6, dan *Active Range of Motion* (AROM) bahu meningkat. Sebulan kemudian, terdapat peningkatan AROM pada sendi bahu pasien. Namun, pada pemeriksaan ultrasonografi, tidak ditemukan perbaikan yang bermakna pada struktur robekan tendon supraspinatus.

Kesimpulan: Sekretom mempunyai efek potensial dalam mengurangi nyeri dan meningkatkan fungsi pada robekan tendon *rotator cuff*. Temuan tersebut meningkatkan potensi sekretom untuk terapi regeneratif robekan tendon *rotator cuff*.

Kata kunci: sel punca mesenkimal terkoneksi-sedang, robekan tendon *rotator cuff*, sekretom, robekan supraspinatus

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INTRODUCTION

Rotator cuff tears are among the most common causes of shoulder pain and limited movement.¹ As the human population ages, the number of outpatient visits and procedures attributed to symptomatic rotator cuff injuries is expected to

climb. It has been reported that the percentage of rotator cuff tears in elderly populations ranges between 25.6% and 50%.² Despite their prevalence, the cause of cuff tears is incompletely understood. Internal factors, external factors, or both may cause rotator cuff injuries. Intrinsic factors relate to the rotator cuff injury caused by the rotator cuff. They are typically degenerative in nature. This includes deterioration associated with aging, inflammation, oxidative stress, and dysmetabolism. External influences are those that originate outside the joint. They may be anatomical, environmental, or the result of an existing impingement.³ It is estimated that shoulder pain prevalence is between 7% and 25%, with an incidence of 10 per 1000 people each year.⁴

As future possibilities for cell-based tendon regeneration, mesenchymal stem cells (MSCs) have garnered significant interest. Positive findings were observed in most in vivo investigations that utilized acute transection or window defect models to simulate the surgical application of MSCs with or without a scaffold.^{5,6} MSCs are increasingly used for musculoskeletal diseases due to their excellent regenerative potential.⁷ It is hypothesized that MSCs can stimulate angiogenesis, decrease inflammation and cell proliferation, and boost collagen deposition. These functions are probably paracrine effects of MSCs, especially those mediated by exosomes.⁸

This case study reveals that a week following the injection of secretome, a reduction in pain scale and improved functional outcomes have already occurred without any surgeries needed. Additional time and research are required to comprehend the secretome's significance in tendon repair completely. This is a novel discovery, considering that secretome injection is rarely implemented because it is still under research. Nevertheless, it has potential treatment for functional and structural clinical improvement in soft tissue injuries in Indonesia.

CASE PRESENTATION

A 42-year-old woman arrived with right shoulder pain and an arm-lifting issue that had been persistent for more than a year. Lying on the affected side also causes some pain. The patient is a housewife, doing housework every day. The patient was a badminton athlete 20 years ago. She is able to do her daily activities independently. The patient has a history of hypertension, chronic cephalgia et causa, and multiple bilateral anterior cerebral artery stenosis on therapy. The patient also has Sjogren syndrome, controlled by medication from Internal medicine department. The patient agreed to be the research subject and signed the informed consent to be the research subject; moreover, existing data is used for research purposes.

During the physical examination, the patient demonstrated pain in the shoulder AROM starting in 60° of abduction and 80° of flexion with a positive drop arm test, empty can test, and Hawkins-Kennedy test. Ultrasound confirmed a complete tear of the supraspinatus (Figure 1). The patient has already received physical therapy programs and steroid injections but she is still suffering from pain.

