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Case Report

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Remarkable pain control and functional improvement in clubfeet-related ankle osteoarthritis post autologous expanded mesenchymal stem cell therapy

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Abstract

Ankle joint osteoarthritis (OA) is not as common as knee and hip OA but it causes a significant socioeconomic burden in society. The causes of ankle OA could be primary or secondary to previous ankle trauma, inflammatory arthritis like rheumatoid arthritis, avascular necrosis, post-infectious, clubfoot, and other rare causes. Ankle OA is hard to treat conservatively. Limited options, including physiotherapy, supportive custom-made braces, weight reduction, and anti-inflammatory medicines. Standard surgical options are joint arthrodesis and ankle replacement. Arthrodesis can limit the movement of talar and subtalar joints, making it difficult to be accepted by athletes who require functional joint movement. Ankle replacement might last between five and ten years and is sometimes technically challenging.

Herein we report a case of a seventy-one-year-old male property investor. His past medical history of bilateral congenital clubfeet with the left foot more affected and pointed backward required three surgeries at the age of two through five to align the foot in the correct direction, and his left ankle was fused. In his mid-forties, he had mild ankles discomfort which was managed by suitable orthotics, despite the ankle pathology he enjoys various recreational physical sports at a premium competitive level with determination. At the age of sixty-seven, his symptoms increased gradually. He was diagnosed with severe secondary severe subtalar and mild talar OA, confirmed by X-rays; by the age of seventy-one, he had significant pain and loss of ankle function to the extent he could hardly walk five steps or play any sport. He failed conservative management with various supportive orthotics and long-term anti-inflammatory medicines. He elected experimental autologous fat-derived expanded mesenchymal stem cells (MSCs) combined with platelet-rich plasma (PRP). After two doses nine months apart, he responded superbly to become pain-free. Three months after the second dose, he was able to walk normally, play sports, and intend to return to competitive table tennis, but we recommended continuing using supportive orthotics. We predict MSCs slow the progression of OA. We believe this is the future medicine to try efficiently and safely regardless of the number of booster doses given.

Keywords: Ankle; Clubfoot; Mesenchymal stem cell; Osteoarthritis; PRP.

Introduction

Osteoarthritis (OA) of the ankle joint is less common than knee and hip OA, but it causes a significant socioeconomic burden in society [1].

From the biomechanical point of view, the ankle movement affects primarily rolling, whereas the knee moves with a mixture of gliding, rolling, and rotating movements. The significant range of mobility of the knee predisposes it to develop primary osteoarthritis, while the ankle remains relatively protected [2].

Anatomical studies imply that despite the ankle joint having thinner cartilage than the knee or hip joints, the ankle cartilage is more even, stiffer, and resilient to indentation. More than that, ankle cartilage is less sensitive to the effects of cytokines that cause primary osteoarthritis [3]. In addition, it does not generate matrix metalloproteinase, an enzyme that is expressed by normal knee cartilage, which predisposes to cartilage degradation.

The aetiology of OA could be primary or secondary. The latter could be related to local trauma, pre-existing structural disease like rheumatoid arthritis, avascular necrosis, post-infectious, clubfoot, and other rare causes [4].

The management of ankle OA includes non-operative and operative approaches. The non-operative treatment involves weight reduction, walking aids, and avoidance of impact sports: ankle braces and shoe outsole modifications to a rocker sole limit

ankle joint motion [5]. In addition, physiotherapy, analgesics, and non-steroidal anti-inflammatory medications (NSAIDs) should be trialed before any surgical intervention. Intra-articular steroid injections help reduce joint synovitis and thus impact arthritis-related pain, but the effect only lasts a few weeks [6]. Steroid injections can carry a small risk of infection, and frequent use might thin the cartilage [7].

Intra-articular hyaluronic acid (HA) injections are thought to help lubricate the synovium. Still, the studies were of poor quality and showed the benefits of HA injections compared with placebos were non-significant [8]. In addition, intra-articular HA injections compared with oral NSAIDs did not show a statistically significant difference in symptom control [9].

The surgical option is the last resort for end-stage ankle OA. Ankle arthrodesis, arthroscopic or open, remains the gold standard surgery for severe symptomatic ankle OA. Total ankle replacement is also a popular surgical option in advanced arthritis [10]. Both types of surgeries with pros and cons, but they can limit strenuous weight activities, especially in athletes.

Through this case, we demonstrate a dramatic symptomatic and functional response of severe ankle osteoarthritis secondary to congenital clubfeet following two doses of expanded autologous mesenchymal stem cells (MSCs) combined with platelet-rich plasma (PRP).

Case Report

A seventy-one-year-old male property investor. His past medical history with bilateral congenital clubfeet with the left foot more affected and pointed backward required three corrective surgeries at the age of two through five years old to align the foot in the normal direction, and the left ankle was fused. Other medical histories of Barrett's oesophagus and Low-grade dysplasia were treated with HALO radiofrequency ablation, regular endoscopy, and long-term omeprazole.

