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Case Report

Dynamic Observation of Vascular Regeneration in Femoral Head Necrosis: a 5-Year Follow-Up Case Report

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Abstract

Femoral Head Necrosis (FHN) is an invasive hip disease of skeletal system, which associated with vascular dysfunction. Therefore, vessels regeneration and follow the posterolateral direction are regarded as a potential therapy target for FHN. We report a case of FHN that was treated by successful regeneration of the internal circumflex femoral artery via targeted Lipoaspirate (LPS) infusion and biomechanical support. A 35-year-old man with FHN involved. LPS isolated from the abdominal subcutaneous fat and infuse into the internal circumflex artery approximately seven times at every 1.5 months in both femoral heads. Besides, the porous tantalum rod was grafted after the first LPS infusion on each side. After the 5-year follow-up study, the primary outcomes showed obvious improvement in the number, distribution, and diameter of blood vessels in the ischemic area. In addition, the patient was now able to perform the daily activities; the congestive area increased from 73.4% to 94.2% on the left side and from 0% to 71.8% on the right side. The Harris Hip Score improved from 22 to 91. Multiple LPS infusions via the internal circumflex femoral artery combined with porous tantalum rod grafting offers an alternative treatment option for FHN.

Keywords: Femoral head necrosis; Angiogenesis; Lipoaspirate

Abbreviations

FHN: Femoral Head Necrosis; LPS: Lipoaspirate; HHS: Harris Hip Score; DSA: Digital Subtraction Angiography; BMSCs: Bone Marrow Mesenchymal Stem Cells

Introduction

Femoral Head Necrosis (FHN) is an invasive hip disease with multiple etiologic factors, such as corticosteroid use, alcohol overdoses, suffered trauma, and hemoglobinopathy [1,2]. During the progression of femoral head necrosis, there is a critical decrease in the blood vessel density and an increase in the intraosseous pressure. Although the pathogenic process has not been identified for FHN, femoral head ischemia can lead to the necrosis of bone tissues, and the resulting collapse of the necrotic segment has been reported [3]. Much research has been devoted to improving angiogenesis and avoiding this collapse [4]. More recently, an increasing number of pre-clinical and clinical studies have reported the limited efficacy of core decompression and mechanical support therapy. Consequently, the use of core decompression and mechanical support therapy has been increasingly debated [5]. Simultaneously, stem cell therapy has been proposed as an appropriate treatment for FHN. A systematic review of pre-clinical studies reveals that the use of stem cells containing uniformly improved osteogenesis and angiogenesis. In clinical studies, the effect of stem cells treatment showed significant improvements in patient-reported outcomes. Unfortunately, hip survivorship was not affected [6].Our team has reported on a combination treatment of biomechanical support and targeted intra-arterial infusion of stem cells [7]. Patients in that previous study received only one stem cell infusion, which was too limited to investigate the progression of tissue regeneration and angiogenesis. In this study, we report a case of FHN treated by multiple infusions of Lipoaspirates (LPSs) in combination with mechanical support therapy provided by implantation of a porous tantalum rod graft.

Case Presentation

History

The patient was a 35-year-old male who worked as a manager and experienced idiopathic deafness in May 2000. Hip joint dysmotility onset gradually more than one year after he began glucocorticoid treatment for the deafness. Conservative therapies, such as physical treatment and medical treatment, did not provide a satisfying curative effect. The patient characterized the bilateral pain of the hips as having intensified to the extent that he could not put on socks by himself, walk for several blocks, or sit for one hour.

Clinical manifestation

The physical examination showed a Harris Hip Score (HHS) of 22. X-ray examination of the femoral head reported heterogeneity

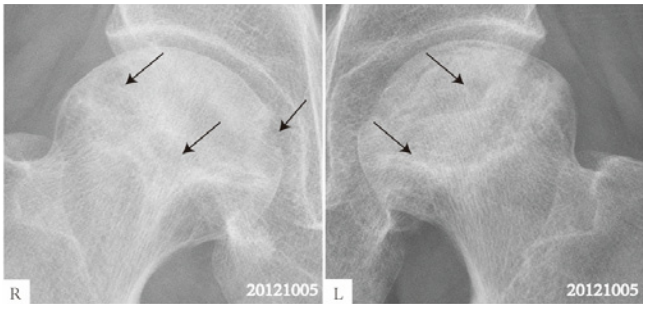

Figure 1: X-ray detection of hip joints before treatment. The arrows show the pathological area.

