Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jcot

Case report

Leukocyte-poor platelet-rich plasma to treat degenerative meniscal tear: A case report

J.P. Betancourt^a, W.D. Murrell^{b,c,*}^a Department of Internal Medicine, University of Puerto Rico, San Juan, PR, USA^b Dr. Humeira Badsha Medical Center, Dubai, United Arab Emirates^c Orthopaedics, Rehabilitation, and Podiatry Department, Ft. Belvoir Community Hospital, Ft. Belvoir, VA, USA

ARTICLE INFO

Article history:

Received 14 April 2016

Received in revised form

1 May 2016

Accepted 5 May 2016

Available online 22 June 2016

Keywords:

Leukocyte-poor

Platelet-rich plasma

Meniscus

Knee

Osteoarthritis

ABSTRACT

A traumatic and/or degenerative meniscus lesion is thought to be a clinical manifestation of early-onset osteoarthritis (OA), which is a chronic progressive condition that can cause substantial pain and disability. Platelet-rich plasma (PRP) is an emerging treatment option that has been reported to improve healing. Here, we present a case of a 29-year-old woman, with left anterior and medial knee pain, without history of trauma or injury. The patient was managed with leukocyte-poor PRP injections derived from her peripheral blood with high concentrations of platelets, platelet-derived growth factors, and bioactive proteins, with a total follow-up of 30 months. Post-treatment patient was evaluated at every follow-up for improvement using three independent measures, VAS, GROG, and KOOS. There was considerable improvement in the pain symptoms from baseline (VAS: 70 mm; GROG: n/a; and KOOS: 39) to 30 months (VAS: 40 mm; GROG: 5; and KOOS: 63.1) indicating that PRP injections can serve as therapeutic intervention for treatment of pain associated with early onset of OA. To further validate these results, more longitudinal and evidence-based studies are recommended, which may further guide the clinicians to manage early-onset OA with PRP.

© 2016

1. Introduction

The menisci, attached between the lateral and medial articular surface of the femur and tibia, are two wedge-shaped, semicircular, fibrocartilaginous structures that provide shock absorption and load transmission during dynamic movements by having an innate resistance to compression, tension, and shear forces.¹ A traumatic meniscus lesion is thought to be

a clinical manifestation of early-onset osteoarthritis (OA) since they have been shown to lead to fibrocartilage loss and eventual joint space narrowing.² The use of magnetic resonance (MR) imaging increases the ability to evaluate suspected meniscal tears, and the severity of the meniscal tear was assessed in terms of grades (0–III). This grading was given based on the MR images³ (Fig. 1). OA itself is a chronic progressive condition that affects 13.9% of adults aged ≥25 years, 33.6% of adults, and a total of 27 million adults in the

* Corresponding author at: Dr. Humeira Badsha Medical Center, Dubai, United Arab Emirates. Tel.: +971 508921587; fax: +1 8779943500.
E-mail address: doctormurrell@gmail.com (W.D. Murrell).

<http://dx.doi.org/10.1016/j.jcot.2016.05.002>

0976-5662/© 2016

Fig. 1 – Meniscal tear classification.⁶

United States with its prevalence increasing with age.⁴ OA has multiple manifestations such as osteophyte and subchondral cyst formation, loss of joint cartilage with associated joint space narrowing, synovial inflammation, and sclerosis of subchondral bone and radiographic manifestations. Additionally, clinical complaints of pain, associated neuropathy, crepitus, and mechanical symptoms such as knee joint “locking”, or “lagging” during dynamic movement.^{1,2}

Although multiple conservative and surgical modalities exist to combat OA symptoms, their efficacy is limited mostly to short-term improvement with minimal to no impact on the natural progression of the disease, with the exception of joint replacement, which effectively cures the disease by replacing the entire joint itself, but with great risk and at a high financial cost.³ The aging, baby-boomer population is expected to place a higher cost burden on existing health care systems and as such more treatment options have emerged to improve patient symptoms and functional outcomes. One emerging option is leukocyte-poor platelet-rich plasma injections (LP-PRP), which have been reported to improve wound and bone healing.⁵ PRP injections are autologous, derived from the patient's peripheral blood with high concentrations of platelets, platelet-derived growth factors and bioactive proteins such as platelet-derived growth factor (PDGF) that influence healing on muscle, tendons, ligament, and bone.⁶ Our purpose is to document significant improvement in validated-patient reported outcomes in a patient with grade 3a medial meniscus rupture with a total follow-up of 30 months following LP-PRP injection.