He believed the ankle corrective surgery had transformed his life to maintain normal daily activities for a long time. In his mid-forties started to get bilateral ankle discomfort that was managed well with custom orthotics and occasional use of analgesia. He has always been an active sportsman with determination despite the ankles' discomfort; he represented local junior soccer, competitive junior and senior tennis, squash, and table tennis in senior and veterans' international events. He is as well a keen gardener and does a lot of walking.

At the age of sixty-seven in 2017, he started to have increasingly bilateral ankle pain and began to seek medical advice from his family doctor. X-rays of both ankles revealed bilateral significant subtalar and mild talar osteoarthritis (OA); in late 2018, he started to have substantial bilateral ankle pain, which limited his ability to walk for a distance and play sport; thus, he was dependent on NSAIDs. He developed an inversion injury while walking on his right ankle in 2019. He saw an orthopaedic surgeon performing an MRI scan of the right ankle, that showed diffuse full-thickness chondral loss on both sides of the lateral and posterior subtalar joints with hindfoot valgus positioning and ankle joint synovitis (Figure 1a and b). He was treated conservatively as was not keen on any surgical intervention, particularly arthrodesis, as this will limit joints' movement and affect his sports life. His condition progressed in 2020, and he could hardly walk five steps despite regular use of NSAIDs and modified orthotics to stabilize the joint movements. He stopped all sports that he enjoys.

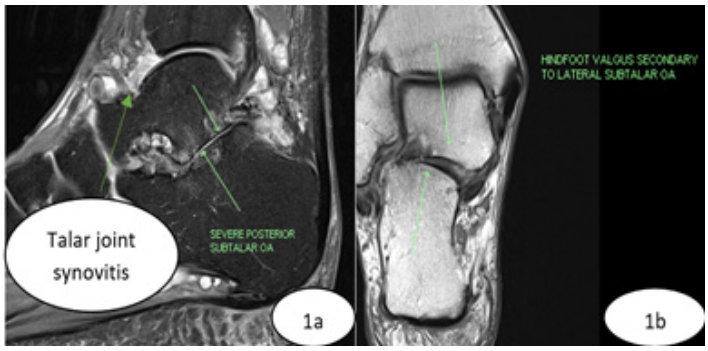

Figure 1: a) and b): MRI of the right ankle shows severe Subtalar OA, talar synovitis, and hindfoot valgus.

The patient elected for experimental autologous expanded mesenchymal stem cells (MSCs) therapy. He had abdominal fat harvesting to get the MSCs for purification, sterilization, and expansion in our specialized laboratory for a few weeks.

Before the MSCs implantation, gross examination of his feet grossly revealed hindfoot valgus with bony swellings related to OA and clubfeet (Figure 2a and b). There was a left foot scar from previous surgeries and mildly limited talar movement with slight right ankle synovitis, but severely limited subtalar movements. His feet X-rays demonstrated severe subtalar and mild talar OA with bilateral joint effusions (Figure 3).

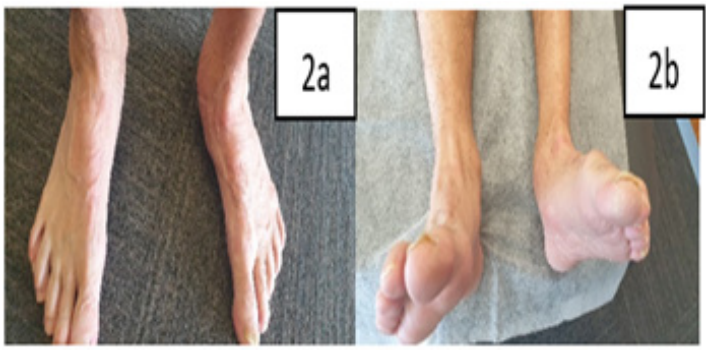

Figure 2: a) and b): shows valgus hind feet with bony changes due to osteoarthritis

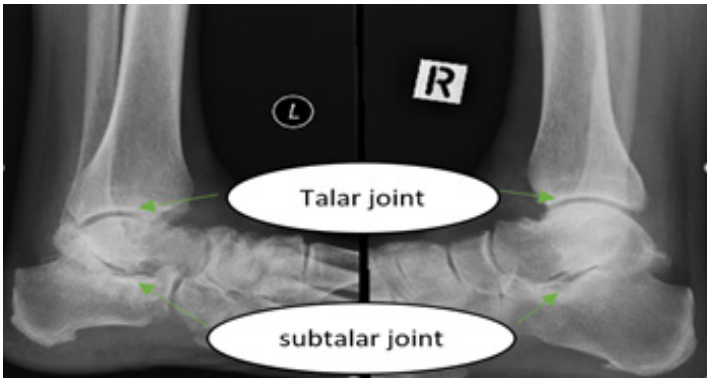

Figure 3: Pre- stem cell therapy x-ray shows bilateral severe osteoarthritis subtalar and mild talar OA.

