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CASE REPORT

Adipose derived stromal vascular fraction cells therapy in hemophilic arthropathy: A case report

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SUMMARY

Stromal vascular fraction (SVF) is a heterogeneous collection of cells obtained from adipose tissue through lipoaspiration and is an alternative intraarticular treatment option, especially in osteoarthritis (OA). The anti-inflammatory and extracellular tissue repair-stimulating properties of SVF increase its effectiveness in regeneration and repair mechanisms. One of the most common symptoms of hemophilia A and B is hemophilic arthropathy (HA). If HA is not adequately managed initially, patients may require major surgery, including total joint arthroplasty. In a 34-year-old male patient who was treated with intraarticular adipose-derived SVF with the diagnosis of hemophilia B and right grade 4 hemophilic knee arthrosis, clinical and radiological scores showed significant improvement in the 3rd month, 6th month, and 1st year controls after the procedure. Intraarticular adipose-derived SVF treatment should be kept in mind as an effective treatment option with minimal invasiveness and few side effects in HA that does not respond to conservative treatments.

Keywords: Hemophilic arthrosis; intraarticular injection; mesenchymal stem cells; stromal vascular fraction.

Introduction

Stromal vascular fraction (SVF) is a heterogeneous collection of cells (stem cells, progenitor cells, and adult cells) obtained from adipose tissue through lipoaspiration. With the ability of mesenchymal stem cells (MSC) to differentiate into other cells, such as chondrocytes, it appears as an alternative treatment option, especially in osteoarthritis (OA), and in bone and cartilage grafts. The anti-inflammatory and extracellular tissue repair-stimulating properties of SVF increase its effectiveness in regeneration and repair mechanisms.[1,2] One of the most common symptoms of hemophilia A and B is musculoskeletal problems, which are challenging for physicians to treat. If hemophilic arthropathy (HA) is not adequately managed initially, patients may require major surgery, including total joint arthroplasty.

In this case report, we wanted to share our experience of applying SVF in our 34-year-old male patient with a diagnosis of hemophilia B and right grade 4 hemophilic knee arthrosis.

Case Report

A 34-year-old male patient with a diagnosis of hemophilia B was admitted to the pain clinic with symptoms of severe pain in the right knee, limited movement, and difficulty in walking. On physical examination, both knees had a limited range of motion and diffuse crepitation. He was regularly receiving factor replacement for the treatment of hemophilia B. A knee X-ray of the patient was compatible with grade 4 gonarthrosis, and he stated that he did not benefit from previous conventional treatments such as physical therapy and intra-articular injection treatments.

Intra-articular SVF treatment was planned for the patient, and pre-operative preparation was performed by consulting the hematology physician, under whose follow-up he was. An informed consent form was obtained from the patient before the application.

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The patient was placed on the operating table in the supine position under operating room conditions and was monitored. After sterile cleaning and dressing, sedo-analgesia and local anesthesia were applied, and approximately 100 mL of fat was collected from the abdomen using a 3-mm aspiration cannula with prior administration of tumescent solution. The collected fat was placed into sterile disposable 250 mL conical centrifuge tubes. The adipose tissue was washed twice in phosphate-buffered saline (PBS) and digested using collagenase at 37 °C for 30 min with agitation at 5-min intervals.

The suspension was then divided into four 50-mL centrifuge tubes and centrifuged at 500×g for 5 min to collect the SVF as a pellet. The pellet was washed twice with normal saline to remove any residual enzyme and resuspended in PBS. The SVF suspension was filtered through a 100-µm cell strainer and centrifuged at 500×g for 5 min. The supernatant was discarded. The pellet was resuspended in normal saline and filtered through a 40-µm cell strainer. Samples were taken to determine cell quantity, viability, and to culture and characterize the stem cells.

Intra-articular SVF was administered to the right knee under the guidance of fluoroscopic imaging. The procedure was terminated by performing abdominal bandaging, and the patient was followed up in the inpatient ward.

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and six-minute walk distance (6MWD) were used to evaluate clinical effects, including a measure of the patient's subjective assessment of pain, joint mobility, and physical disability. The WOMAC score, 6MWD, and laboratory tests were repeated at 3 and 6 months and 1 year. X-rays (Fig. 1) and magnetic resonance imaging (MRI) were completed at 1 year.

The WOMAC pain scores during walking, using stairs, in bed, sitting or lying, and standing were also recorded. The patient demonstrated a significant reduction in pain from 73.9% at baseline to 50% at 3 months, 28.1% at 6 months, and 14.5% at 1 year. The patient walked an average of 600 metres at baseline and demonstrated a statistically significant improvement to 635 metres at 1-year post-treatment.

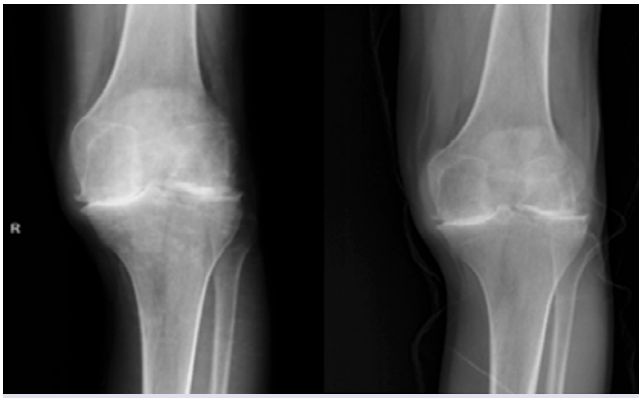

Figure 1. Right knee X-ray image at baseline and 1 year post-injection.

