

CASE REPORT

Is Prolotherapy Effective in the Treatment of Avascular Necrosis of the Femoral Head?

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ABSTRACT

Introduction • Avascular necrosis of the femoral head (ANFH) is one of the most common diseases, accompanied by varying degrees of functional limitation and reduced quality of life, especially in younger individuals. Various conservative and operative options are available for the treatment of this disease.

Methods and Results • We report a case with ANFH that occurred from long-time and uncontrolled glucocorticoid use. In the treatment of the case, we used prolotherapy injections, whose efficacy and reliability were proved in the treatment of other chronic musculoskeletal problems. After the sixth session of prolotherapy injections, the

patient was able to do daily activities as the same as the previous physical and effort capacity. The WOMAC osteoarthritis index was decreased from 92 preinjections to 12; the Likert pain scale was decreased from 5 preinjections to 1 after the injections.

Conclusions • We obtained successful outcomes in terms of patient satisfaction and clinical and radiological parameters with prolotherapy injections. Prolotherapy may be useful as an easily applicable and satisfying auxiliary method for the treatment of ANFH. (*Altern Ther Health Med*. [E-pub ahead of print.]

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Avascular necrosis of the femoral head (ANFH) is described as the death of the subchondral bone as a result of repetitive or complete deterioration of bone vascularity.¹ The collateral circulation is usually restricted, and this results in a necrosis of the femoral head.¹ The disease commonly occurs in weight-bearing bones such as the femoral head, femoral condyles, proximal tibia, and ankle. Alcohol and glucocorticoid are the most common reasons of nontraumatic ANFH, at a ratio of 60% to 90%. Glucocorticoids are commonly used medications, and they provide immunosuppressive and

antiinflammatory effects at proper therapeutic doses.² Too many complications have been declared with the use of glucocorticoids; however, avascular necrosis is a rare and destructive complication of these medications.²

The popularity of prolotherapy has increased in the management of chronic musculoskeletal problems.³⁻⁵ The injection solutions are prepared as the combination of hypertonic dextrose and anesthetic agents. Its effect is known to be an increase of osmotic gradient in the extracellular matrix, which leads to proliferation of growth factors and subsequent healing.⁶ Prolotherapy injections are successfully used in the treatment of chronic sprained and degenerated ligaments, dense connective tissue structures, entheses, and osteoarthritis.^{3,5} Most related studies have declared high rates of treatment success and low rates of complications.^{2,4} Despite numerous studies, which have focused on similar indications, no opinion or evidence about the effectiveness of prolotherapy in the treatment of ANFH can be found. Chronic musculoskeletal pain and disability are usually assessed as secondary to degeneration of ligamentous and tendinous attachments and adjacent joint structures. Prolotherapy has been suggested to improve this degeneration at the tissue level.⁷ We hypothesized that ANFH can be considered as a type of degeneration, which can be improved at the tissue level by prolotherapy. When the mechanism of action was investigated,

Figure 1. Effects of Repeated Prolotherapy Injections on WOMAC and Likert Scores

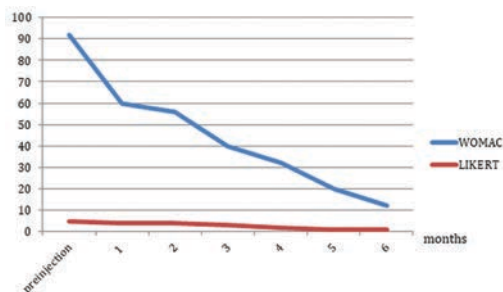
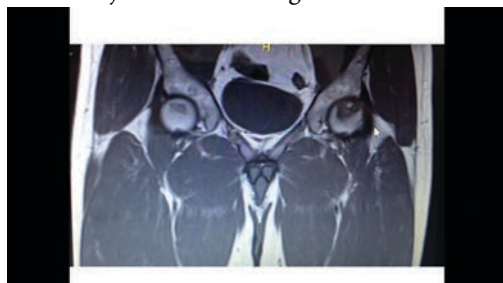