In March 2021, we implanted the MSCs with a dose of 90 X 10^6 in each ankle. The sample was divided into three syringes. Those were injected into the talar joint medially, the subtalar, sinus tarsi, and ATFL areas. In each syringe was 30 X 10^6 of MSCs in 2 MLS combined with 3 MLS platelet-rich plasma (PRP) to a total of 5MLS.

We prepared the PRP using sterile ACD-A tubes centrifuged it with good plasma separation over eight minutes.

The procedures were done under the aseptic technique and ultrasound guidance (Figure 4a and b). We used ropivacaine 0.25% in the skin to anaesthetize the needle entry using a 25G 1.5 inch needle. No local anaesthetic solution was used in the joints to avoid damaging the MSCs and PRP.

On verbal follow-ups, he reported pain improvement, but he was still unable to walk for a long distance. We saw him five months following the first therapy, a stable condition with minor discomfort; his physical examination revealed no synovitis or tenderness and reasonable movement of the talar joint but a limited subtalar movement. His repeat x-rays did not show any changes in the joint spaces compared to the initial x-ray but no joint effusions.

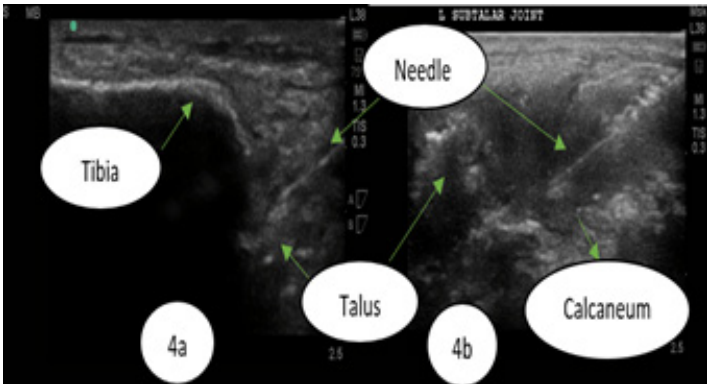

Figure 4: a) and b): shows ultrasound-guided needle trajectory in talar and subtalar joints.

He continued taking NSAIDs. We decided on a booster dose which was done nine months following the first implantations. The amounts and technique used were precisely the same as the first one. We reviewed him three months later; he reported no pain and dramatic improvement of the ankle functions with a return to sports twice a week, and he was able to walk comfortably with confidence. He intends to return to a competitive sport, particularly table tennis, while using rigid supportive braces to enhance recreational activities performance. We proposed further booster doses in the future if needed as we have stored his MSCs at our specialized lab using liquid nitrogen.

Discussion

Advanced Ankle joint OA is hard to treat conservatively with limited options including; physiotherapy, weight reduction, and supportive orthotics. Intra-articular steroid and HA injections are of limited use, and frequent steroid injections might affect the cartilage thickness [6-8]. NSAIDs carry some risks of gastrointestinal bleeding when used for the long term [11]. They can also cause renal and liver impairments, especially when comorbidities like diabetes, hypertension and polypharmacy are used.

Arthrodesis can limit the patient's function, particularly in athletes who require a good joint range of motion. Joint replacement might not be feasible in the mal-aligned ankle, and the probability of success of the implant parts was 94% after five years and 84% after ten years. Revision might be technically challenging [12].

MSC therapy is promising science as it can provide appropriate cellular signals to promote tissue regeneration with a superb anti-inflammatory effect. MSCs are presently being investigated in numerous research facilities and clinical practices to establish efficacy and safety [13,14]. Furthermore, randomized controlled trials implied the optimistic outcome of MSCs in OA management [15].

Our patient had superior clinical and functional responses following the experimental management with combined autologous expanded MSCs combined with PRP. His pain score dramatically improved when he could not walk for a short distance before the MSC therapy. This has transformed his life to return to his beloved sport comfortably. The X-rays finding did not show any progression of the talar and subtalar joint degeneration. Clinical studies showed MSCs slow or stop the progression of OA [16], and similar results were noticed in our private practice while treating many hundreds of cases with MSCs for various joints OA including upper and lower limb large and small joints.

Conclusion

We hypothesize that the use of expanded mesenchymal stem cells combined with platelet-rich plasma has resulted in significant pain control from advanced ankle osteoarthritis secondary to bilateral clubfeet. This therapy improved the patient's quality of life and returned to his beloved sport. We predict MSCs slow the progression of OA. We need to confirm those findings are consistent in broad randomized controlled trials.

Acknowledgment

Thanks to my awesome wife, Zahraa. She supported me with my challenging therapy by helping me with the paperwork and reducing my stress to deal with the evolving regenerative alternative medicine challenges, especially the skepticism of stem cell therapy. Thank you so much, dear Zahraa.

Competing Interest

The author has declared that no competing interests exist.

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