Chapter 15
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Successful Treatment with Expanded Mesenchymal Stem Cell Therapy for Muscle Wasting Post-Surgical Repair of Achilles Tendon

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ABSTRACT

This study investigates the efficacy of local implantation of biological therapy to repair injured calf muscles and tendons. The Achilles tendon (AT) is one of the most frequently ruptured lower leg tendons. AT rupture occurs when sudden forces apply upon the Achilles tendon during vigorous physical activities that involve abrupt swivelling on a foot or a fast burst of speed. Chronic AT rupture generally occurs 4-6 weeks after injury; symptoms include pain, ankle stiffness, and reduced strength. There is no typical treatment, mainly when a significant gap between the tendon ends; it warrants reconstruction, commonly with flexor hallucis longus tendon (FHLT) transfer for all defects over 2 cm. This case study features a 44-year-old female patient who suffered a left AT rupture during a netball game. Initially, she had conservative treatment, but it spontaneously ruptured again, necessitating reconstruction surgery with FHLT transfer. She developed calf muscle weakness and atrophy at the grafted musculo-Achilles junction. Her symptoms included the inability to perform a single heel raise, decreased recreational activities, and calf muscle wasting and weakness. The Foot & Ankle Disability Index (FADI) score was 74. Her orthopaedic surgeon declined any further surgical intervention, given it will not offer any benefit to the patient. She has opted for a trial of autologous adipose-derived expanded mesenchymal stem cell therapy (MSCs) combined with platelet-rich plasma (PRP). Six months following the treatment, she had a good outcome evidenced by improved daily activities, heel-raise, and running slowly for the first time after several years post reconstruction surgery. Her FADI score rose to 91.3, and a six-month post-treatment MRI revealed an increased signal at the musculo-Achilles junction suggesting a healing process. This case presents a successful outcome with a single MSCs and PRP, indicating we can try MSC therapy to repair wasted calf muscle and tendon from previous scars.

Keywords: Achilles Tendon (AT); Rupture; Mesenchymal stem cells (MSCs); Platelet-rich plasma (PRP); rupture; surgery; wasting.

1. INTRODUCTION

The Achilles tendon (AT) is the strongest one in the human body, but it is the most frequently ruptured tendon of the lower limb [1].

Chronic AT rupture is typically described 4 to 6 weeks following injury [2], characterized by pain, reduced strength, and ankle stiffness. A noticeable gap between the ruptured ends can be observed on physical examination.

AT rupture is diagnosed by clinical examination, but an ultrasound scan enables rapid bedside confirmation of the diagnosis; MRI provides more anatomic details with greater accuracy and looks for other pathologies.

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Initial management of AT rupture comprises a conservative approach with rest, non-steroidal anti-inflammatory medicines, and ankle immobilization. If those measures were unsuccessful, then consider surgical intervention.

Surgical repair diminished the risk of recurrent tendon rupture compared with conservative management [3], but it raises the probability of complications, particularly with open repair [4]. Around 80 % of athletes return to sports following AT rupture [5].

Chronic AT rupture can be directly attaching end-to-end; however, there is no standard treatment for chronic AT rupture with significant gaps. Generally, a gap between 2-4 cm makes flexor hallucis longus tendon transfer is a good option with a favourable outcome [6-10]. Despite an excellent surgical approach, long-term complications of scarring and some limitation of achieving competitive sports compared to pre-rupture status. There is growing evidence that MSCs can improve the tendon's function and repair [11]. We have accomplished that target in our clinical case study.

2. CASE REPORT

A Forty-four-year-old female patient works as a development Planner, usually fit and healthy; she ruptured her left Achilles tendon (AT) in March 2012 when she was playing netball; she felt as though someone kicked her in the back of the leg. She had conservative treatment with a standard leg cast, followed by moon boot, a non-weight-bearing, then weight-bearing until May 2012, and physiotherapy helped her recovery. In August 2012, she felt a slight pull in her AT, with a non-painful limp, so she did not do much about it. Ultrasound scan in the community revealed the AT appears functionally ruptured with disorganized scar tissue in the tendon gap.

