Injury, Int. J. Care Injured 45 (2014) 369–373

Contents lists available at ScienceDirect

Injury

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

Treatment of AVN using the induction chamber technique and a biological-based approach: Indications and clinical results

G.M. Calori [a,*], E. Mazza [a], M. Colombo [a], S. Mazzola [a], G.V. Mineo [b], P.V. Giannoudis [c]

[a] Orthopaedic Reparative Surgery Department, Orthopaedic Institute Gaetano Pini, University of Milan, Italy
[b] University Department of Orthopaedics, Orthopaedic Institute Gaetano Pini, University of Milan, Italy
[c] Academic Department of Trauma and Orthopaedics, School of Medicine, University of Leeds, Leeds, UK

ARTICLE INFO

Article history:
Accepted 17 September 2013

Keywords:
Avascular necrosis
AVN
Mesenchymal stem cells
Core decompression
rhBMP
Osteonecrosis
Femoral head
Early stage
Autologous implantation
Biological chamber

ABSTRACT

Objective: To determine the efficacy of core decompression (CD) technique combined with recombinant morphogenetic proteins, autologous mesenchymal stem cells (MSCs) and xenograft bone substitute into the necrotic lesion of the femoral head on clinical symptoms and on the progression of osteonecrosis of the femoral head.
Patients and methods: A total of 38 patients (40 hips) with early stage osteonecrosis of the femoral head were studied over a 4-year period.
Results: CD technique combined with recombinant morphogenetic proteins, autologous MSCs and xenograft bone substitute was associated with a significant reduction in both pain and joint symptoms and reduced the incidence of fractural stages. At 36 months, 33 patients achieved clinical and radiographic healing.
Conclusion: This long-term follow-up study confirmed that CD technique combined with recombinant morphogenetic proteins, autologous MSCs and xenograft bone substitute may be an effective treatment for patients with early stage osteonecrosis of the femoral head.

Introduction

Avascular necrosis (AVN) of the femoral head is a common cause of hip disability that may progress to collapse of the femoral head and hip osteoarthritis in up to 80% of patients if left untreated [1]. Osteonecrosis is the biological death of bone, either partially or completely. It has a variety of potential causes, idiopathic, infective, traumatic, toxic or ischaemic.

Osteonecrosis of the femoral head typically affects patients in their third to fifth decades of life [2]. In the USA in the future, 10,000–20,000 patients are expected to develop femoral head osteonecrosis every year, with 70% of them being males aged 30–40 years old. Over 50% of these patients will develop the disease in both hips within two years [3].

Several risk factors have been reported to be associated with the development of AVN, including alcohol abuse, excessive use of corticosteroids, haemoglobinopathy, Gaucher's disease, pregnancy, coagulopathies, Caisson disease, organ transplantation, hyperbaric exposure, inflammatory or autoimmune disease, antiretroviral therapy, smoking [4,5], cancer chemotherapy [6,7] trauma and other idiopathic mechanisms [8–10]. Despite the plethora of causative factors, the pathophysiology of AVN remains uncertain [11–13].

The factors that influence the progression of AVN from the appearance of the necrotic lesion to subchondral fracture and femoral head collapse are not yet fully understood, but size and stage of osteonecrosis have been shown to be predictive of the clinical outcome [14].

The pathogenesis of osteonecrosis is still unclear, but it can be seen as a vascular and bone disease. On one hand, the function of the capillaries that serve as a conduit for the stem cells and bone cells needed in the bone remodelling unit and providing blood supply could be altered by emboli or thrombosis [15,16]. On the other hand, autologous mesenchymal stem cells (MSCs) and osteoblasts that could potentially induce bone formation have been shown to be decreased in number and activity [17,18]. Moreover, osteocytes and bone-lining cells in the necrotic lesion and the proximal femur undergo apoptosis [19,20]. This altered bone remodelling may be associated with three different events in the pathogenesis of osteonecrosis: the appearance of osteonecrosis itself, the insufficient bone repair that occurs after osteonecrosis, and its evolution to the subchondral fracture.

* Corresponding author at: Orthopaedic Reparative Surgery Department, G. Pini, University of Milan, P.za Cardinal Ferrari 1, 20122 Milan, Italy.
?Tel.: +39 02 58296903; fax: +39 02 58296905.
E-mail address: gmc@studiocalori.it (G.M. Calori).

0020–1383/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.injury.2013.09.014

The gold standard therapy for early stage osteonecrosis of the femoral head (stage I of the Ficat [21] classification) is a conservative treatment comprising a symptomatic therapy, electrostimulation or extracorporeal shockwave therapy (ESWT). For later stages of osteonecrosis (stages II–III of the Ficat [21] classification), therapy comprises surgical treatment, such as vascularised fibula grafting, core decompression (CD) technique or total hip arthroplasty (THA); surface replacement arthroplasty offers a minimally destructive procedure. When the joint is irreversibly compromised (stage V), the most effective treatment solution is total hip replacement [22–24].

