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Case report

Case report: adipose–derived mesenchymal stem cells combined with core decompression in the treatment of early-stage avascular necrosis of the femoral head

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ABSTRACT

Introduction: Core decompression is a well-known modality for treating the early stages of avascular necrosis of the femoral head (AVN), however, several methods have been suggested to augment this procedure and improve the outcomes.

Case report: A 52 male was diagnosed with a stage I AVN of the femoral head and treated with core decompression (CD) and injection of adipose-derived mesenchymal stem cells (AD-MSCs). The MRI showed full healing of the lesion after 3 months with significant clinical and functional improvement.

Discussion: AD-MSCs could have the same capabilities as bone marrow-derived stem cells with many advantages, implantation of AD-MSCs in orthopedics and as an augmentation of core decompression has been tried before, but no clear guidelines nor methods of application are well established in the literature.

Conclusion: Implantation of AD-MSCs with Core decompression could be an effective modality to treat osteonecrosis of the femoral head in pre-collapse stages, however, we need bigger clinical studies to determine the actual effectiveness of this method.

1. Introduction

Avascular necrosis of the femoral head is a condition characterized by the death of the cellular component of the subchondral bone due to a vascular insult ultimately leading to osteoarthritis [1], the lack of blood supply could be the result of many factors: traumatic, genes predisposition, metabolic factors, systemic diseases, drugs and local factors [2,3]. The development mechanism is not clear but the result is replacing the dead bone with a weaker thinner trabecula that could fracture and collapse under stresses [1]. Different Treatment modalities are indicated based on the modified Ficat classification [4,5], in early stages core decompression is supported by the literature as a safe common procedure with a wide range of success, yet it may be augmented with the addition of bone grafting, bone morphogenic protein and Mesenchymal stem cells (MSCs) from adult bone marrow [5,6]. Various applications of MSCs and regenerative medicine has been done in orthopedic practice, bone marrow-derived MSCs (MD-MSCs) is the most studied, however, adipose-derived MSCs show similar properties with less donner morbidity and a less invasive technique [7,8]. This article presents a case of a combination of core decompression and AD-MSCs in the treatment of stage I femoral head osteo necrosis, knowing that we relied on MRI, clinical examination, and the Harris Hip score (HHS) which is a clinical score that provides a functional picture of the hip and the higher the score the better the function [9].

This case report has been reported in accordance with SCARE 2020 standards [10].

2. Case presentation

A 54-year-old Caucasian overweight male with a history of smoking, metabolic syndrome, ischemic heart disease, and a herniated nucleus disc for 4 years that was treated conservatively had a gradual onset of severe low back and right buttock pain that progressed over weeks until the patient was barely able to ambulate even with crutches without any history of traumatic events. He sought his neurosurgeon for treatment, his neurological examination and X-rays were normal, an MRI of the

Abbreviations: CD, Core decompression; ADMSCs, adipose-derived mesenchymal stem cells; MDMSCs, marrow-derivedmesenchymal stem cells; AVN, Avascular necrosis; MSCs, mesenchymal stem cells; HHS, Harris hip score.

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lumbar spine was obtained and he was referred to the pain management clinic as his MRI revealed degenerative irrelevant findings of L1-L2 and L2-L3 but importantly an increased signal of the right femoral head on the T2 and STIR weighted images (Fig. 1).

On 30-5-2021 he was referred to us by the neurosurgeon, and avascular necrosis of the femoral head was suspected. Clinical examination revealed right-sided hip pain along the groin with an antalgic gait and decreased function and inability to do daily activities. Tender range of motion where internal rotation and flexion were restricted, his HHS was 42, and examination of the remaining musculoskeletal system was unremarkable, hip X-rays were normal while MRI confirmed the diagnosis of FICAT stage I osteonecrosis of the right femoral head which is also a stage 1 AVN of the femoral head based on the ARCO classification with normal X-ray and abnormal MRI [11]. He had no history of blood transfusion, coagulopathy, or steroid use; all the biochemical studies were within normal limits (Fig. 2).

