Transplantation of tissue-engineered cartilage for excessive osteochondritis dissecans of the elbow

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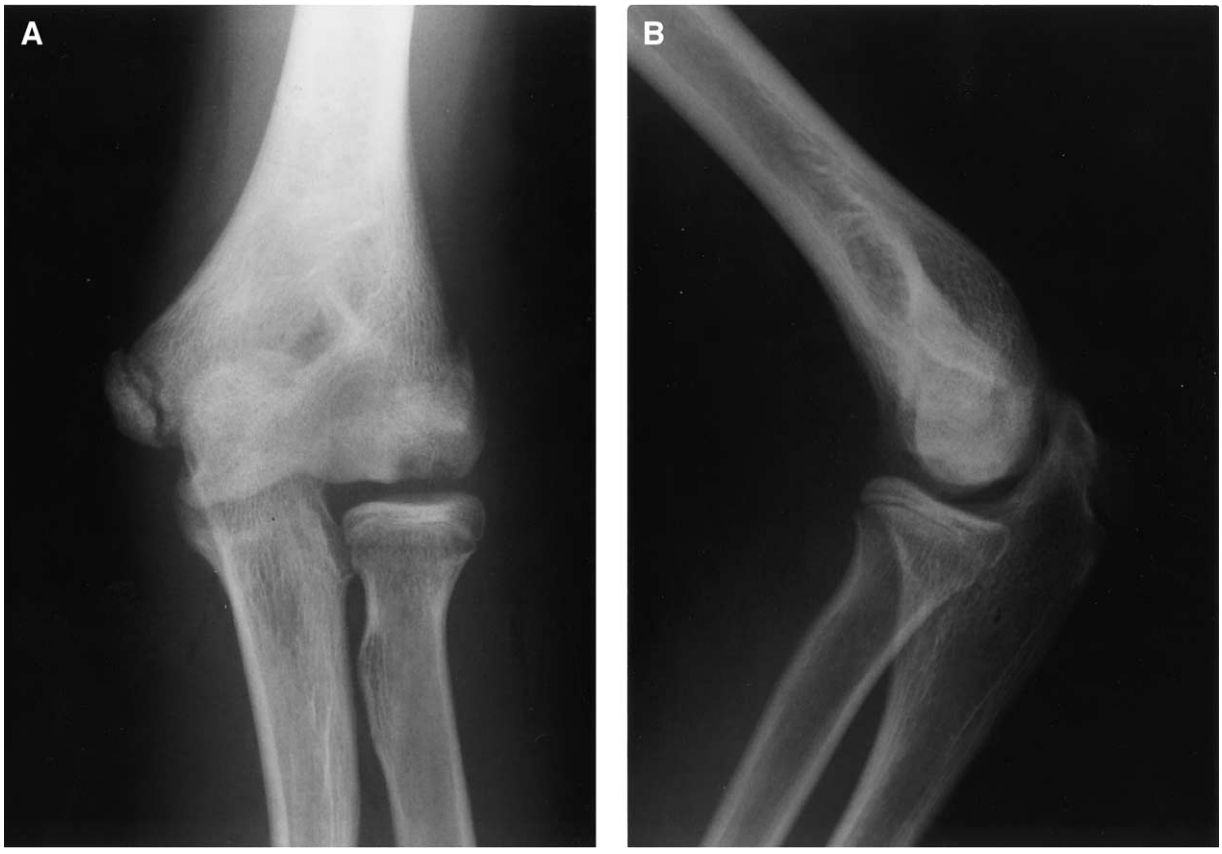

Figure 1 A, An anteroposterior radiograph taken with the elbow in 45° of flexion clearly shows the lesion. **B**, Lateral radiograph of elbow joint.

