Core decompression and implantation of calcium phosphate cement/Danshen drug delivery system for treating ischemic necrosis of femoral head at Stages I, II and III of antigen reactive cell opsonization

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Objective: To introduce a new method using calcium phosphate cement/Danshen drug delivery system for treating ischemic necrosis of the femoral head and evaluate its curative effect.

Methods: From May 2000 to June 2005, 48 adult patients (54 hips) with ischemic necrosis of the femoral head at Stages I, II and III of antigen reactive cell opsonization (ARCO) were treated with implantation of calcium phosphate cement/Danshen drug delivery system in the involved femoral head. The operation consisted of removal of the necrotic bone under weight-loading cartilage and the implantation of phosphate cement/Danshen drug delivery system, and all manipulations were made percutaneously through a bone tunnel in the trochanter. The functions of the hip joint were evaluated and X-ray films were taken preoperatively and postoperatively.

Results: Postoperative follow-up was 45.5 months on average, ranging from 27 to 78 months. According to the evaluation criterion of “Dandong 1995” for therapeutic effect of adult ischemic necrosis of the femoral head, the therapeutic effects were excellent in 33 hips, good in 17, fair in 3 and poor in 1, with the excellent and good rate of 92.6%.

Conclusions: This method is relatively simple with little invasion. It not only improves the microcirculation of the femoral head by local application of traditional Chinese medicine, but also provides mechanic buttress in the weight-loading area to prevent collapse during repairing, which is beneficial to repair and reconstruction of femoral head. It may be a choice of minimal invasion surgery for ischemic necrosis of the femoral head at Stages I, II and III of ARCO.

Key words: Calcium phosphates; Medicine, Chinese traditional; Drug delivery systems; Osteonecrosis
the necrotic bone. Besides its roles of provision of mechanical buttress and prevention of cartilage collapse, combined with local application of traditional Chinese medicine, this method is beneficial to the reconstruction of local microcirculation and repair of the necrotic femoral head.

METHODS

General data of patients

From May 2000 to June 2005, 48 patients (54 hips) with early or middle stage of osteonecrosis of the femoral head were admitted to our hospital. Among the patients, 32 (36 hips) were male and 16 (18 hips) were female, and their mean age was 38.7 years (range, 26-68 years). Twenty-one patients were alcoholic, 15 had a history of long-term steroid use, 2 had slight sprain in the involved hips and the others had idiopathic osteonecrosis. The diagnosis of osteonecrosis was based on the clinical history, anteroposterior (AP) and frog-leg lateral radiographs, and computed tomography (CT) or magnetic resonance imaging (MRI). According to the International Association Research Circulation Osseous (IARCO) System 6 (Table 1), 8 hips were diagnosed as Stage I, 32 as Stage II, and 14 as Stage III.

Surgical technique

The patients were placed in a supine position with both legs abducting for 30° and the affected limb intorting for 15° after epidural anesthesia became effective. A midlateral longitudinal incision about 1.5 cm in length was made 2 cm distal to the greater trochanter, the iliotibial band was split longitudinally, and the vastus lateralis fascia and fibers were elevated off. A Kirschner pin of 2.5 mm in diameter was used as a guide pin (Fig. 1A). Under the monitoring of G type X-ray machine, the pin was drilled into the cystic destruction or cirrhosis area of the femoral head through the neck of femur 1 cm distal to the greater trochanter (Fig. 1B). A hollow trephine of 8 mm in diameter was drilled into the necrotic area along the guide pin (Fig. 1C). The hollow trephine was taken out and a biopsy was obtained from the necrotic region of the femoral head. The necrotic scope was predicted according to the arc, proportion and position of the necrosis on the preoperative imaging findings. Curettage of the cystic tissues and sclerotic dead bone was performed to the normal bone using an eccentric drilling device and a curette, but 0.5 cm of the subchondral bone should be kept (Figs. 1D and 1E). The collapsed articular cartilage should be reduced as far as possible so as to resume the shape of the femoral head. After the intramedullary exuding blood being thoroughly extracted (Fig. 1F), 5-10 g of calcium phosphate cement based on the size of the marrow cavity and compound Danshen injection were mixed in proportion of 2 g of calcium phosphate cement to 0.1 ml of compound Danshen injection. The mixture was injected into the necrotic area and the bone tunnel when it became pasty (Fig. 1G). After solidification for 15-20 minutes, full rinsing was performed to avoid residuals of the compound remaining in the soft tissues and inducing foreign body rejection, then the incision was sutured in layers (Fig. 1H).