Under spinal anesthesia while using the orthopedic table, core decompression was done with a DHS drill pit (6.5 mm) to drill one hole in the femoral head, bone wax was used to plug the hole and AD MSCs were injected through the bone wax plug. The AD MSCs were prepared by utilizing a LIPOGEMS kit (Fig. 3), liposuction of abdomen fat was done after infiltration of 400 ml of saline and adrenaline (2 μg/ml) into the lower abdomen and then the lipoaspirate was processed using the kit with sterile saline solution to remove contaminants and rinsing and resizing the fat into smaller clusters and filtering it following manufacturer instructions to get 20 ml of LIPOGEMS final product ready to be injected [12].

The patient was dismissed the next day with the protection of weight bearing and allowed the full range of motion of the hip and walking on crutches, oral anti-coagulation medicine was used for three weeks. After 6 weeks the patient was allowed gradual progressive weight bearing and achieved it fully at 8 weeks without crutches. At 6 weeks the patient had mild pain and was pain-free at 10 weeks. At 3 months he had a very mild limp with occasional pain, especially while standing from a seat, and repeated MRI showed healed femoral head with a recession of the lesion, his HHS was 92 (Figs. 4, 5, 6).

3. Discussion

Bone is a living material thus the lack of blood supply leads to the death of cellular components and ultimately necrosis and failure of bone tissue [1], the femoral head is the most common site for aseptic necrosis

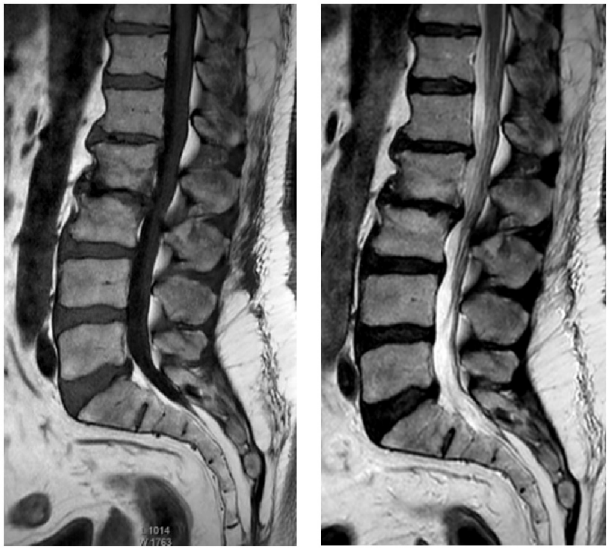

Fig. 1. Sagittal MRI T1 and T2 weighted images of the lumbar spine showing irrelevant findings.

to occur, and atraumatic AVN could happen due to medications use like steroids, systematic diseases like; SLE, autoimmune diseases and could be idiopathic [13].

In our case, the patient had metabolic syndrome and smoking as risk factors though many other risk factors have been recognized in the literature as alcohol overconsumption, hyperlipidemia, radio and chemotherapy, and anything that leads to small vessels blood flow impairment [1].

The natural history of AVN is total hip arthroplasty within 4 years if left untreated so early diagnosis and appropriate treatment are mandatory regarding prognosis [14].

Ficat modified his original classification in 1985, going through five stages from 0 to IV early stages contain 0, I, and II while the late stages are III and IV considering the crescent sign and losing the contour of the femur head as a threshold and luckily for our patient, he was diagnosed in stage I when he was symptomatic with negative X-rays and positive MRI [4].

There is no definitive role for conservative treatment in AVN, in pre-collapse stages preserving the hip joint is possible, yet when the subchondral bone collapse THA is indicated [15].

Core decompression has been the gold standard treatment of choice in the early stages, when the right indication is made it is considered a safe effective procedure [16].

In 1995 Fairbank et al. reported survival of the core decompressed hips in stages I and II after 15 years of follow-up to be 90 % and 66 % respectively [17].