CD is a widely accepted procedure for treatment of hip osteonecrosis in its early stages (before mechanical failure has occurred) [25–29]. The outcome of CD is not always satisfactory: the reconstruction of the necrotic area by this method may remain incomplete because of inadequate creeping substitution and bone remodelling [30]. This is attributed to the relative insufficiency of osteoprogenitor cells in the proximal femur of the osteonecrotic hip [31,32]. Recent pioneer studies by Hernigou et al. and Gangji et al. have shown the efficacy of implantation of autologous MSCs into the CD tract during early-stage AVN [33–36]. There is evidence to indicate that implanted MSCs promote both osteogenesis and angiogenesis in the femoral head [34,37]. These beneficial effects may be mediated, at least in part, by MSCs and endothelial precursor cells [37].

The efficacy of growth factors, particularly recombinant human bone morphogenetic protein (rhBMP)-7, in orthopaedic surgery has been shown in several clinical studies, including in the treatment of non-union and bone defects [38–40,51–53]. The purpose of the current study is to evaluate the results of treatment using a new biological-based approach. The aim of this retrospective clinical study is to examine the effectiveness of CD and implantation of MSCs and growth factors (rhBMP-7) with flexible xenograft bone substitute [41] for the treatment of early-stage AVN to create a biological chamber [42] based on the principles of the polytherapy [43–45].

Patients and methods

Study design

This retrospective clinical study of prospectively documented data was conducted in the Orthopaedic Institute G. Pini (Milan) on patients treated between March 2007 and June 2011. The objective of this study was to assess the efficacy of the diamond-based approach to bone regeneration following CD combined with implantation of MSCs and growth factors (rhBMP-7) with a xenograft (equine origin) bone substitute partially demineralised (flexible) for the treatment of early-stage AVN.

AVN was classified according to the Ficat [21] classification: stage 0: asymptomatic, normal MRI and radiograph; stage 1: normal or minor changes on plain radiograph and MRI, sometimes groin pain; stage 2: sclerosis, or cysts of femoral head with diffuse porosis, geographic defects on MRI; stage 3: pain and stiffness with radiation to knee and limp, radiographs and MRI show broken contour of the head; stage 4: collapse, flattened contour, decreased joint space and osteoarthrosis (Fig. 1 and Table 1).

Participants

Inclusion criteria were age greater than 18 years, clinical signs of hip pain and radiological features on the MRI scan of stages I–III osteonecrosis (Ficat [21] classification).

Exclusion criteria were pregnancy, active infection, skeletal immaturity, stage IV osteonecrosis, immunosuppressive drug therapy, history of inflammatory arthritis, hypersensitivity to rhBMP-7, contraindication to bone marrow harvest, severe osteoporosis, neuromuscular deficits or physical condition that may interfere with the ability to limit the load, autoimmune disease, cancer near to the site of surgery, previous treatment with rhBMP and mental health problems.

Procedure

Patients received antibiotic prophylaxis with 2 g cephalosporin when they arrived in the surgical room (i.e. before surgery), then 1 g cephalosporin at both 8 h and 16 h after surgery.

The first step of the procedure was bone-marrow blood aspiration. The patient was placed on the operating table in a supine position with arms stretched out to the sides. The needle for bone-marrow blood aspiration was introduced at the level of the anterior iliac crest and the bone marrow blood was aspirated. The second step of the procedure was CD. A c-arm fluoroscope was draped with a sterile sleeve and positioned over the hip region to enable an anteroposterior view. Under fluoroscopic control, a Kirschner wire was inserted in the direction of the osteonecrotic lesion; the access of the wire was controlled with the two standard fluoroscopic projection. When the Kirschner wire was positioned at the lesion site, a 2 cm incision was made laterally through the skin and the fascia at the level of, or just distal to, the greater trochanteric. With the help of the Kirschner wire and a soft tissue protector, an 8-mm reamer was then inserted under fluoroscopic control through the trochanter, the femoral neck, and the femoral head in the direction of the osteonecrotic lesion. This procedure was then repeated with a specially shaped 12-mm reamer for retrograde removal of the osteonecrotic lesion. The reamer was directed towards the necrotic zone until it reached the pathologic area without reaching the joint. Concentration of the bone marrow sample was achieved by washing using physiological water to remove bone spicules, fat and cellular debris

Growth factors (rhBMP-7), a scaffold of xenograft (equine origin) bone substitute and autologous bone MSCs was inserted inside the tunnel of the femur using special instrumentation; the bone substitute was inserted at the end to close all the components of the polytherapy [43–45] in the biological chamber [42]. The patient was usually discharged two days after surgery and was advised 20 days with no weight-bearing using two crutches, then 10 days with partial-weight bearing before returning to normal deambulation.

Outcome assessments

Patients underwent clinical and radiological evaluation (X-ray, MRI, and CT scan) before surgery; then were classified using Ficat [21] classification. Follow-up was scheduled at 1, 3, 6, 9, 12, 24 and 36 months after the intervention. The primary outcome was clinical and comprised evaluation with the Harris hip score (HHS), which measures the pain, function, activity and motion of the hip. The secondary outcome was the radiological evaluation of the collapse of the femoral head. The tertiary outcome was the MRI-CT evaluation of the progression in osteonecrotic stages. The last outcome was the evaluation of the number of patients who went on to have a total hip replacement. Peri- and post-operative complications were recorded and classified as severe, moderate or mild. All adverse events were classified as serious or non-serious.

Results

A total of 47 patients were enrolled in the current study between March 2007 and June 2011. Nine patients were lost to follow up, therefore 38 patients (40 hips) were available for the final follow up. Patients comprised 25 males and 13 females with a