Possibility of “distraction arthrogenesis”: first report in rabbit model

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Abstract We investigated the possibility of articular cartilage distraction for use in reconstructing joint structure and for increasing the donor site of osteochondral grafts. Intraarticular osteotomy was performed at the femoral condyle in 12 Japanese white rabbits. The bone segment was fixed with a specially designed external fixator. After a 3-week waiting period, distraction was performed intermittently for 3 weeks (0.7 mm × 3 times per week) in the distraction group (n = 7) and, in the remaining animals (gap group; n = 5), a gap of 6.3 mm in length was made at surgery. All rabbits received etidronate injections (20 mg/kg × 2 times per week) for 5 weeks, to slow mineralization. The femoral condyle was harvested 9 weeks postoperatively and decalcified sagittal sections were stained and evaluated, using a histological grading scale. In the distraction group, distraction of 4.2 ± 1.4 mm was achieved, and the distracted cartilage area was filled with regenerated cartilage, without any gap between the regenerated and the adjacent articular cartilage. This regenerated cartilage showed metachromasia with toluidine blue. In the gap group, newly formed cartilage tissue was folded from the edge of the osteotomy site and fibrous tissue was interposed in the gap. The histological grading score was significantly lower in the distraction group (P < 0.02). Our preliminary results demonstrated the possibility of cartilage distraction; however, long-term observation will be necessary to confirm the characteristics of the distracted cartilage. We may call the process “distraction arthrogenesis”, because the entire articular entity, which consists of cartilage, subchondral bone, and bone, could be distracted at once.

Key words Cartilage regeneration · Distraction · External fixator

Introduction

Joint dysplasia is a disease in which joint structure is not sufficiently developed. These structural deficiencies cause degeneration of the joint cartilage, resulting in joint pain and dysfunction. For example, acetabular dysplasia is a major cause of coxarthrosis. Recurrent patellar dislocation is brought about by dysplasia of the intercondylar groove of femur.

Osteotomy and bone graft are operations employed to change the joint structure and supply bony coverage. However, as these operations cannot augment the surface of articular cartilage, this may be one of the reasons that joint degeneration is not always prevented by these operations. Accordingly, the regeneration of both articular cartilage and bone is indispensable for the treatment of joint dysplasia.

Distraction osteogenesis has been established to regenerate bone for limb-lengthening and treatments of bone defects.1,2 It has been reported that slow distraction stimulates osteogenesis.15 Distraction does not act on the bone itself, but acts on the callus that is formed by cells from bone marrow and periosteum.6,22 When this technique is applied to the articular cartilage, it is considered that intrarticular osteotomy through the articular cartilage leads to the supply of mesenchymal cells to the osteotomy site. It is generally accepted that the repair of cartilage defect is mediated wholly by the proliferation and differentiation of mesenchymal cells from bone marrow.13,17 We hypothesized that these mesenchymal cells may differentiate to articular cartilage when they are exposed to the intrarticular environment.

In this study, we performed intrarticular osteotomy at the femoral condyle in rabbits, and gradual distraction was achieved with a specially designed distraction apparatus. We now describe the surgical technique and report our histological findings, using a histological grading scale.
Materials and methods

Twelve Japanese white rabbits (male, weighing 2.5–3.0 kg) were used. The rabbits were anesthetized with an intramuscular injection of a mixture of ketamine (50 mg/ml; 1.0–1.5 ml/kg body weight) and xylazine (20 mg/ml; 1.0–1.5 ml/kg body weight). The fur around the knee was removed and the knee was disinfected with iodine. The femoral shaft and knee joint were exposed, and a specially designed external fixator was attached to the lateral side of the femur (Fig. 1). The external fixator consists of two parts; an angled bar with a sliding table, and a half ring connected to the sliding table. The femoral shaft was fixed to the bar with two pins, and the femoral condyle was fixed to the half ring with two wires. Intrarticular osteotomy was performed at the femoral condyle through the articular cartilage (Fig. 2). We took care not to create any step-off at the osteotomy site.

To prevent infection, cefpirome sulfate (75 mg/kg) was injected intravenously immediately after the operation. All rabbits were returned to their cages after the operation and were allowed to move freely. To slow bone mineralization, etidronate (20 mg/kg, × 2 times per week) was subcutaneously injected during the initial 5 weeks.

The rabbits were divided into two groups:

1. Distraction group (n = 7). Three weeks postoperatively, distraction was initiated and was performed intermittently for 3 weeks (0.7 mm × 3 times per week). Three weeks after the last distraction, the femoral condyle was harvested.

2. Gap group (n = 5). A gap of 6.3 mm in length was made at the operation site, and the femoral condyle was harvested 9 weeks postoperatively.

Decalcified sagittal sections of the femoral condyle were stained with hematoxylin-eosin and toluidine blue for microscopic evaluation. The sections were examined blindly and scored independently by two of the authors, using a histological grading scale consisting of five categories, with a score range of 0 to 14 points (Table 1).

Statistical analysis of the data for the distraction group and the gap group was performed using the Mann-Whitney U-test.