2. Case report

JN, a 29-year-old female with an unremarkable past medical history, was referred for a secondary injection after incomplete pain relief after a first series with hyaluronic acid derivative. She defined a left anterior and medial knee pain since 3 months before evaluation, without history of trauma or known mechanism of injury that has worsened since initial injection. Pain is described as sharp and intermittent with a Visual Analog Scale (VAS) Pain scale of 70.00 mm and a Knee Injury and Osteoarthritis Outcome Score (KOOS) of 39. She described a non-painful clicking as her only mechanical symptom, with pain being generated throughout ambulation, while running, transferring weight from chair, and squatting. Also, it should be mentioned that JN works as a flight attendant, and the very nature of her job requires that she stands and walks for very long periods of time. At the time of case study, the patient status was post two right meniscus debridements, the last, May 2005 on her right knee and her only medication was an oral contraceptive. She was married and self-described athletic with no pertinent family history of OA.

On initial examination, patient's left knee was without effusion or muscle strength deficit, but had palpable tenderness in the pes anserine region. Her patella had normal glide and tilt and her stability tests were normal. Her range of motion on her left knee was between 0° and 130°, which was diminished in comparison to her right knee (0°–145°). A McMurray test reproduced pain in her posteromedial left knee.

Magnetic Resonance Imaging (MRI) of the left knee revealed a grade 3a medial meniscus tear (Fig. 2).³ Plain right posterior-anterior and lateral radiographs showed narrowing of medial tibiofemoral compartment, and posterior facial compartment. The patient was assessed as having early-onset OA in bilateral knee, a left knee meniscal tear with concurrent synovitis and chondromalacia. She did not wish to undergo surgery nor did she meet indications for surgical treatment by her treating orthopedic surgeon, at this time she was scheduled for LP-PRP injection 4 days later with informed consent.

Afterwards, 120 cc of whole blood was taken from the patient and placed in 180 cc closed angel blood separator system with 12 cc ADCA citrate. This was then processed with the counterweighted angel centrifuge for 15 min at 3200 rpm. The platelet-poor plasma (PPP) is automatically transferred into the PPP compartment, and then the desired buffy coat is separated and was placed into a 20 cc syringe by way of a different portal after being optically separated on 2% hemoglobin setting to limit red cells and white blood cells (Angel Blood Separator-Cytomedix, Maryland, USA).

The left lateral knee was anesthetized with 10 cc, 7.5 mg/ml (0.75%) ropivacaine (AstraZeneca, London, UK), given intra-articularly. Ultrasound-guided with linear probe (Acuson X300-Seimens AG, Munich, Germany), LP-PRP was then injected intra-articularly, that would be activated following contact with free ends of articular collagen found in a joint that has osteoarthritis. The patient tolerated the procedure and was given outpatient ambulatory clinic follow-up.

The patient follow-up was evaluated using three different and independent scoring outcomes used to objectively

Fig. 2 – Magnetic resonance imaging of knee: pre- and post-treatment.

measure patient progress; these were the Global Rating of Change (GROC: 0 (about the same) to –7 (a very great deal worse) and 1 (a tiny bit better) to 7 (a very great deal better), worse and better score, respectively), VAS and Knee injury and

Osteoarthritis Outcome Score (KOOS, normalized score: 100 indicating no symptoms and 0 indicating extreme symptoms). These measures accurately reflect patient improvement across follow-up evaluations, with consistently better outcomes throughout the follow-up period when compared to baseline (Table 1). The patient tolerated the procedure well and reported only mild joint swelling and pain during initial follow-up that dissipated after few follow-up evaluations.