She has subsequently referred to the orthopaedic surgeon for an assessment, and an MRI scan was obtained and showed complete rupture of the distal tendo-Achilles. There is moderate thickening at the myotendinous junction and some disuse oedema within the soleus (Fig. 1).

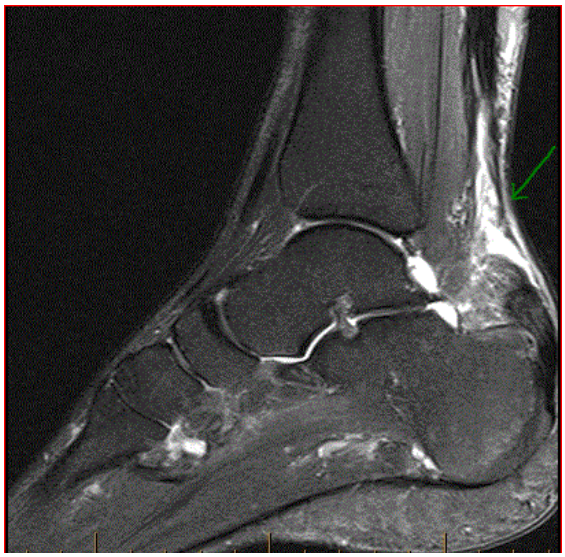

Fig. 1. Sagittal T2 MRI Pre-surgery MRI demonstrating evidence of AT rupture

The surgeon felt it was difficult to stitch together the ruptured tendon. He recommended AT reconstruction to reduce Achilles scar tissue and advised FHLT transfer in November 2012. She underwent several years of the rehabilitation program. Despite that, she developed calf muscle weakness and atrophy. In June 2020, the orthopaedic surgeon noted calf muscle weakness and atrophy, and she could not perform a single heel raise. The Foot & Ankle Disability Index (FADI) score of 74 and a follow-up MRI revealed remodelling of the left tendo-Achilles with surgical changes at the reconstruction site. There were tendinopathy/post-surgical changes in the distal tendo-Achilles and

soleus tendon insertion zones. There was a partial thickness tear at the soleus musculotendinous junction (Fig. 2).

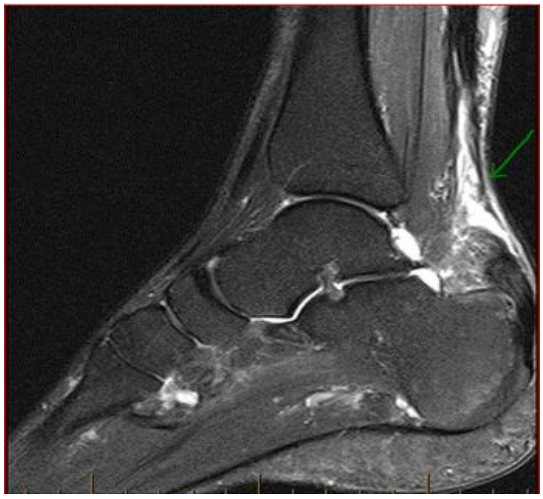

Fig. 2. Sagittal T2 MRI showed post-surgery muscle atrophy and partial thickness tear

The surgeon advised her against any further surgical intervention, given it has a high chance of failure or minimum benefit due to chronic tendon scarring. Because the gastric-soleus muscle complex was short for so long, the risk of surgery outweighs the benefit. She researched alternative therapy options, and she discovered a non-invasive treatment in New Zealand using adipose-derived expanded MSCs combined with PRP.

In August 2020, we assessed her at our regenerative clinic. The findings were post-surgery mid-calf scar with soleus muscle wasting at the tendo-muscular junction; she could not perform heel raise. She was concerned about her inability to carry out recreative sports or running. After discussing the pros and cons of the MSCs therapy, she decided to proceed.

