ABSTRACT

Aim: The following case has the objective to show how mesenchymal cells from the same patient, are a better treatment option for osteoarthritis by means of decreasing pain and increasing functionality.

Case: Male patient, 64 with history of diabetes and osteoporosis. Patient refers pain at the base of his right thumb for the last three years. Pain causes dysfunctionality of right hand, patient unable to write and shake hands.

Findings and Treatment: Patient is unable to shake hands, patient refers pain when pressure is applied to the carpometacarpal joint, as well as when trying to press the thumb and the index finger together, and patient cannot hold this position for a long time. X-ray examination reveals arthrosis of the carpometacarpal joint, the articular space has been reduced to 2 mm, osteophyte deformity of trapezium and metacarpal bone. The patient is prepared for mesenchymal cell aspiration from the anterior iliac crest and to receive the cells as treatment for osteoarthritis.

Conclusion: Treatment osteoarthritis with autologous mesenchymal stem cells, is a very effective therapeutic alternative. With this approach patient can avoid surgery and greatly improve articular function and diminish pain.

Keywords
Adult stem cells, Mesenchymal, Autologous, Osteoarthritis.

Introduction
Articular cartilage is an avascular tissue, with chondrocytes as the main cell type. Chondrocytes equilibrate synthesis and degradation of the extracellular matrix macromolecules, such as type II collagen and proteoglycans [1], exerting regulation at the structural and functional level of the cartilage [2].

Osteoarthritis is a joint degenerative disease, which is characterized by progressive loss of articular cartilage. As a consequence, the patient experiments severe pain and finally disability [1]. The development of osteoarthritis is characterized by protein cleavage of type II collagen fibers and proteoglycans. The enzymes responsible of this process are matrix metalloproteinases and aggrecanases. Proteolysis results in cartilage altered mechanical properties [1].

Chondrocytes are surrounded by the pericellular matrix that together forms the functional unit known as the chondron. The main component of the pericellular matrix is type VI collagen [1]. The chondron is remodelled during osteoarthritis. This remodelling includes swelling and distension of the microenvironment, leading to chondrocyte proliferation to occupy the expanding microenvironment, a decline in pericellular fibrillar collagens, and upregulation of matrix metalloproteinase and aggrecanases [3].

Cartilage self-renewal potential is limited due to the absence of a
dense population of progenitor cells [4]. It has been demonstrated that dysfunction of the cartilage can extend to the subchondral bone and therefore cartilage, exhibits some ability to repair itself, probably as a result of the release of bone marrow-derived stem cells, from the subchondral bone [4]. Considering the pluripotential ability of mesenchymal stem cells, they have been used therapeutically for the purposes of cartilage repair [5].

Arthrosis of the carpometacarpal joint is common in postmenopausal women and requires surgical treatment [6]. Mesenchymal stem cells have been used as donors of connective-tissue progenitors from the anterior and posterior iliac crest [7].

Osteoarthritis is considered a public health problem, it is estimated that 15% of the world’s population over 60 years old suffer from it [8]. In the United States, over 27 million people suffer from osteoarthritis, resulting in a total annual economic burden of over 80 billion dollars [1].

In Mexico, is estimated that 14% of people over 60 years old suffer from osteoarthritis and about 0.4% of the gross domestic product has been used to treat musculoskeletal diseases [9,10].

Due to the high incidence of osteoarthritis worldwide, and the economic burden that it represents, it is very important to use different therapeutic approaches to help patients recover from pain and cartilage dysfunction. In this work we present the use of mesenchymal stem cells from the anterior iliac crest as treatment for osteoarthritis.

Case Report
The following case has the objective to show how mesenchymal cells from the same patient, are a better treatment option for osteoarthritis by means of decreasing pain and increasing functionality.

Male patient, 64 with history of diabetes and osteoporosis. Patient refers pain at the base of his right thumb for the last three years. Pain causes dysfunctionality of right hand, patient unable to write and shake hands.

Evaluation and Treatment
Patient is unable to press his right hand when shaking hands, patient refers pain when pressure is applied to the carpometacarpal joint, as well as when trying to press the thumb and the index finger together, and patient cannot hold this position for a long time.

X-ray examination (Figure 1) reveals arthrosis of the carpometacarpal joint, the articular space has been reduced to 2 mm, osteophyte deformity of trapezium and metacarpal bone.

The patient is prepared for mesenchymal cell aspiration (Figure 2) from the anterior iliac crest. Patient is advised to drink 2 liters of water 6 hours before the procedure.

