

Case Report

New Trends in Treatment of Osteoarthritis: “From Cells to Metal”. A Case Report of Simultaneous Different Approach to Bilateral Hip Osteoarthritis

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Citation: De Caro F, Russo A, Cortina G, Collarile M, Condello V, et al. (2019) New Trends in Treatment of Osteoarthritis: “From Cells to Metal”. A Case Report of Simultaneous Different Approach to Bilateral Hip Osteoarthritis. Ann Case Report 11: 247. DOI: 10.29011/2574-7754/100247

Received Date: 15 August, 2019; **Accepted Date:** 04 September, 2019; **Published Date:** 09 September, 2019

Introduction

Osteoarthritis (OA) is one of the most common sources of pain and disability worldwide. Although it can potentially affect any type of joint, it typically involves hip and knee. Nowadays there is a remarkable demographic change towards a more elderly population [1] and this has led to a dramatic increase of prosthetic implants [2,3]. Furthermore, the number of total joint arthroplasty has increased even in younger patient (< 65 years of age) and this could lead to enormous repercussions on health costs, in terms of periprosthetic infection, aseptic mechanical failure and wear of prosthetic implants that can lead to revision surgery [4], considerably more frequent in younger patients [5].

In this sense a valid therapeutic option, useful at least to alleviate pain and reduce functional disability, could be infiltrative therapy. In the current state of the art there are several infiltrative options like hyaluronic acid, Platelet-Rich Plasma (PRP) and Mesenchymal Stem Cells injections [6]. Each of these techniques have shown beneficial effects on pain relief and recovery of an acceptable Range of Motion (ROM) [6-9]. The main objective is not recover from OA but delaying the implantation of a prosthesis as much as possible. A recent and interesting therapeutic option

in the conservative treatment of OA is the use of Peripheral Blood Mononuclear Cells (PBMCs). Several studies have already highlighted the ability of tissue regeneration of monocytes given their ability to differentiate towards different mesenchymal cell lines such as osteoblast or chondroblast cells [10,11].

Case Report

A 59 years old, very active female, come to our attention in our outpatient clinic for a bilateral hip pain. On the right side she reported high impairment, with limping after a short walk. On the left side she referred a continuous pain with a slight limitation of the Range of Movement (ROM) that was clinically painful only at maximum degrees of passive motion. At the x-rays she reported Tonnis grade 2 osteoarthritis on the right side and Tonnis grade 1 on the left side (Figure 1). She had already done physical therapy, shock wave therapy and pharmacological treatment with NSAID without resolution of the symptoms and ROM limitation on both sides. Since clinically she was less painful on the left side, we decided to treat her with a total hip arthroplasty on the right side (Figure 2) and a percutaneous x-ray guided injection of monocytes (MonoCytes TissYou Biological Company) in the left hip.

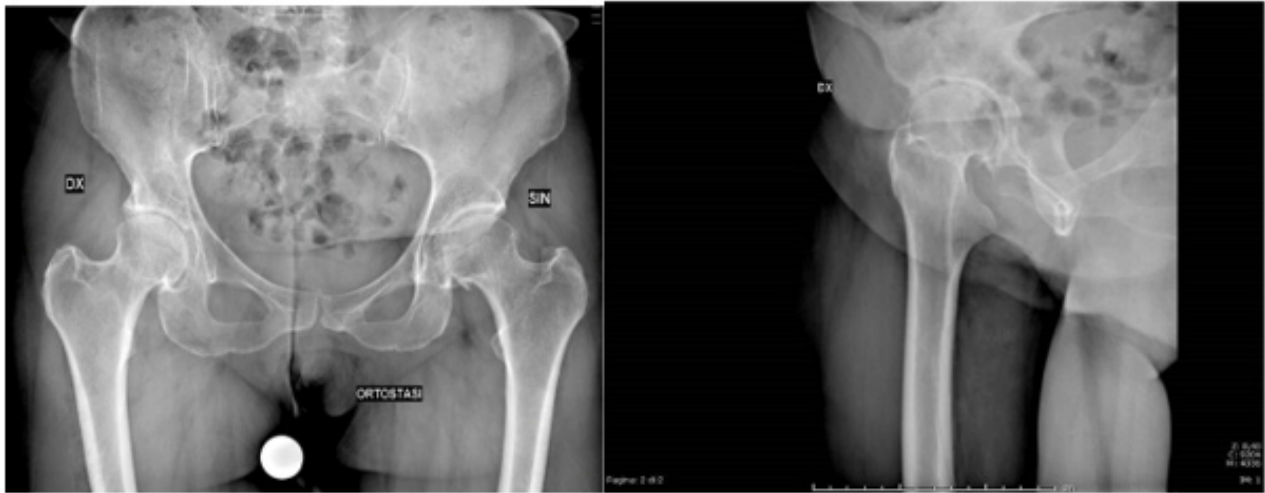


Figure 1: Pre-operative x-ray. (A) AP pre-op view. (B) Lequesne pre-op view of the right hip.