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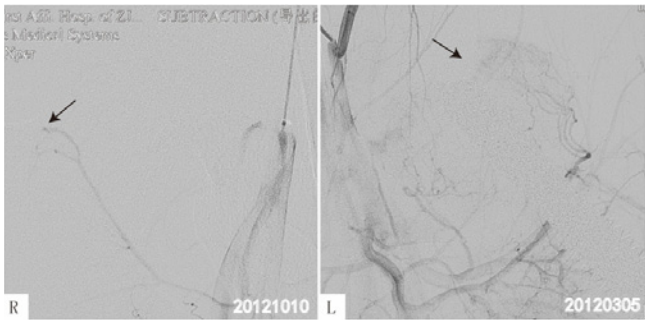

Figure 2: DSA images show the vessels of both sides femoral head before treatment. The arrows show the ischemic area.

of necrotic tissue density, sclerosis, and cyst formation (Figure 1). In addition, examination of the internal circumflex femoral artery found a weakly positive artery in the right-side femoral head and no severe defects of either the superior retinacular artery or the inferior retinacular artery in the left side (Figure 2).

Therapy

A treatment protocol was established after discussing it with the patient and obtaining informed consent. The LPSs were isolated from the patient's abdominal subcutaneous fat. Before injection, the LPSs were cultured for several days in vitro until the cell count exceeded 10^7. The LPS infusion (10mL) was administered via the internal circumflex femoral artery using Digital Subtraction Angiography (DSA) technology. Subsequently, mechanical support was provided by grafting porous tantalum rods bilaterally to the hips, which our group had demonstrated previously [7,8]. The tantalum rods were 10mm in diameter and 90mm long, and the two sides were grafted one month apart. Due to the perceived beneficial effects, the patient received further LPS infusion six times, approximately at every 1.5 months, from October 2012 to August 2014. The patient delayed treatment twice for personal reasons. The treatment effect was assessed by Digital Subtraction Angiography (DSA) detection, X-ray evaluation, and Harris Hip Score. The angiography results were quantitatively analyzed using Image J software (NIH, USA) to identify the congestive area rate (S).

Results

At the 5-year follow-up, the patient's HHS was 91, and he described a release from pain and the ability to walk and climb stairs without help. Bilateral examination of the femoral head found that the blood vessels had regenerated at the necrotic area (Figure 3). The number, distribution, and diameter of vessels had improved gradually over the 5-year period. The quantity results showed that the congestive area increased from 73.4% to 94.2% on the left side and from 0% to 71.8% on the right side. X-ray examination of the femoral head reported that the bone marrow gradually became uniform, the cystic area became indistinct, and the bone density increased to a more significant extent (Figure 4). Although femoral head collapse still happened bilaterally, especially on the left side, the patient's clinical symptoms resolved and he was discharged from the hospital with follow-up recommended as needed.

Discussion

Several studies have demonstrated the value of stem cell

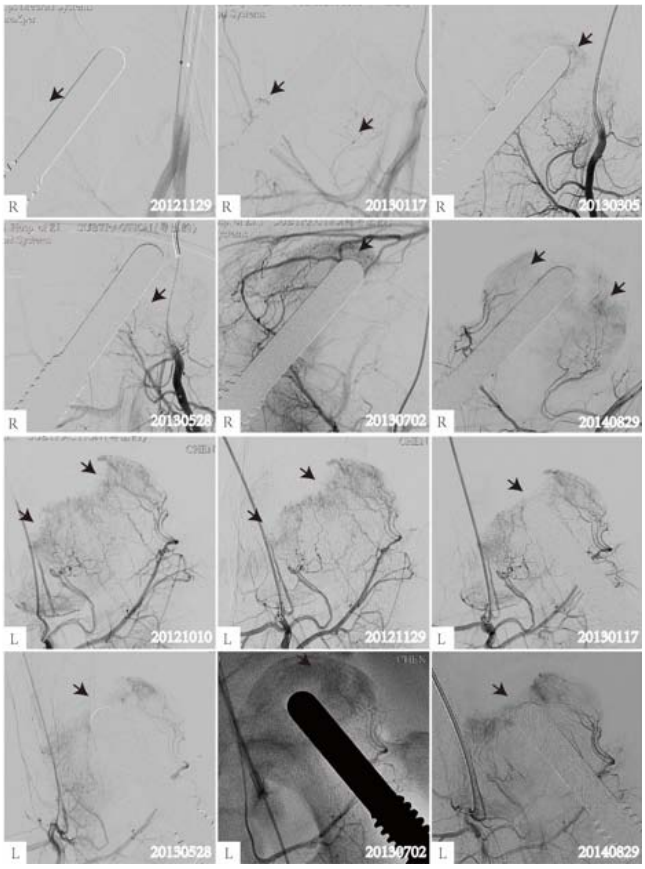

Figure 3: DSA images show the vessels of both sides femoral head during the treatment. The arrows show the angiogenesis area.