Controversy surrounds the treatment of osteochondritis dissecans (OCD) of the elbow. Until now, OCD has been treated by arthrotomy with debridement, drilling of subchondral bone,[15,22] and surgical reattachment of the fragment.[3,9-12] In cases in which there are excessively detached fragments of the OCD without a bony segment, however, no previous reports have demonstrated an advantage to fragment fixation or replacement.[2,14,24]

Recently, Brittberg et al[4,5] introduced a new cell technology to treat a cartilage defect of the knee joint, in which cultured autologous chondrocytes in suspension are injected into a cartilage defect after covering the defect with a flap of the periosteum to repair the hyaline cartilage. We modified their surgical procedure using a tissue-engineering technique, in which we cultured au-

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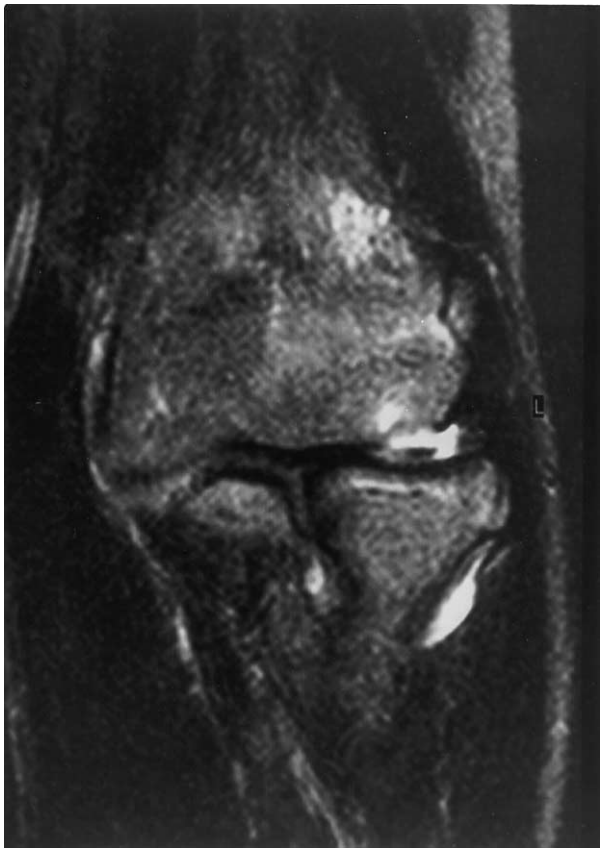

Figure 2 Subsequent magnetic resonance image shows an OCD lesion in the capitellum of the left elbow joint. Detachment of the fragment is seen based on the presence of intervening fluid on T_2-weighted images.

tologous chondrocytes in Atelocollagen gel (Koken, Tokyo, Japan) for 3 weeks before transplantation. This

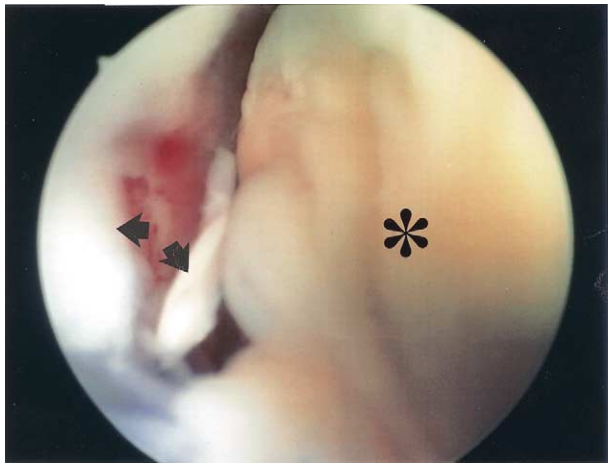

Figure 3 Arthroscopy shows a large articular cartilage defect on the left capitellum. The *down-side arrow* indicates the detached fragment. The *left-side arrow* indicates widely exposed subchondral bone. The *asterisk* indicates the radial head.