Table 1 – GROC, VAS, and KOOS scores before and after PRP (30 months' follow-up).

	GROC ^a	VAS ^b (mm)	KOOS ^c
Pre-PRP	n/a	70.00	39
Post-PRP			
7 weeks	7	25.00	81.9
12 weeks	7	25.00	66.9
6 months	7	20.00	67.8
14 months	7	30.00	74.1
25 months	6	35.00	69.1
30 months	5	40.00	63.1

Pre-PRP, pre-platelet-rich plasma; GROC, Global Rating of Change; VAS, Visual Analogue Scale; KOOS, Knee injury and Osteoarthritis Outcome Score.

^a GROC scales ask that a person assess his or her current health status, recall that status at a previous time-point, and then calculate the difference between the two. The magnitude of this difference is then scored on a numerical or Visual Analogue Scale. Such scales have been recommended for use as a core outcome measure for chronic pain trials.

^b VAS: A horizontal line (100 mm in length) the patient marks on the line the point that they feel represents their perception of their current state of pain.

^c KOOS: KOOS consists of 5 subscales; pain, other symptoms, function in daily living (ADL), function in sport and recreation (Sport/Rec) and knee-related quality of life QOL. Standardized answer options are given (5 Likert boxes) and each question gets a score from 0 to 4. A normalized score (100 indicating no symptoms and 0 indicating extreme symptoms) is calculated for each subscale. The result can be plotted as an outcome profile.

3. Discussion

A variety of epidemiological factors such as age, gender, obesity, heavy physical activity, and trauma have been associated with an increased risk for developing OA.¹ Given rising healthcare costs, nonsurgical management is preferred over the permanent treatment of joint replacement, especially in the younger population. Oral NSAIDs, intra-articular corticosteroid or hyaluronic acid (HA) injections, and activity modification are among the many treatment modalities being studied in efficacy for lifestyle improvement, and certified pain resolution for OA.⁷ The reason behind PRP injections stems from the potential activity of growth factors and cytokines contained inside platelet granules (insulin-like growth factor – IGF-1, transforming growth factor – TGF- β , among others) to regulate and facilitate cartilage repair.⁸ A systematic review found that significantly improved patient outcomes were reported with PRP injection, including significant differences between PRP vs placebo or HA injections.⁶ Specifically, a higher neutrophil content in PRP injections, unlike those in our study, has been associated with a greater inflammatory response and delayed wound healing.⁶

All three outcome measures score in our study showed consistent improvement from baseline levels, but seemed to peak between 6 and 14 months follow-up; coincidentally,

multiple studies have also found that statistically significant improvement in outcome measures after PRP administration could not be sustained past 1 year.^{4,9,10} However, systematic reviews have also reported areas of improvement such as the need to document WBC concentration, the type of PRP injection used, presence of an activating agent, longer term follow-up, among others.^{4,7,9}

The question of cost is also a significant concern; however, conservative therapies accepted by this patient had been exhausted, as the hyaluronic acid injections and oral medication no longer relieved pain. The kit used to prepare the LP-PRP cost 140.00 USD, but in comparison to surgical intervention, this is nominal especially in consideration of 30 months of pain relief. It is well known that LP-PRP can be prepared manually in the lab at very low cost, basically the cost of anticoagulant, 5 or 10 cc syringes, and a centrifuge.^{11,12}

The mechanism of symptom relief is largely believed to be the result of microenvironment modification by activation of endogenous mesenchymal stem cells.¹³ Tissue regeneration has also been seen inconsistently experimentally in human subjects, and the mechanism is a result of platelet granule release of a multitude of growth factors, that promote a healing response demonstrated by cellular, matrix proliferation, and ultimately the formation of vascular channels in the injured meniscus.¹⁴

In conclusion, our study documents the clinical efficacy of ultrasound-guided LP-PRP administration using a myriad of validated pain outcome measures (KOOS, VAS, GROG) alongside the longest follow-up (30 months) known to this author. Our findings provide evidence for LP-PRP injections for treatment of pain associated with medial meniscus tear, which is associated with early-onset OA.^{1,2,6} Despite the fact, the number of clinical studies showing significant improvement following PRP injections continue to grow. More longitudinal, evidence-based research is needed in order to better guide future treatment guidelines and validate this regimen as another treatment modality in the fight against OA and rising health care costs.