Several methods have been proposed to augment CD, autologous bone grafting, fibular vascularized graft, Bone marrow aspirate, and MSCs implantation [18].

MSCs are multipotent cells, they can differentiate into various mesenchymal cells including osteoblasts [19], and not only have osteogenesis properties but also osteoinduction and immune response-modulating effects that could contribute to the preservation of healthy bone and enhance regeneration [20].

AD MSCs are easier to obtain and while they share many biological features and properties as MD MSCs, considerably larger amounts of MSCs can be harvested without the need for ex-vivo culturing [8].

It is thought that the ischemic environment lowers the number of osteoprogenitor cells in the uninvolved part of the femoral head thus giving the necrotic process an advantage and progress of the lesion due to failure of repair [21].

So, the rationale behind our choice of treatment is that preserving the hip joint is essential at any cost and while CD alone could promote healing, the addition of MSCs could enhance that process ultimately leading to better clinical and functional outcomes, and adipose-derived MSCs preparation is technically easy with low risks and complications and could be reproducible in other centers that don't necessarily have advanced and high technology equipment.

Pak J reported clinical and radiological improvement in two patients after injection of the diseased femoral heads with AD-MSCs aspirate combined with PRP and hyaluronic acid in a scaffold suggesting the possibility of achieving similar outcomes to bone marrow-derived stem cells [21].

Hamid Namazi commented on this paper suggesting a molecular mechanism that might explain the role of AD-MSCs in reproducing bone in AVN of the femoral head [22], however, Hee Joong Kim disagreed with the original author suggesting that the reproduced tissue is fat-like tissue, not bony tissue and the author had misread the MRI [23].

Later on, in 2014 Pak J et al. reported a case of a 43 years old Korean male with early-stage AVN of the femoral head treated with AD-MSCs and PRP injection into the diseased head with a 21-month follow-up and complete resolution of the lesion on MRI and good functional improvement [24].

Lee K et al. explained the reparative potential of human AD-MSCs when transplanted into mice by inducing an increased number of osteoblasts and osteoclasts activity in bone tissue, and concluded that AD-

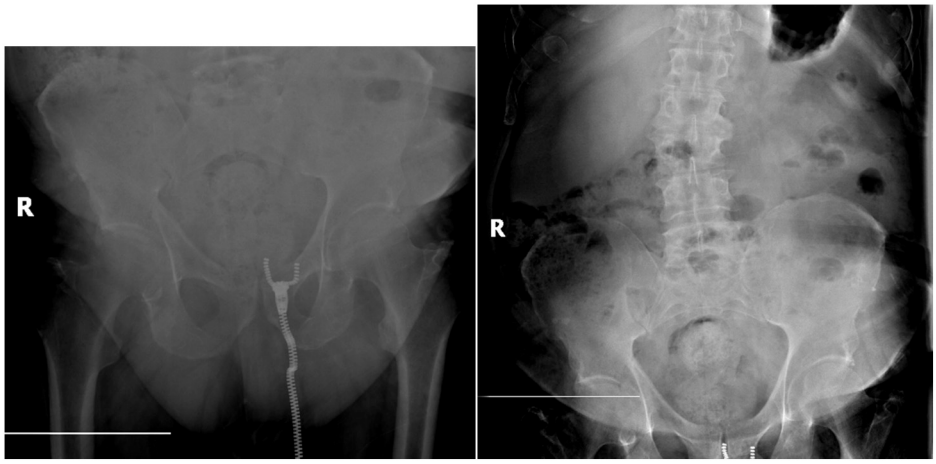

Fig. 2. Plain X-ray of the hips obtained at the start of the patient's complaint with no abnormalities.