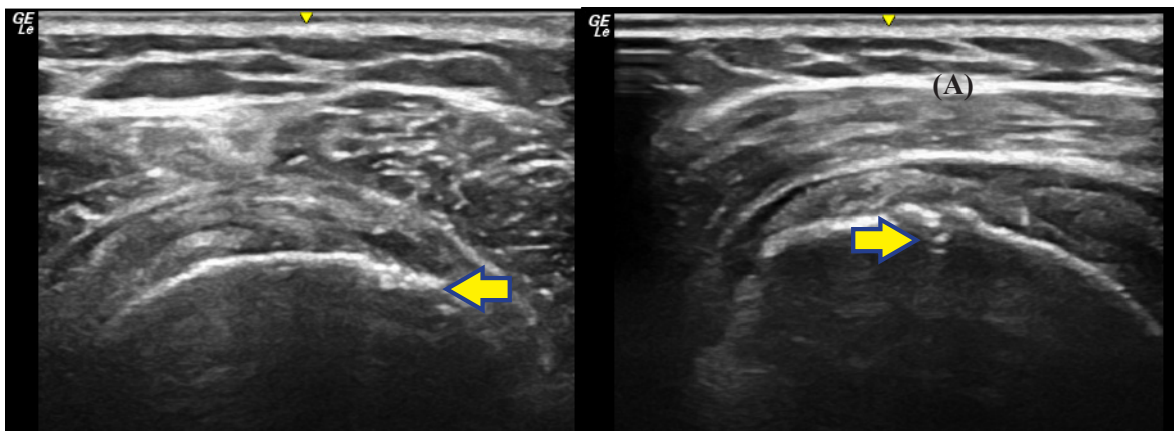


Figure 1. Ultrasound confirmed full-thickness supraspinatus tear. A. Short Axis View, B. Long Axis View

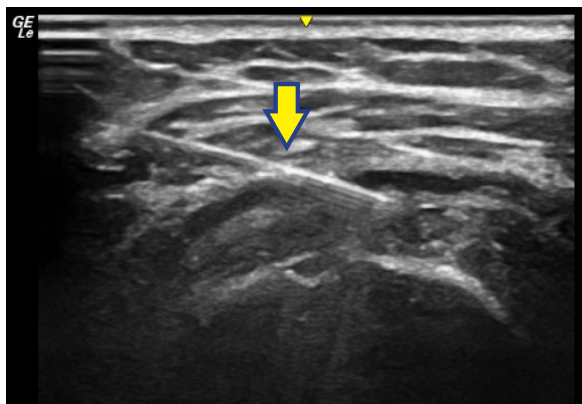


Figure 2. The 2 ml umbilical cord MSCs secretome was injected by ultrasound-guided into the supraspinatus tendon

At the second examination, the patient had an ultrasound-guided injection of 2 ml of umbilical cord MSCs secretome into the supraspinatus tendon (Figure 2). The patient is scheduled for an examination, repeating the ultrasound injection the following week, and receiving joint protection therapy for the right shoulder. At the one-week follow-up, the patient showed a reduction in pain scale (from 8 to 6), improvement of shoulder AROM, and a SPADI score (from 56,9% to 48,5%). Joint Protection therapy continued, and the patient did an ultrasound examination; which it seems to be no significant structural improvement (Figure 3).

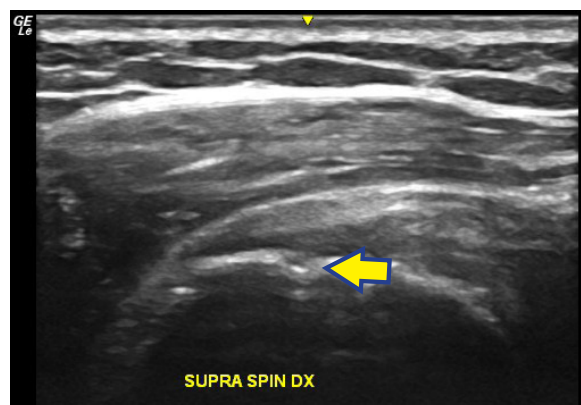


Figure 3. The ultrasound Long Axis View shows that there is still an improvement in cortex irregularity without supraspinatus tear significant to structure improvement.

After one month of follow-up, the ultrasound shows no structural improvement in the supraspinatus tear after the secretome injection. AROM has increased.

DISCUSSION

A 42-year-old woman arrived with right shoulder pain and an arm-lifting issue that had been persistent for more than a year. Lying on the affected side also causes some pain. The patient is a housewife, doing housework every day. The patient was a badminton athlete 20 years ago. She is able to do her daily activities independently. Based on these, the extrinsic risks, such as occupations and sports activities, cause excessive mechanical loading on it, involving rotator cuff injury.⁹ A repeated and biomechanical loading on the rotator cuff tendon increases the risk of rotator cuff injury.¹⁰ The most general pathology of the shoulder is dysfunction of the rotator cuff, including inflammation and physical tearing that results in

shoulder discomfort, weakness, and instability. This condition affects 30 to 50% of patients over 50 at some point in their lives; nevertheless, it is prevalent across all ages and activity levels.^{11,12}

During the physical examination, the patient had shoulder AROM pain beginning at 60° of abduction and 80° of flexion, along with a positive drop arm test, empty can test, and Hawkins-Kennedy test. Ultrasound confirmed a complete tear of the supraspinatus. The patient has already received physical therapy and steroid injections but still suffering from pain. At the second examination, the patient had an ultrasound-guided injection of 2 ml of umbilical cord MSCs secretome into the supraspinatus tendon. The patient is scheduled for an examination, repeating the ultrasound injection the following week, and receiving right shoulder joint protective therapy. At the one-week follow-up, the patient's pain scale had decreased from 8 to 6, his shoulder AROM had improved, and his SPADI score had decreased from 56.9% to 48.8%. The patient did an ultrasound examination; which it seems to be no significant improvement in the supraspinatus tear structure.