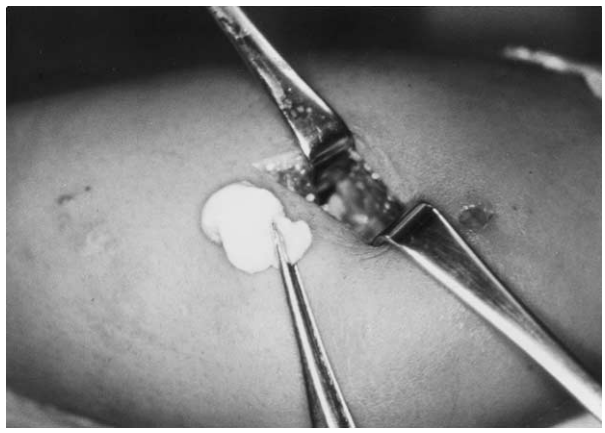

Figure 4 Arthrotomy reveals a large 1.0 × 1.8–cm detached fragment.

modified technique maintains the chondrocyte phenotype, there is little leakage of the grafted chondrocytes from the grafted sites, and the cells in the defect are evenly distributed. We have reported good clinical and arthroscopic outcomes after using the treatment for cartilage defects in the knee joint that resulted from trauma, OCD, chondromalacia, and osteoarthritis.[19-21] We present a patient with OCD of the elbow who underwent transplantation of tissue-engineered cartilage, with a good clinical and arthroscopic outcome after a 2-year follow-up.

CASE REPORT

A 14-year-old boy, who had been a baseball player for 5 years and was a left-handed pitcher, presented with a history of a painful left elbow of 4 years' duration and restricted range of motion of 2 months' duration. He complained of pain in the left elbow while pitching. Physical examination revealed slight swelling of the left elbow, tenderness on the capitellum, and limited range of motion from 15° to 135° with pain during maximal extension. Pronation and supination were not restricted.

Radiographs showed an extensive lucent area and a small loose fragment with peripheral bone sclerosis in the left capitellum (Figure 1, *A* and *B*). Magnetic resonance imaging (MRI) documented an OCD lesion in the capitellum of the left elbow. Detachment of the fragment was noted based on the presence of intervening fluid seen on T_2-weighted images (Figure 2). Arthroscopy showed a large articular cartilage defect on the capitellum, with widely exposed subchondral bone (Figure 3). A fragment of peeled cartilage was attached loosely to the front of the lesion. The detached fragment was 1.0 × 1.8 cm, which was larger than expected (Figure 4). To prevent progression of the osteoarthritic change, we treated the cartilage defect with transplantation of a cartilage-like tissue (a tissue-engineered cartilage) using a tissue-engineering technique.

The gel was transplanted 21 days after harvest of the cartilage. With the patient under general anesthesia, the capitellum was exposed through a lateral approach under