On 21/10/2020, after informed consent, the abdominal fat was harvested by a qualified general surgeon. The MSCs were extracted and expanded at our licensed private Auckland lab, New Zealand, according to the approved protocol. The lipo-aspirate was washed and then digested with 0.2 U/mL collagenases. The stromal vascular fraction (SVF) was separated from the digested adipose tissue through density centrifugation. The SVF was plated down and cultured using Dulbecco's Modified Eagle Medium (DMEM) and 10% human platelet lysate (HPL) to expand the MSCs population. Cells were grown to 90% confluence over eight weeks and then cryopreserved until injection. The implants got prepared on the date of treatment. The cells were washed and filtered before being resuspended in Hartmann's solution with 10% HPL in syringes for administration. Cell count was measured manually and confirmed by a hemocytometer, and the viability test was calculated by trypan blue exclusion dye, which ranged from 95-98%.

On 16th December 2020, we performed the stem cell implantations after informed consent. Under complete aseptic technique, we used 100×10^6 of MSCs (2mL) combined with PRP (prepared on the day of the procedure, 8 ml); the PRP was prepared by using an Anticoagulant Citrate Dextrose Solution-A (ACD-A) tubes and placed in a centrifuge for eight minutes. We added the PRP to the expanded stem cells for the total amount of 10 ml; we injected the mixture in multiple areas of the soleus-Achilles junction under ultrasound guidance, using a 1.5-inch 25Gauge needle. The injectate was distributed in a fan-shaped fashion penetrating the scar tissues.

Six months post the stem cell implant, she clinically reported a positive outcome to heel raise and started running slowly. The FADI score rose from 74 to 91.3. An MRI in June 2021 revealed an increased heterogeneous signal within the distal myotendinous junction of the soleus. This is thought to be due to an inflammatory healing response (Fig. 3).

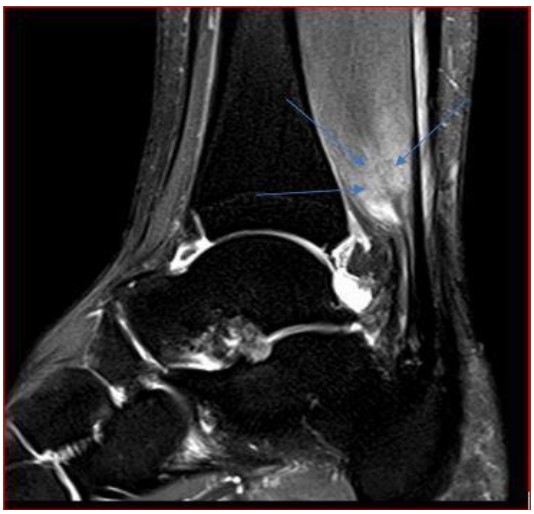

Fig. 3. Sagittal T2 minor increase in signal may be due to post-treatment changes (healing response)

3. DISCUSSION

Some studies showed aggressive surgical intervention was the preferred option over conservative management. Based on early findings, conventional treatment is associated with high re-rupture rates [3]. Regardless of the treatment modality, aggressive early rehabilitation is recommended for acute AT ruptures to allow for an early return to activities of daily living, high patient satisfaction, and functional improvement.

There is growing interest in providing biological stimuli to heighten the tendon reparative response. MSC therapy is a promising science that can give an appropriate cellular signal to promote new tendon formation (neotendon) during repair rather than scar tissue. Currently, this is being studied in various research facilities and clinical practices to ascertain efficacy and safety [12,13]. We believe the significant outcome in our patient could be related to a high number of MSCs with the scaffolding PRP that has the growth factors for a synergistic effect. Also, precise implantations of the mixture under ultrasound guidance in multiple areas with various depths at the affected musculo-Achilles junctions. The FADI score rose from 74 to 91.3; the improvements mainly; came up to her toes and doing complex works. The MRI finding of increased signals six months post-treatment could be a good sign of healing, but it is worth repeating it in the future to see the progress.

We propose future randomized controlled trials to test this therapy and standardize the technique used for consistent results.

4. CONCLUSION

We hypothesize the use of expanded mesenchymal stem cells combined with PRP produced a dramatic effect on the tendon healing with symptoms improvement and high signal of the inflammatory healing evidence on MRI. We recommend a large-scale study to see those findings are reproducible.

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COMPETING INTERESTS

The author has declared that no competing interests exist.

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Biography of the author(s)

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DISCLAIMER
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