Postoperative management

Postoperatively, the patients walked with crutches and no weight-bearing was made on the affected limb for one month, then with partial weight-bearing for three months and finally with full weight-bearing six months after surgery.
RESULTS

None of the patients had any complications, such as deep vein thrombosis of leg or foreign body rejection. The incisions were all healed by first intention. The average follow-up was 45.5 months, ranging from 27 to 78 months. According to the evaluation criteria of “Dandong 1995” for adult osteonecrosis of the femoral head, the clinical score of the patients was 60 points and X-ray score was 40 points. The scores were calculated before operation and at the final follow-up, and the preoperative score was 76 points and postoperative score was 96 points for the 8 hips of stage I patients. The scores were 62 points and 55 points preoperatively, 92 points and 78 points postoperatively for the 32 hips of stage II patients and 14 hips of stage III patients, respectively. The total score >90 points was considered as excellent, 75-89 points as good, 60-74 points as fair, and <60 points as poor. In this group, 33 hips were excellent, 17 were good, 13 were fair and 1 was poor. The excellent and good rate was 92.6%.

Typical case

A 46-year-old man complained of exacerbated pain and lameness in the right hip 9 months ago. And 3 months later, he also felt pain in the left hip. Physical examination showed tenderness in the middle of inguina and percussion pain in the greater trochanter. There was restriction of motion in both hips, the ranges of motion of the right hip were 15° of extension, 90° of flexion, 15° of intorsion, 25° of extorsion, 25° of adduction and 20° of abduction, and the restriction of intorsion in the left hip was 10°. X-ray photographs showed that the bone density in the right hip was uneven and there were local cystic destruction and cirrhosis. In the left hip, the bone density was uneven (Fig. 2A) and necrosis was further proved by MRI (Fig. 2B). Focal cleaning and implantation of calcium phosphate cement/Danshen drug delivery system were performed after admission. Two weeks postoperatively, pains in the hips disappeared and normal walk was obtained. The ranges of motion of the right hip were 5° of extension, 125° of flexion, 25° of intorsion, 35° of extorsion, 25° of adduction and 25° of abduction. The examinations one year and 6 months after operation found that the patient felt no discomfort in the hips and there was no influence on his daily life. X-ray photograph showed normal femoral head and fine combination of implant and its surrounding bone tissues (Figs. 3A and 3B).
DISCUSSION

Osteonecrosis of the femoral head seemingly has a wide range of etiology and a poorly-understood pathogenesis. No matter what reason leads to osteonecrosis of the femoral head, the key reason is local microcirculation disturbance. Its basic pathologic changes include bone necrosis, local cystic destruction, cirrhosis and collapse of the femoral head. Therefore, the aim of treating necrosis of the femoral head is to improve and reconstruct the local blood circulation, clear away local sclerotic bone, supply timely and proper local mechanical supporting and prevent the femoral head from collapsing. Osteonecrosis of the femoral head is a progressive disease. When it happens, the intramedullary blood vessel is gradually forced into the necrotic area trying to repair the necrotic bone. However, its self-repair ability is limited and drugs are difficult to get to the necrotic site in the state of ischemia. Sclerotic belt is finally formed on the edge of the necrotic area. Once the sclerotic belt is formed, self-repair is stopped, cystic destruction occurs, and the subchondral bone shape is difficult to be repaired in the weight-bearing area. This is the main reason for the progress of the disease. If there are not any interventions, such as operations or other invasions (like extracorporeal wave of oscillation), it is impossible for the necrotic area to be repaired. In view of this knowledge, local treatment of osteonecrosis of the femoral head is drawing more and more attentions. The methods include: (1) clearing the necrotic focus by operations or other invasive methods, (2) promoting the reconstruction of blood circulation and focus repair by local application of drugs, cell factors or stem cells, and (3) local implantation of auto-graft or bone succedaneum so as to resume the normal mechanical circumstances and prevent the femoral head from collapsing in the course of repairing.