Figure 1: X-ray examination shows arthrosis of the carpometacarpal joint, the articular space has been reduced to 2 mm, osteophyte deformity of trapezium and metacarpal.

Figure 2: Mesenchymal cell aspiration, upper left panel shows site of injection. Right panels show the BMAC Terumo System, used for aspirate centrifugation. Left bottom panel shows the syringe containing the cells ready to apply to same patient.

The patient is admitted into de OR to undergo sedation under the supervision of an anesthesiologist. To initiate the mesenchymal cell aspiration procedure, patient should be facing up, and the aseptic technique is used in region of the anterior crest. Ropivacaine is
infiltrated; patient is required to be under anesthesia for at least three hours. A two centimeter area on the anterior superior iliac spine is chosen trying to avoid the ligaments and is manually palpated to identify the injection site. A 3mm incision of the skin to canulate with a Jamshidi needle and repeated hammer strokes are performed until the spongy bone is reached. Then, 20 cubic centimeters of bone marrow are aspirated using the BMAC Terumo System kit (according to manufacturer’s instructions) with anticoagulant, up to 60 cubic centimeters can be obtained.

The bone marrow sample is centrifuged at 3,200 rpm for about 14 minutes. The bone marrow sample will be about 9 to 12 ml, which are ready to be injected back to the same patient. Four years after receiving stem cells (Figure 3), osteophytes are no longer seen, articular space is much wider, and apparently there has been remodeling from the subchondral bone. Patient does not refer pain and has regain functionality of his right thumb. Patient is under antiresorptive medication and is under diabetes control.

![Figure 3: X-ray examination shows a 4 year follow up of the patient. Osteophytes are no longer seen, articular space is much wider, and apparently there has been remodeling from the subchondral bone.](image)

Discussion

Traditional therapy for osteoarthritis includes anti inflammatories, hyaluronates and chondroprotective agents. Patients experience loss of function and a lot of pain. Besides from that, patients skip days of work and this disability has a big impact in everyday activities.

Treatment with autologous mesenchymal stem cells offers many advantages to the patient. Is less invasive than any surgery, patient walks back home on the same day of the procedure and is able to initiate rehabilitation. Patient understands that the burden caused by pain medications is gone, that pain itself and loss of function will gradually improve with this kind of therapy.

In the Center for Regenerative Medicine, we are very interested in improving our osteoarthritis treatment, including 3D-bioprinting of molds replacing dysfunctional areas and enriched them with autologous mesenchymal stem cells. This will provide a much efficient therapeutic approach to osteoarthritis.

Conclusion

Treatment of degenerative osteoarthritis with mesenchymal stem cells, is a very effective therapeutic alternative. With this approach patient can avoid surgery and greatly improve articular function and diminish pain.

References

1. Wilusz RE, Zauscher S, Guilak F. Micromechanical mapping of early osteoarthritic changes in the pericellular matrix of human articular cartilage. Osteoarthritis and cartilage. 2013; 21: 895-1903.
2. Musumeci G, Castrogiovanni P, Trovato FM, et al. Biomarkers of chondrocyte apoptosis and autophagy in osteoarthritis. Int J of Mol Sci. 2015; 16: 20560-20575.
3. Poole AC. Articular cartilage chondrons: form, function and failure. J Anat. 1997; 191:1-13.
4. Mazor M, Lespessailles E, Coursier R, et al. Mesenchymal stem-cell potential in cartilage repair: an update. J. Cell. Mol. Med. 2014; 18: 2340-2350.
5. Xin T, Greco V, Myung P. Hardwiring stem cell communication through tissue structure. Cell. 2016; 164: 1212-1225.
6. Armstrong AL, Hunter JB, Davis TR. The prevalence of degenerative arthritis of the base of the thumb in post-menopausal women. J Hand Surg Br. 1994; 19: 340-341.
7. Pierini M, Di Bella C, Dozza B, et al. The posterior iliac crest outperforms the anterior iliac crest when obtaining mesenchymal stem cells from bone marrow. Bone Joint Surg Am. 2013; 19: 1101-1107.
8. Wieland HA, Michaelis M, Kischbaum BJ, et al. Osteoarthritis—un treatable disease? Nat Rev Drug Discov. 2005; 4: 331-344.
9. De Pavia-Mota, Larios.-González MG, Briceño-Cortés M. 2005. Manejo de la osteoarthritis. Med. Fam. 2005; 7: 93-98.
10. March LM, Bachmeir CJ. 1997. Economics of osteoarthritis. A global perspective. Baillieres Clin Rheumatol. 1997; 11: 817-834.