Conflicts of interest

The authors have none to declare.

Acknowledgement

Jigoo Sison, RN for manuscript data preparation.

REFERENCES

1. Englund M. Meniscal tear – a feature of osteoarthritis. *Acta Orthop Scand Suppl.* 2004;75:1–45.
2. Blanke F, Vavken P, Haenle M, von Wehren L, Pagenstert G, Majewski M. Percutaneous injections of platelet rich plasma for treatment of intrasubstance meniscal lesions. *Muscles Ligaments Tendons J.* 2015;5:162–166.
3. Reicher MA, Hartzman S, Duckwiler GR, Bassett LW, Anderson LJ, Gold RH. Meniscal injuries: detection using MR imaging. *Radiology.* 1986;159:753–757.
4. Lai LP, Stitik TP, Foye PM, Georgy JS, Patibanda V, Chen B. PRP in intra-articular knee injections for OA: American Academy of Physical Medicine and Rehabilitation. *PM&R.* 2015;7:637–648.
5. Davis VL, Abukabda AB, Radio NM, et al. Platelet-rich preparations to improve healing. Part II. Platelet activation and enrichment. Leukocyte inclusion, and other selection criteria. *J Oral Implantol.* 2014;40.
6. Meheux CJ, McCulloch PC, Lintner DM, Varner KE, Harris JD. Efficacy of intra-articular platelet-rich plasma injections in knee osteoarthritis: a systematic review. *Arthroscopy.* 2016;32:495–505.
7. Campbell KA, Saltzman BM, Mascarenhas R, et al. Does intra-articular platelet-rich plasma injection provide clinically superior outcomes compared with other therapies in the treatment of knee osteoarthritis? A systematic review of overlapping meta-analyses. *Arthroscopy.* 2015;31:2213–2221.
8. Saito M, Takahashi KA, Arai Y, et al. Intraarticular administration of platelet-rich plasma with biodegradable gelatin hydrogel microspheres prevents osteoarthritis progression in the rabbit knee. *Clin Exp Rheumatol.* 2009;27:201–207.
9. Ornetti P, Nourissat G, Berenbaum F, et al. Does platelet-rich plasma have a role in the treatment of osteoarthritis? *Jt Bone Spine.* 2016;83:31–36.
10. Duif C, Vogel T, Topcuoglu F, Spyrou G, von Schulze Pellengahr C, Lahner M. Does intraoperative application of leukocyte-poor platelet-rich plasma during arthroscopy for knee degeneration affect postoperative pain, function and quality of life? A 12-month randomized controlled double-blind trial. *Arch Orthop Trauma Surg.* 2015;135:971–977.
11. Bausset O, Giraudo L, Veran J, et al. Formulation and storage of platelet-rich plasma homemade product. *BioRes Open Access.* 2012;1:115–123.
12. Fukaya M, Ito A. A new economic method for preparing platelet-rich plasma. *Plast Reconstr Surg Global Open.* 2014;2:1–7.
13. Murrell WD, Anz AW, Badsha H, Bennett WF, Boykin RE, Caplan AI. Regenerative treatments to enhance orthopedic surgical outcome. *PM&R.* 2015;7:S41–S52.
14. Arnoczky SP. Biologic adjuncts to connective tissue healing. Can we improve Mother Nature's recipe? In: Day AS, ed. *Las Vegas: AANA Specialty Day 2009.* Las Vegas: AAOS; 2009:101–107.