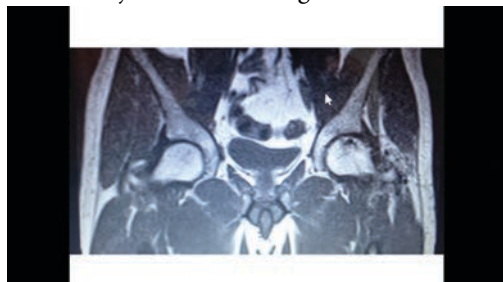
Figure 2. Preinjection MRI Images of the Patient^a



^aCoronal T1A-weighted MRI of the patient showing a large hypointense avascular area in the left femoral head.

Abbreviation: MRI, magnetic resonance imaging.

Figure 3. Postinjection MRI Images of the Patient^a



^aObtained after 6 sessions of injections. Coronal T1A-weighted MRI of the patient showing a considerable decrease in the size of hypointense avascular area. These new hypointense areas refer to the granulation tissue in the bone marrow.

Abbreviation: MRI, magnetic resonance imaging.

clear evidence could not be found, but many logical opinions are present in the literature. Injected irritant solutions produce fibroblastic stimulation. Active fibroblasts provide secretion of new collagen fibrils needed for healing damaged ligaments, and healing occurs.⁸ Hypertonic dextrose can cause osmotic rupture of local cells and cause growth factors to grow in different types of human cells. In addition, a hypertonic environment may cause the release of DNA-encoding growth factors.⁹ In light of these facts, we chose prolotherapy as a treatment modality for ANFH. Prolotherapy injections were planned to reduce pain and muscle atrophy, and also to regenerate joint structures. We report a case of a patient with

ANFH who had been diagnosed a long time ago and took glucocorticoid drugs uncontrolled, and we report the results of our prolotherapy treatment.

METHODS AND RESULTS

A 30-year-old man presented to our clinic with complaints of pain and restricted motion of the right hip. He had received corticosteroid therapy for the treatment of atopic dermatoid for 15 years. He had moderate pain for 2 years, but it was exacerbated 6 months before presentation. He also felt difficulty in his gait; pain became extreme when he walked for 30 meters, and he needed to rest. He had awakened several times at night because of hip pain.

Atrophy was determined in his right gluteus maximus and gluteus medius muscles with palpation and inspection. Right hip pain was spread from his thigh to knees. Right hip of motion was restricted and painful, and 10 degrees of flexion contracture was determined with a Thomas test. His right leg was 2 cm shorter than his left leg. His gait was antalgic with bearing lower weight to right extremity and used walking sticks. He hardly climbed up a 10-step ladder with holding banisters. FABER and FADIR tests were positive in the right hip. In the anteroposterior and lateral radiographies joint space right hip was narrowed, and the femoral head was irregular and compressed. The biochemical values were consistent with corticosteroid use.

The prolotherapy injections were planned to the patient. A total of 30 mL of prolotherapy solution was used (10 mL to hip joint and capsule [9 mL, 25% dextrose and 1 mL, 0.2 lidocaine]) and 20 mL was used for soft tissues around the hip joint (gracilis and other adductor tendons; 18 mL, 15% dextrose and 2 mL 0.2 lidocaine). Injections were repeated with an interval of 30 days. After the injection sessions, the patient was instructed to perform an active-assistive exercise program to strengthen the dorsolumbar region and hip muscles. In addition, a rehabilitation program consisting of gaiting with a walker, balance, and coordination education in bed, chair and standing, and weight transfer in parallel bar, was started for the patient.

Pain was investigated using a visual analog scale (VAS), with 0 for no pain and 10 for severe pain. Hip functions were evaluated with the Western Ontario and McMaster Universities arthritis index (WOMAC). The total score ranged from 0 to 100, with a higher score indicating worse function. A Likert pain scale was used for pain and stiffness. The total score ranged from 0 to 5, with a higher score indicating much pain and stiffness.