Assessment of cartilage repair using the MRI observation of cartilage repair tissue (MOCART) score indicated considerable cartilage repair at 1 year, with a mean MOCART score of 73.7 out of a maximal score of 100.

Discussion

Adipose tissue is a rich source of cells that can be used in the repair and regeneration of musculoskeletal tissues. SVF is a heterogeneous collection of cells (stem cells, progenitor cells, and adult cells) obtained from adipose tissue by various methods. With the ability of MSCs to differentiate into other cells, such as chondrocytes, it is an alternative treatment option for OA, bone and cartilage injuries, soft tissue damage, and esthetic purposes. SVF's anti-inflammatory and extracellular tissue repair-stimulating properties also increase its effectiveness in regeneration and repair mechanisms.[1–3]

In an animal study investigating the effect of SVF and adipose tissue-derived stem cells (ADSCs) on diabetic chronic wound healing, it was found that SVF and ADSCs improved fibroblast and endothelial cell functioning, regulated gene expression, and promoted skin healing.[2] Adipose tissue is a good reservoir for MSCs because it is rich in capillaries, which are thought to be located in the perivascular region in connection with blood vessels. MSCs derived from adipose tissue are referred to as ADSCs. ADSCs are an alternative to bone marrow-derived mesenchymal stem cells because they are easily isolated under sedation and local anesthesia and are cheaper.[4]

The generally accepted practical application is the production of SVF from adipose tissue taken from the abdominal region by lipoaspiration. Autologous treatments using adipose tissue-generated SVF (AD-SVFs)

and MSCs (AD-MSCs) require careful preparation of harvested adipose tissue. However, there is no standardized protocol.[5] SVF is usually administered together with platelet-rich plasma (PRP) by intra-articular injection. The advantages of using PRP as an adjuvant are the acceleration of stem cell proliferation with the release of growth factors and its effect of increasing the attachment of cells to the damaged cartilage area.[6,7]

In a study, the MSC isolation method, which combines enzymatic digestion with mechanical degradation, was considered a standardized and easy-to-use method to achieve significantly higher MSC yields (by increasing the surface area of adipose tissue) compared with traditional enzymatic isolation protocols. With this method, it was determined that the amount of adipose tissue required to reach a sufficient amount of MSCs and the in vitro expansion time decreased. It did not require increasing amounts of collagenase, and the MSC yield increased threefold without impairing the viability or differentiation of MSCs.[1]

Yokota et al.[8] compared ADSCs and uncultured SVF with intra-articular injection in the treatment of knee osteoarthritis. It was found that although the clinical response was similar in both groups, ADSCs outperformed SVF in reducing symptoms and early pain with less comorbidity.

In another study in which six patients with hip osteoarthritis were treated with intra-articular injections of autologous fat-derived MSCs and followed up for 6 months, MSCs were evaluated as an effective treatment method.[9]

In a review analyzing the long-term effects of MSC treatments in intra-articular joint injections, stem cell studies performed on patients with osteoarthritis and chondral defects were evaluated. Ankle (n=61) and hip (n=5) joints were treated intra-articularly. In some studies in this review, it was stated that radiologic improvement was observed, and intra-articular stem cell therapy was an effective and generally safe treatment option.[10]

Hemophilia is a sex-linked recessive inherited bleeding disorder. Deficiency of coagulation factor VIII causes hemophilia A, and deficiency of factor IX causes hemophilia B. Disease prevention and management require an intravenous infusion of the missing factor. One of the most common symptoms of hemophilia A and B is musculoskeletal problems. Multi-joint joint degeneration (hemophilic arthropathy) secondary to recurrent hemarthroses is challenging for physicians to treat.[11] If hemophilic arthropathy is not adequately managed initially, patients may require major surgery, including total joint arthroplasty.

A thorough understanding of the pathophysiology, diagnosis, and both medical and surgical interventions is critical in establishing an appropriate treatment regimen for these patients. A truly multidisciplinary approach is required for patients with HA, including hematology, orthopedics, and physical therapy and rehabilitation departments.

Insufficient studies have evaluated the effectiveness of MSC treatment in HA. However, experimental studies published to date show promise for HA treatment.[12]

We aimed to share the positive clinical response and experience we received with adipose-derived SVF treatment in our case with HA and to contribute to the literature.

Conclusion

Multi-joint joint degeneration (hemophilic arthropathy) secondary to recurrent hemarthroses is frequently seen in patients with hemophilia. This situation causes both pain and limitation of movement, leading to a deterioration in the quality of life. Intra-articular ADSC/SVF treatment should be approached with a multidisciplinary perspective in the treatment of HA that does not respond to conservative treatment methods. It should be considered a minimally invasive and effective treatment option with few adverse effects.

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