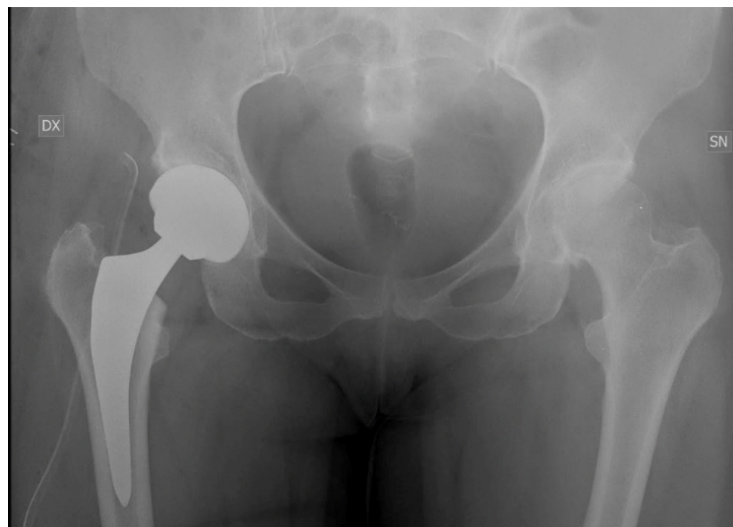


Figure 2: THA post-op control.

We wanted to evaluate the results of the MonoCytes injection, though the patient compiled clinical (HHOS and HHS) and Quality of Life (SF12) questionnaires pre-op and at 2 months follow up for the left hip, the one treated by injection. HHOS pre-operative was 71,3% while the post-operative HHOS was 91,3% at two months' follow-up. The HHS pre-operative was 70,65% and the two months post-operative HHS was 79%.

An increase also of the SF12 was found at 2 months' follow-up (pre-op SF-12: PSC 24,25 and MCS 42,16; post op SF-12 PCS 47,84 and MCS 59,93). PROM of the left hip is complete and pain free. PROM on the right side was 100° of hip flexion, 30° of internal rotation and 45° external rotations, 40° of abduction and 20° of adduction. The patient reported muscle hypotrophy on the right

side, compatible with normal outcome of total hip replacement at 2-month post-op. The patient is happy and very satisfied of the procedure, stating she would repeat it in the future.

Procedure

The procedure is easy and reproducible, consisting in four standardized steps. It is not necessary to undergo the procedure in the operating room. In this case, since the patient was operated contra laterally for a total hip replacement, we decided to undergo the procedure in the operating room at the same moment. The first step consists of a withdrawal of 80-120 ml of peripheral blood in a 60 ml syringe with 5ml of ACD-A or 1ml of heparin sodium 5000 UI/ml. The second step is the processing of the withdrawal through

a closed sterile kit: the entire blood sample is injected inside the first upper bag of the system. The filter circuit is then activated by opening the clamps. In a few minutes all the blood flows through the filter. The scrap is deposited into the second lower bag while the cells are trapped inside the membrane.

Filtration occurs by gravity. No centrifugation or other action, that might alter or stress out the cells, is needed. Monocytes technology is able to select blood cells in a size-dependent fashion. Mononuclear cells with regenerative potential, after obstructive-trapping, are recovered with a gentle basckwash. This occurs in the third step of the procedure. The lower and upper clamps must be closed to exclude the filter circuit. The side clamp is opened. 10 ml of sterile saline solution are injected trough the lower side door: the first 2-3 ml of sterile saline solution must be pushed in a very strong way and the remaining 7-8 ml with extreme slowness.

Once the filter wash operation is finished, retrieve the contents from the collection bag with a new syringe. The fourth and last step of this procedure is the infiltration of the joint, or tendon that needs to be treated. In this case, we injected under fluoroscopy the left hip. The MonoCytes kit is already available on the market. All the assembled components are manufactured according to quality systems conform to ISO standards 9001:2008 and ISO 13485:2003 and the 94/42/EEC.

Discussion

The treatment of cartilage pathologies and osteoarthritis is one of surgeons most compelling challenges. The term orthobiology is becoming very common in the orthopaedic field. Different injective regenerative treatments have been used in the last years such as PRP and adipose derived stem cells. Recently a new focus on peripheral blood cells and their regenerative properties has enlightened between surgeons. Krupps in 1972 confirms us what Cohnheim et al described for the first time in 1867: peripheral blood monocytes participate in the normal tissue renewal of various organs [12]. The monocytes/macrophages and lymphocyte exert a crucial role in arterio-arterial collateral growth. They promote vascular growth through paracrine mechanisms, including extracellular matrix remodelling, endothelial progenitor cell recruitment, trophic support for neo-endothelium and finally, the promotion of de novo arteriogenesis [13].

Macrophages can be either pro-inflammatory (M1 activation) or anti-inflammatory (M2 activation) depending on the micro-environment stimuli, as the same happen for some lymphocytes, moreover an anti- dogma of circulating monocytes as multipotent progenitors has been investigated by Seta et al. [10]. More recent papers describe the chondrogenic potential of the peripheral blood mononuclear cells [14,15]. Histologic and Magnetic Resonance Imaging (MRI) evaluation of articular cartilage regeneration in patients with chondral lesions treated by arthroscopic subchondral

drilling followed by postoperative intra-articular injections of Hyaluronic Acid (HA) with and without Peripheral Blood Stem Cells (PBSC) has been completed in a randomized study by Saw et al. [16]. The results of this randomized controlled trial showed a significant statistical improvement in histologic and MRI scores at two years' follow-up in the 25 patients that underwent the PBSC injection.

In our case report, the patient is, at short term follow-up, very happy about the injection. She has no pain during mobilizations of the injected hip. She moreover reported an increase of the clinical and quality of life questionnaires at two months' follow-up. No adverse event occurred right after injection or during follow-up. Results might be slightly affected by the patient undergoing total hip replacement on the contralateral hip. More studies, randomized controlled trials, are for sure required to certify the efficacy and safety of this easy, reproducible and promising nonsurgical technique.

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