After 3 injection sessions for the patient, VAS scores decreased from 8 (preinjection) to 3.5. The patient was able to walk without crutches, climb stairs without support, and to do daily activities without help. After the sixth session, the patient was able to do daily activities with the same previous physical and effort capacity. The WOMAC osteoarthritis index was decreased from 92 at preinjection to 12, and a Likert pain scale was decreased from 5 at preinjection to 1 (Figure 1). A remarkable improvement was seen the in the last magnetic resonance imaging (MRI) when compared with preinjection (Figures 2 and 3).

CONCLUSION

ANFH is one of the common diseases, described as the necrosis of bone tissue after deterioration of vascular support of the femoral head. Several methods have been described literature, but no standardized consensus has been formed owing to incompatibility of the studies' results with each other.¹ In the treatment of this case, we used prolotherapy injections, whose efficacy and reliability was proved in the treatment of other chronic musculoskeletal problems and obtained successful outcomes in terms of patient satisfaction and clinical and radiological parameters.

The management of the disease differs for each author and usually depends on clinical experiences and knowledge. Surgical and nonsurgical methods are available in the treatment of the disease. Recently, there has been growing interests in nonsurgical and minimal invasive methods. Many investigators have contributed to this issue; however, an inadequate number of treatment agents have been described in the literature. Medical treatment, hyperbaric oxygen (HBO), extracorporeal shockwave therapy (ESWT), and stem cell therapy are the most suggested nonsurgical methods.¹⁰ HBO provides high oxygen pressure to improve angiogenesis that will provide healing of osteonecrosis and also stimulate osteoblasts and osteoclasts.¹¹ Koren et al¹¹ investigated HBO in the treatment of early stages of ANFH and declared that an improvement was found in 80% of the patients' MRI findings when compared with pretreatment MRI images. Harris hip scores and SF-12 scores confirmed this success. ESWT has also been used in the treatment of femoral head avascular necrosis in early stages. Ludwig et al¹² declared significant improvements in VAS scores and Harris scores at 1 year after first treatment of ANFH with ESWT. Some of the patients' lesions completely recovered in the MRI images. A recent study comprised the long-term results (8-9 y) of ESWT and surgery (core decompression). and a remarkable ratio of the patients had excellent and good results in the ESWT group; however, that was lower in the surgery group.¹³ We used prolotherapy in our ANFH case, and our results were as successful as the other nonsurgical methods. But ultimately, this is the report of only 1 case. If more advanced studies prove significant evidence in the future, one day prolotherapy might be considered a valid alternative to surgery.

Prolotherapy has gained popularity, and application fields have increased continuously.^{3,5} Easy application, success rates, associated low-complication risks, and the short rehabilitation process are the reasons why prolotherapy is the preferred treatment for these conditions.^{3,4} It also facilitates healing of the degenerated and damaged musculoskeletal structures, and then their functions have been restored.^{3,12,14} Moreover, the injections have been reported to be safer than other similar methods.^{3,12} To our knowledge, there is no study that has reported the effects of prolotherapy in the treatment of ANFH. For the treatment in this case report, we used prolotherapy injections and obtained successful results as the other indications of prolotherapy.

Palpation- or ultrasound-guided prolotherapy injections have been preferred by different authors for similar indications. Most of the studies used 1 of the 2 methods, and

all have declared successful results. No study has compared palpation- or ultrasound-guided prolotherapy injections. Chen et al¹⁵ compared these 2 methods (ultrasound and palpation guided) for steroid injections and declared that ultrasound-guided methods had significantly better therapeutic outcomes. They also stated that the effectiveness and duration of action is enhanced when injections were performed into the target points. We preferred the use of ultrasound-guided injections in our study, based on our clinical experiences. We thought that the help of ultrasound was crucial for this indication. The joint space and hip capsule must be clearly visualized before the injections. A randomized double-blind controlled clinical study by Rezasoltani et al¹⁶ reported that periarticular prolotherapy was significantly superior to intraarticular prolotherapy in reducing pain and improving function. In our study, we used both intra-articular and periarticular prolotherapy. Maybe only periarticular prolotherapy is sufficient, but we used both methods, and we cannot explain this situation. Comparative studies are needed to explain this issue.