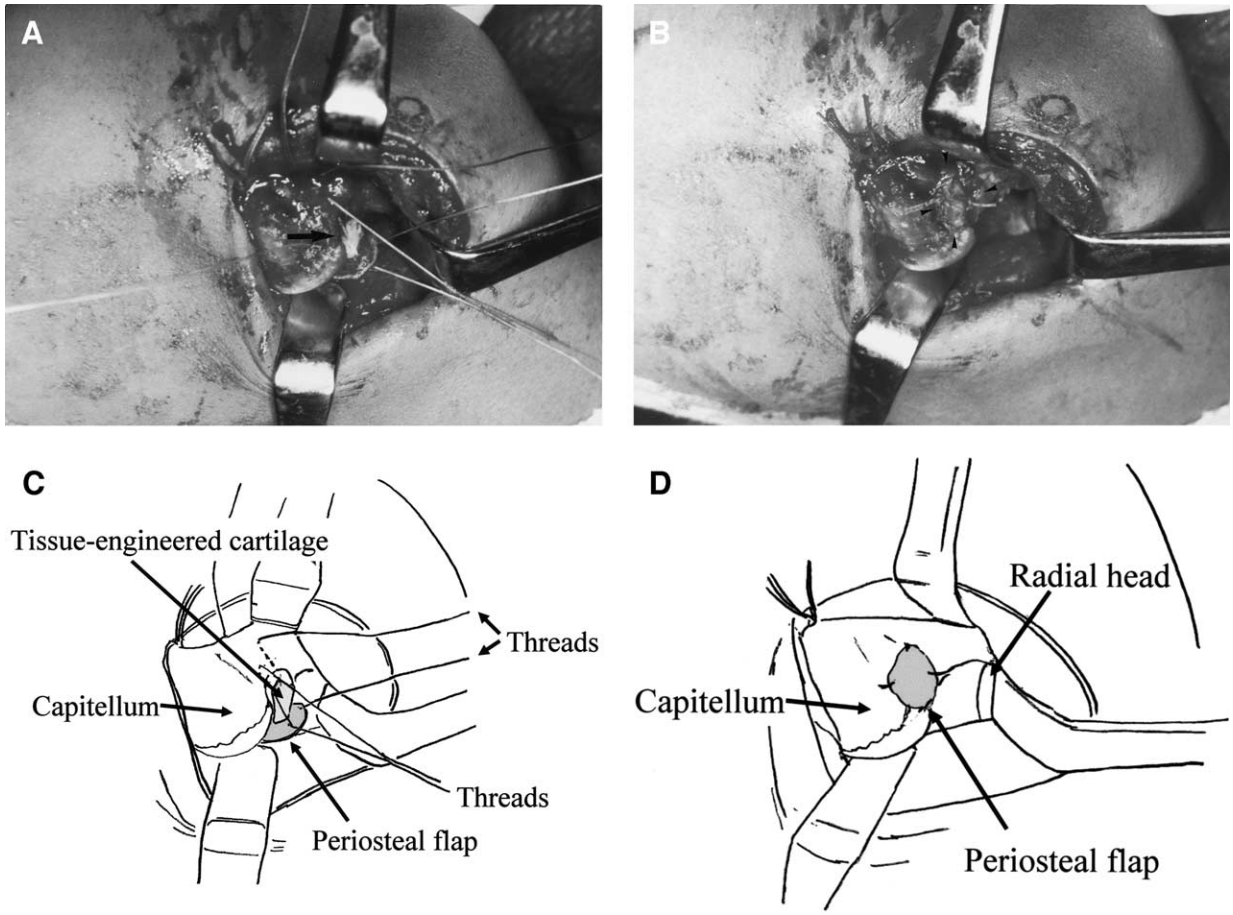

Figure 5 Transplantation of tissue-engineered cartilage into the cartilage defect of the humeral capitellum. **A**, Our surgical procedure. The *arrow* indicates the transplant beneath the periosteal flap. **B**, Complete suture of the periosteal flap. The *arrowheads* indicate the graft site. **C**, The schematic diagram of figure A. **D**, The schematic diagram of figure B.

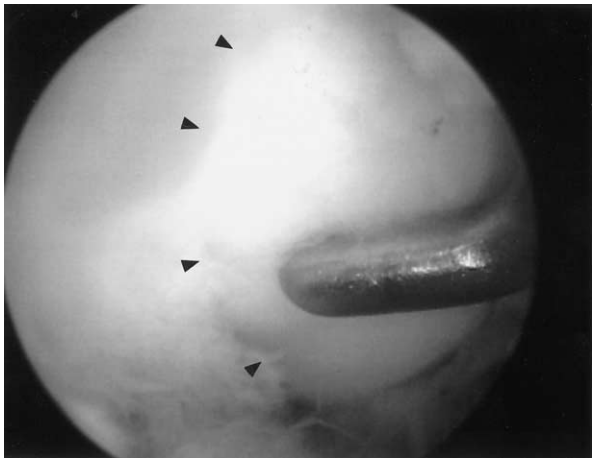

Figure 6 Arthroscopy 24 months after transplantation. The arrowheads indicate the grafted border.

tourniquet control. The chondral lesion was debrided as far as the normal surrounding cartilage and subchondral bone was visible. The defect was covered with a sutured periosteal flap taken from the proximal medial tibia. The flap was fitted and sutured to the surrounding rim of the normal cartilage with interrupted 5-0 nylon and partially pulled out 4-0 Vicryl sutures (Matudaika Co, Tokyo, Japan) with the deep cambium layer facing the subchondral bone plate. After half of the border of the flap was sutured, the tissue-engineered cartilage was placed into the defect, and the remaining border of the flap was sutured (Figure 5, *A* and *B*). The joint capsule, fascia, and skin were sutured in separate layers.