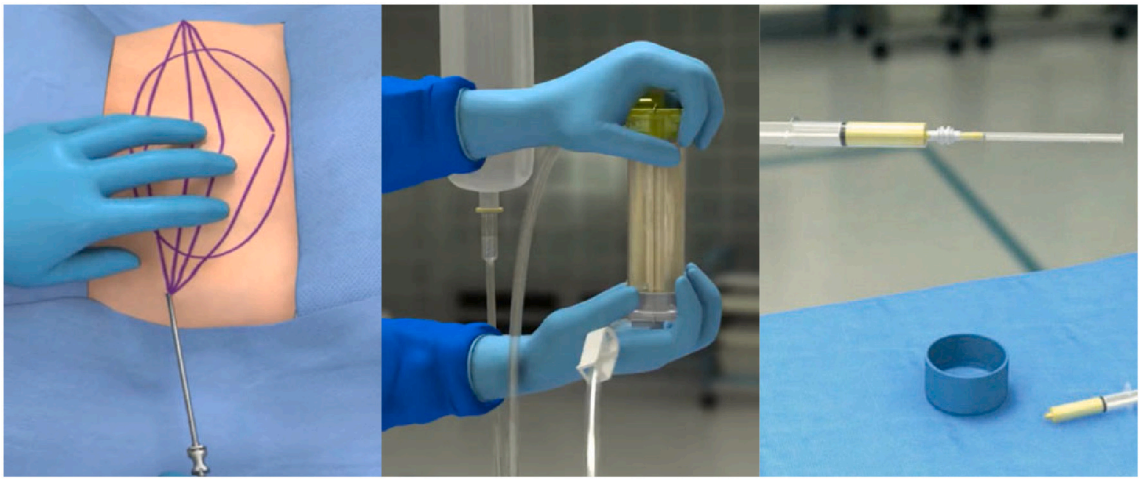

Fig. 3. AD-MSCs preparation starts from liposuction of lower-abdomen fat then processing the aspartate in the kit and infringing the fat and filtering the product into AD-MSCs rich aspirate ready to be injected.

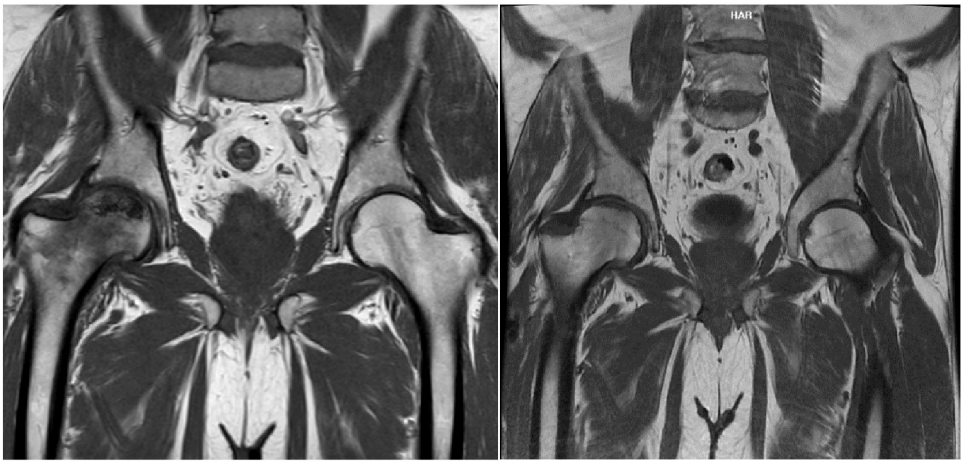

Fig. 4. On the lift T1 MRI weighted coronal image of the hips preoperatively and on the right 3 months postoperatively.

MSCs can be a useful tool in treating osteoporosis and bone repair [25].