Further case series are required to confirm the effect of prolotherapy injections in the treatment of ANFH. Prolotherapy may be very useful as an easily applicable and satisfying auxiliary method for the treatment of ANFH.

REFERENCES

1. Ali SA, Christy JM, Griesser MJ, Awan H, Pan X, Ellis T J. Treatment of avascular necrosis of the femoral head utilising free vascularised fibular graft: A systematic review. *Hip International*. 2014;24(1):5-13.
2. Fardet L, Kassir A, Cabane J, Flahault A. Corticosteroid-induced adverse events in adults: Frequency, screening and prevention. *Drug Saf*. 2007;30(10):861-881.
3. Akpancar S, Seven MM, Tuzun HY, Gurer L, Ekinci S. Current concepts of prolotherapy in orthopedic surgery. *Arch Trauma Res*. October 2016; https://www.researchgate.net/publication/309277636_Current_Concepts_of_Prolotherapy_in_Orthopedic_Surgery. Accessed March 14, 2018.
4. Seven MM, Ersen O, Akpancar S, et al. Effectiveness of prolotherapy in the treatment of chronic rotator cuff lesions. *Orthop Traumatol Surg Res*. 2017;103(3):427-433.
5. Seven MM, Koca K, Akpancar S, et al. Prolotherapy injections in the treatment of overuse injuries. *BMMR*. Online First: 15 May, 2016.
6. Krump E, Nikitas K, Grinstein S. Induction of tyrosine phosphorylation and Na⁺/H⁺ exchanger activation during shrinkage of human neutrophils. *J Biol Chem*. 1997;272(28):17303-17311.
7. Carayannopoulos A, Borg-Stein J, Sokolof J, Meleger A, Rosenberg D. Prolotherapy versus corticosteroid injections for the treatment of lateral epicondylitis: A randomized controlled trial. *PM R*. 2011;3(8):706-715.
8. Hackett GS, Hemwall GA, Montgomery GA. *Ligaments and Tendon Relaxation Treated by Prolotherapy*. 5th ed. Madison, WI: Hackett Hemwall Foundation; 2008.
9. Murphy M, Godson C, Cannon S, et al. Suppression subtractive hybridization identifies high glucose levels as a stimulus for expression of connective tissue growth factor and other genes in human mesangial cells. *J Biol Chem*. 1999;274(9):5830-5834
10. Rajpura A, Wright AC, Board TN. Medical management of osteonecrosis of the hip: a review. *Hip Int*. 2011;21(4):385-392.
11. Koren L, Ginesin E, Melamed Y, Norman D, Levin D, Peled E. Hyperbaric oxygen for stage I and II femoral head osteonecrosis. *Orthopedics*. 2015;38(3):e200-e205.
12. Ludwig J, Lauber S, Lauber HJ, Dreisilker U, Raedel R, Hotzinger H. High-energy shock wave treatment of femoral head necrosis in adults. *Clin Orthop Relat Res*. 2001;119-126.
13. Wang CJ, Huang CC, Wang JW, Wong T, Yang Y. Long-term results of extracorporeal shockwave therapy and core decompression in osteonecrosis of the femoral head with eight- to nine- year follow-up. *Biomed J*. 2012;35:481-485.
14. Hackett GS, Hemwall GA, Montgomery GA. *Ligament and Tendon Relaxation Treated by Prolotherapy*. 5th ed. Oak Park, IL: Institute in Basic Life Principles; 1991.
15. Chen C-M, Chen J-S, Tsai W-C, Hsu H-C, Chen K-H, Lin C-H. Effectiveness of device-assisted ultrasound-guided steroid injection for treating plantar fasciitis. *Am J Phys Med Rehabil*. 2013;92(7):597-605.
16. Rezasoltani Z, Taheri M, Mofrad MK, Mohajerani SA. Periarticular dextrose prolotherapy instead of intra-articular injection for pain and functional improvement in knee osteoarthritis. *J Pain Res*. 2017;17(10):1179-1187.