A plaster cast was applied to the left elbow for 2 weeks. Three weeks after transplantation, active motion of the joint was initiated. Three months after transplantation, the patient had no pain, swelling, or locking of the left elbow joint. The range of motion was from 5° to 140°. Arthroscopy performed 3 months after surgery revealed that the transplants, which were white and slightly fibrillated but soft in both the central and marginal areas, were level with the surrounding articular surface. Arthroscopy 24 months after transplanta-

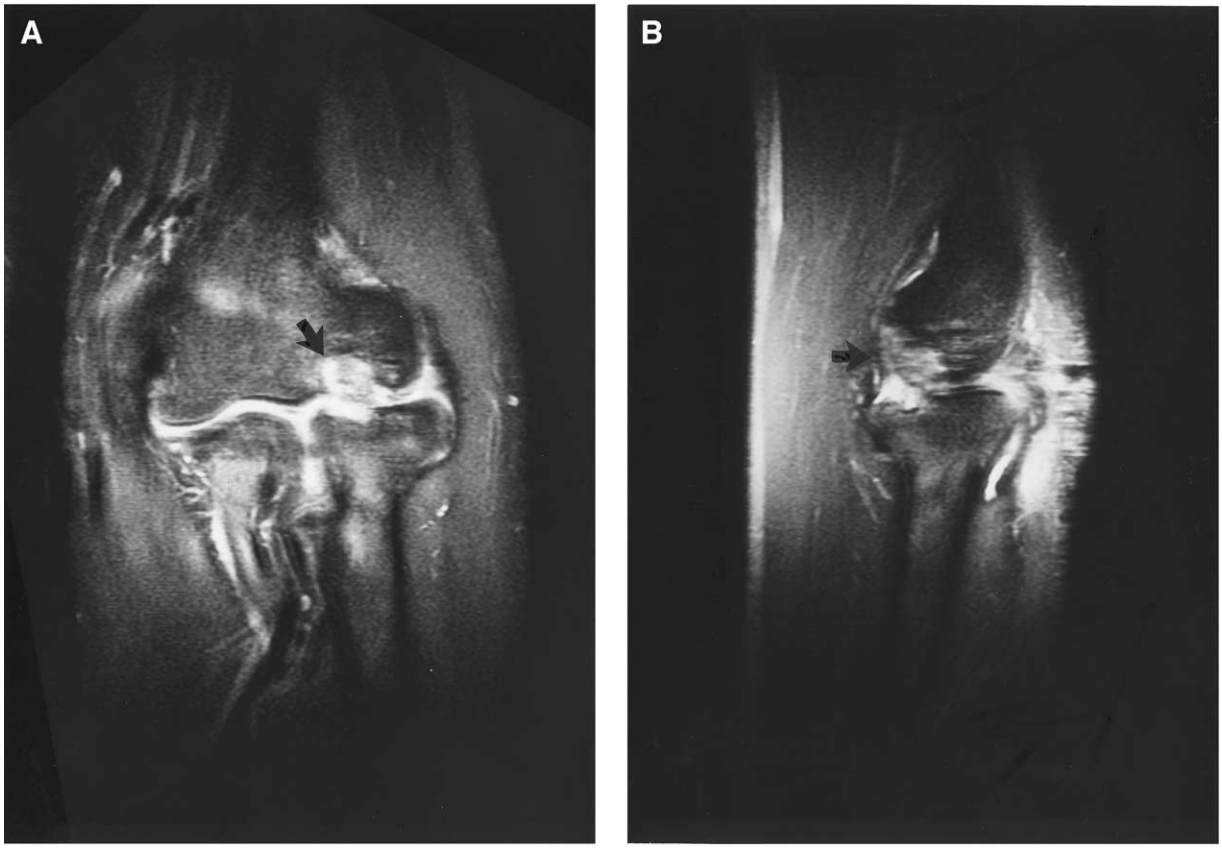

Figure 7 Magnetic resonance images (T_2-weighted) 24 months after transplantation. The *arrow* indicates the transplant beneath the periosteal flap. MRIs show the tissue-engineered cartilage of high signal intensity at the grafted site with a subchondral area of high signal intensity. **A**, Coronal section. **B**, Sagittal section.

tion revealed that the transplant had a smoother surface and was more congruous and harder than at 3 months, which was determined by probing without deteriorating the facing cartilage of the radial head (Figure 6). MRI showed the tissue-engineered cartilage with high signal intensity at the grafted site with a subchondral area of high signal intensity (Figure 7). At 24 months after transplantation, the patient had no pain in the elbow and he was able to perform his daily activities without restriction. His elbow could be actively extended to 5° and flexed to 140° without pain, representing an improvement of 15°.