It is well-known now that AD-MSCs have equal reparative and differential potentials compared with MD-MSCs with the clear advantages that we discussed earlier regarding harvesting, culturing, and the safety of the intervention [26], however, research is still looking into further details to optimize the treatment methods in bony defects and lesions, Mihaila, S. M et al. demonstrated that by obtaining the appropriate subpopulation of human adipose tissue it is possible to attain the most

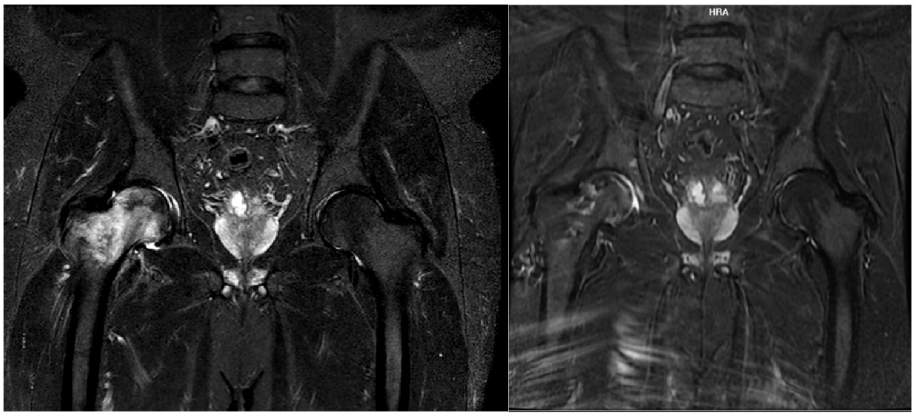

Fig. 5. On the lift STIR MRI weighted coronal image of the hips preoperatively and on the right 3 months postoperatively.

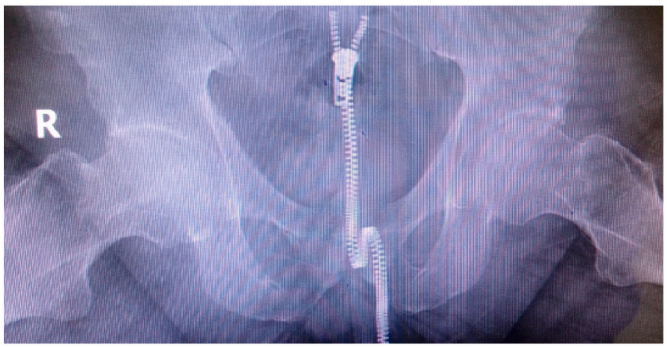

Fig. 6. Follow-up X-ray of the hips 16 months post-surgery.

relevant cell types for the creation of vascularized bone tissue-engineered constructs [27], while Behr, B et al. demonstrated in vitro that the local application of certain growth factors might improve the osteogenesis properties of AD-MSCs [28].

We don't know yet the actual potential of regenerative medicine in orthopedics, whereas many researchers are interested in this field, there are many challenges to overcome like ethical issues, donner morbidity, and possible complications, and we tend to see adipose tissue as a perfectly safe approach to this promising new area of research.

Some limitations we admit are the relatively short follow-up period, though we are still following the patient as he is well-collaborating, also we only relied on MRI and HHS for the evaluation of our treatment outcomes and maybe other clinical and radiographic parameters could have been utilized.

Another limitation is that no biopsy of the regenerated tissue was done to evaluate its nature as the patient refused such an invasive investigation.

4. Conclusion

Core decompression could be an effective modality to treat osteonecrosis of the femoral head in pre-collapse stages, modifications to the technique by implantation of AD-MSCs could improve the outcomes and it is a safe mini-invasive and a relatively easy way to augment the procedure; however, we need bigger clinical studies to determine the actual effectiveness of this method.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

This study was exempted from ethnical approval.

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Author contribution

Doried Diri M.D.: conceptualization, investigation, data curation, writing, editing and reviewing.

Hakam Alasaad M.D.: investigation, data curation, writing, editing and reviewing.

Hussain Muhammed M.D.: investigation, data curation, editing and reviewing.

Jaber Ibrahim M.D. PHD: conceptualization, investigation, data curation, writing, editing.

Guarantor

Doried Diri M.D.

Registration of research studies

N/A.

Declaration of competing interest

The author has no conflicts to disclose.

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