Core decompression of the hip is the most common procedure used to treat the early stage of osteonecrosis of the femoral head. It has such advantages as simple operation, smaller invasion, and short-time staying in bed postoperatively. Some researches found that core decompression could stimulate the angiopoiësis around the decompression canal, enhance the creeping substitution of necrotic bones, and eliminate the focal necrosis. Plenk et al found through histological observation that core decompression could reduce edema of the femoral medullary cavity of femoral head and delay the progress of osteonecrosis. However, core decompression further reduced the weak mechanical buttress of subchondral bone and caused stress concentration and collapse of the femoral head. Schneider et al held that core decompression was effective on the relief of pain, but it had no more values on stopping the development of the pathologic process. Therefore, simple core decompression is used uncommonly now. However, most researchers considered that the method had many advantages, such as smaller invasion, better outcome for suitable indications and patients’ willingness to accept. Many researchers are making efforts in improving this method, especially in the clinical study on improvement of the supporting and osteogenic abilities with the compound implant.

At present, autogenous iliac bone column graft, fibula, bone substitute, hydroxyapatite, bone cement, and titanium alloy are commonly used in the treatment of osteonecrosis of the femoral head. Although core decompression combined with nonvascularized or vascularized grafts is effective, but the success rates for free nonvascularized fibular grafts range from 54% to 95% after a follow-up of 2-12 years, and for their vascularized counterparts, from 67.4% to 92% after a follow-up of 2-7 years. Moreover, this technique requires much technical expertise, time, and expense and the patients must restrict weight-bearing for 6-12 months. It also gives significant morbidity of donor sites, including motor weakness and sensory abnormalities in the surgically-treated leg. In addition, fracture of the proximal femur was reported in 2.5% of hips in another study. Bone cement and titanium alloy are biological inert materials, and they cannot be integrated with bone tissues directly and tend to cause loosening. Their modulus of elasticity is obviously higher than normal bone tissues, which leads to local stress concentration and may speed up cartilage collapse. All of them cannot act as drug carriers and cannot improve and reconstruct the local microcirculation. Calcium phosphate cement is a new artificial non-ceramic hydroxyapatite bone material with biological activity. It is biodegradable in vivo and can be substituted by new bones gradually. Its maximum compressive strength is about 30-50 Mpa, its mechanical strength is higher than that of cancellous bone, its modulus of elasticity is close to cortical bone, and the mechanical strength of bone repair can be offered. Serial studies by Otsuka et al demonstrated that calcium phosphate was an ideal drug...
carrier, with drug loading among them. It not only fills the defect of bone, but also makes the drug slowly release in the local region and maintains a high level of local drug concentration, which plays double efficacies of repairing and supporting.

The basic pathologic change of osteonecrosis of the femoral head is local derangement of microcirculation. In this study, a hole was drilled from the greater trochanter and new circulatory passage was widely and quickly opened to reduce the pressure inside the bone, which made the bone inner microcirculation stasis relieved and the symptoms improved. Then the calcium phosphate cement/Danshen drug delivery system, which was composed of calcium phosphate cement and compound injection of Danshen, was implanted to fill the defected bone and prevent the femoral head from collapsing. The microcirculation would be reconstructed and the necrotic bone would be repaired by local delivered traditional Chinese drug. With the defective part of the femoral head being filled by the implant and combining the bone tissues closely, the mechanical properties of the femoral head were reconstructed and the cartilage collapse was prevented, eventually restored the normal blood circulation and femoral bony structure.

The advantage of calcium phosphate cement/Danshen drug delivery system is easy to use and moulding. After the dead bone being removed and the collapsed articular cartilage reduced, calcium phosphate cement/Danshen drug delivery system sufficiently filled the defected area. It solves the problem that drug could not be delivered to the desired sites, ensures the long-term stability of local drug release, and effectively improves the microcirculation. Implantation of calcium phosphate cement/Danshen drug delivery system is simple and does not need to open the articular cavity, and therefore, the functions of joints are recovered more quickly.

We believe that this technique potentially postpones the need for arthroplasty in young patients and offers the possibility of long-term benefits in selected patients. The short- and middle-term outcomes were satisfactory, but long-term results need further observation.

REFERENCES

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