DISCUSSION

Several long-term follow-up studies of OCD of the humeral capitellum have been published.[2,16,25] According to their results, the residual elbow symptoms related to daily activities in approximately 50% of patients may be associated with advanced lesions, osteoarthritis of the elbow, and a large osteochondral defect. If there is a large osteochondral defect in the capitellum, as in our case, a poor outcome over the long term may be inevitable. Therefore, repair of excessive articular cartilage defects caused by OCD should be considered to prevent future degeneration.

Several authors have reported reconstruction of the cartilage defect by periosteal and perichondral grafting,[1,23] articular cartilage allograft transplantation,[18,26] or autologous osteochondral grafting.[7,8] However, periosteal and perichondral grafting may repair the defect with fibrocartilage without hyaline cartilage, although there is a risk of donor-site morbidity. Osteochondral grafting has the added advantage of not only transplanting articular cartilage but also reconstituting subchondral bone and has been popularized for use in small, isolated, contained articular cartilage defects.[7,8,13] Nakagawa et al[17] reported good results at follow-up 35 months after osteochondral grafting to the capitellum. However, they also pointed out some peculiarities associated with the capitellum, in that the operative field on the humeroradial joint was small and narrow, and they could not properly insert the equipment required for the osteochondral graft perpendicular to the joint surface when they used the osteochondral autograft transfer system. In addition, they stated that an additional wedge osteotomy should be performed to achieve proper alignment of the osteochondral cylindrical grafts and to decrease the pressure on the graft, which are essential to the good outcome of this procedure.

We treated the patient under discussion with transplantation of tissue-engineered cartilage into the excessive cartilage defect without performing an additional osteotomy. We modified the procedure of Brittberg et al[4,5] for cultivat-

ing chondrocytes embedded in the commercially available form of injectable collagen, Atelocollagen.[19-21] In our procedure,[19-21] chondrocytes were isolated from the detached cartilage fragment with enzymatic digestion. The isolated cells were then embedded in 1 mL of Atelocollagen gel and cultured in Ham-F12 medium (Biowhittaker Co, Walkersville, USA) supplemented with autologous serum. We chose Atelocollagen because the antigenic determinants on the peptide chains of type I collagen reside mainly in the telopeptide regions.[6] Atelocollagen has been used clinically in plastic surgery and dermatology. Our in vitro and in vivo experimental results[11,18-21,27] supported the hypothesis that transplanting chondrocytes cultured in Atelocollagen gel would be effective in repairing articular cartilage defect, not only in animals but also in human beings, by maintaining the chondrocyte phenotype, reducing the risk of leakage of grafted cells, and distributing grafted cells evenly throughout the grafted site. The cell density of the chondrocytes in the Atelocollagen gel was 2×10^6/mL. After 3 weeks of culture, the autologous chondrocyte–Atelocollagen gel complex had acquired a jelly-like hardness. Our previous basic studies showed that our technique is more effective than that in monolayer cultivation,[11,27] because it maintains the chondrocyte phenotype, there is a low risk of leakage of the transplanted chondrocytes, and there is homogenous distribution of the grafted chondrocytes in the defect. Although chondrocyte transplantation was proposed as a new approach to treat OCD of the elbow,[22] no report in which this procedure was used has been published. The current case is the first one in which the chondrocyte-Atelocollagen complex made by a tissue-engineering technique (tissue-engineered cartilage) was transplanted into the cartilage defect of the capitellum.

Although this technique requires that a periosteal flap be taken from the anteromedial site of the tibia, no adverse effects have been observed on the leg. Longer follow-up times and comparisons with other techniques are needed from the viewpoint of clinical outcome, arthroscopic appearance, histology, and MRI; follow-up 24 months after the operation, however, indicated that this procedure may achieve a good clinical and arthroscopic outcome for the treatment of excessive OCD of the elbow.

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