and biomechanical support therapies for FHN [9-14]. Another study reported a positive result using autologous bone marrow mesenchymal stem cells (BMSCs) in combination with tantalum rod implantation or vascularized iliac grafting for the treatment of end-stage osteonecrosis of the femoral head [15]. Although this study reported a positive end-stage result, it did not describe the effect on angiogenesis. However, a previous study using the same therapy-BMSCs with mechanical support-suggested that patients who have a large-sized lesion or a laterally located medium-sized lesion would not be good candidates for the head preserving procedure [16,17]. These conclusions were based on the bone characteristics and did not include an assessment of the blood vessels. In the case described here, the patient underwent separate porous tantalum rod implantations bilaterally, which provided rehabilitation training for each joint. After our treatment, the patient had improved hip function and gradually reduced pain, and he continued to work at his job as usual. However, he still felt some discomfort when he walked for too long or exercised too intensely. On examination, we found the integrated regeneration of vessels in the ischemic segment and an apparent improvement of symptoms. The case we report on here is an unfortunate but exceptional chance to study potential mechanisms in FHN pathogenesis, in which multiple factors can induce ischemia at the femoral head. Ultimately, the lack of blood results in osteoporosis, cystic degeneration, and eventual collapse [1]. Thus, it follows that supporting blood vessels may be crucial for treating FHN. In this

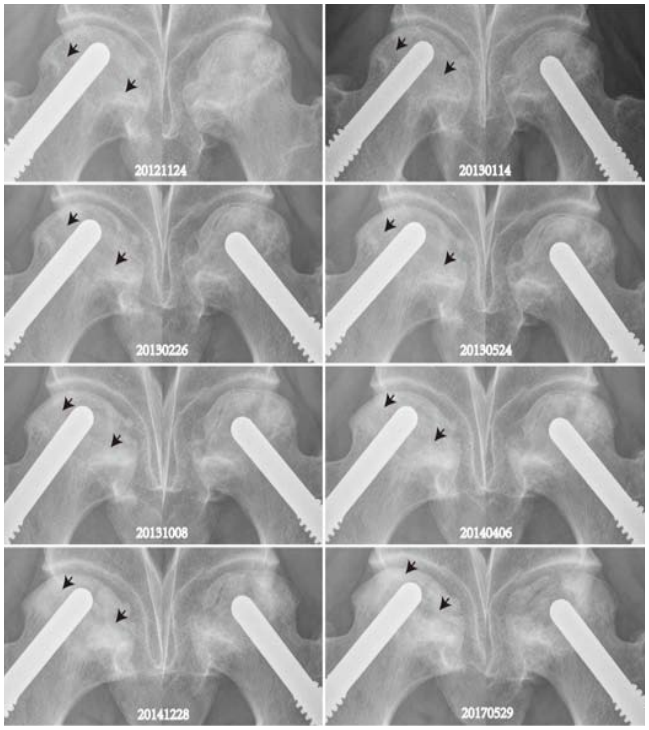

Figure 4: X-ray detection of hip joints during and after the treatment. The arrows show the pathological change area.

case, we repeatedly infused the target vessels with the LPSs, and we assessed the bone density, characteristics of vascular bundles in the necrotic area, and HHS. We found that although the patient's symptoms decreased substantially and angiogenesis was widespread, the femoral head still collapsed. Other studies have also reported angiogenesis and pain relief during FHN recovery [18]. Many studies have reported that stem cells can delay or reverse the progression of FHN and regenerate the necrotic area. The benefits provided by stem cells include multifunctional capacities of surviving, proliferation, and differentiation. LPS therapy has been reported to outperform BMSC therapy with respect to osteonecrosis treatment [19]. Increasingly, basic research has demonstrated that LPS transplantation improved osteogenesis and the microstructure of vascular deprivation-induced osteonecrosis tissue [20]. Core decompression and porous tantalum rod grafts improved intraosseous pressure and provided mechanical support, which created a positive environment for fully functional LPSs. The combined therapy enhanced the functioning of both the LPSs and the porous tantalum rod to reverse the ischemic necrosis. Of course, more evidence to support these findings, and further investigation of the underlying mechanisms is warranted.

Conclusion

FHN is often treated with physical therapy, medications, and a series of surgery options. These therapies are intended to control the pathological development, prevent the collapse of the femoral head, improve hip function, and release the patient from pain. In this case report, we suggest that for patients suffering femoral head necrosis, multiple LPS infusions combined with porous tantalum rod graft implantation may provide pain relief where other treatments have failed. We are planning a clinical series involving more significant numbers of patients to further investigate the therapy and discover the best mechanism for treating FHN.

Declaration

Statement of Ethics: This case is included in a prospective study, which was approved by Zhejiang Provincial hospital of TCM Ethics Committee, started in October 2012 and ended in May 2017 and was registered with the Resman Research Manager (ChiCTR1800020138).

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Authors' contributions: Weixin Zhang and Cheng Zheng have equal contribution to this research. Weixin Zhang and Cheng Zheng were responsible for collecting, analyzing data and writing manuscript. Peijian Tong was involved in planning research ideas and writing the manuscript.

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