Utilizing mesenchymal stem cells (MSCs), which can be derived from numerous sources, including bone marrow (BM), adipose tissue (AD), muscle tissue (MT), and umbilical cord blood (UCB), to repair damaged tissues is a promising therapeutic approach. Recently, a few studies have shown that MSCs effectively regenerated rotator cuff tendons.¹³ It has been demonstrated that MSCs secrete anti-inflammatory cytokines and inhibit immune cell proliferation, development, and in vitro activity. Transplanted MSCs do not induce an immunological response in vivo, allowing their use in allogenic stem cell treatment.¹⁴

MSCs are capable of direct differentiation into musculoskeletal cell types. When implanted in vivo, they do not develop teratomas, making them safe for therapeutic applications.¹⁵

Umbilical cord-derived mesenchymal stem cells (UC MSCs) are fetal MSCs extracted from umbilical cord tissue, frequently thrown as medical waste after birth, and may therefore be collected non-invasively at the collection site and given at a relatively low cost.¹⁶ According to reports, UC MSCs are more proliferative and have a greater capacity for self-renewal than other adult MSCs.¹⁷ UC MSCs can develop towards the myogenic lineage and contribute to anterior tibialis muscle injury-induced muscle regeneration in a rat model.¹⁶

Mesenchymal stem cells can do self-renewal and differentiate the cells into osteoblasts, chondrocytes, and adipocytes. These cells are frequently extracted from various connective tissues. They may be propagated in vitro and contain multilineage potential. Many in vivo investigations have demonstrated that transplanted MSCs can enhance tendon repair in animal models with Achilles tendon abnormalities, rotator cuff problems, and patellar tendinitis.¹⁹ Based on several studies above, the administration of secretome is one of the promising options for structural repair in cases of rotator cuff injuries. Therefore, the administration of secretome is one of our considerations in managing rotator cuff injury cases in this patient.

In our case, after one month, the ultrasound shows no structural improvement in the supraspinatus tear after the secretome injection. AROM has increased. The failure rate for

rotator cuff tendon repair is 20– 90%. The prognosis depends on the patient's age, tear size, chronicity, muscle atrophy, fatty degeneration, tendon quality, surgical technique, and postoperative rehabilitation treatment. Current therapeutic approaches result in suboptimal quality at the distal end of a rotator cuff tendon tear and a lack of physiological restoration; therefore, a new biological treatment creates an optimal environment for the tendon restoration required to regenerate the tendon and reduce scar formation.²⁰ Histological analysis and motion analysis of walking by Rak Kwon et al. were performed four weeks after therapy to determine the efficacy of UCB-MSCs for chronic full-thickness rotator cuff tendon injuries without repair.²¹ Other studies by Yea et al., upon implanted into a rat rotator cuff repair model, UCB-MSCs seeded biomimetic hydroxyapatite-gradient scaffold improved collagen organization, cartilage production, and equivalent biomechanical qualities to the native tendon-bone contact by eight weeks.¹⁶ Sometimes, the lack of tendon structure improvement after secretome administration may warrant further evaluation and research. Possible dose adjustments to consider repeating secretome administration could be studied further.

Secretome is indeed one of the promising treatment options based on our case. However, nowadays, the secretome cannot be implemented in Indonesia because secretome therapy is still under development and research, making it quite expensive and it is not covered by the public health insurance system despite its promising results. Future clinical trials will presumably seek to standardize protocols for secretome therapy. However, we must still wait to develop a 100%

effective and inexpensive clinical procedure, especially in Indonesia. For several countries, cell therapy cannot be carried out on-site due to a lack of adequate facilities and delivery of cell preparations developed by industrialized countries consequently making the cost will be quite expensive.²²

CONCLUSION

In this case report, we conclude that Secretome's injection can alleviate shoulder pain and improve functional outcomes without detrimental effects on this patient. These findings indicate the possibility of using secretome as a regenerative therapy for tendon tears in conjunction with proper rehabilitation exercise programs to enhance recovery, resulting in positive functional outcomes. Hopefully, this report provides some insight for further study, and it is hoped that based on this case, secretome can be considered as one of the treatment options for rotator cuff tears.

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