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Case report

Cartilage regeneration in osteoarthritic knees treated with distal femoral osteotomy and intra-lesional implantation of allogenic human umbilical cord blood-derived mesenchymal stem cells: A report of two cases

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ABSTRACT

Background: To treat lateral compartment osteoarthritis caused by a valgus deformity, partial or total knee joint arthroplasty is recommended. However, for young patients, joint preservation surgery such as distal femoral osteotomy (DFO) can be an alternative treatment option. Combined cartilage defects of lateral compartment osteoarthritis can be restored by human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSCs). This case report presents the results of DFO and hUCB-MSC implantation for treating two patients with valgus deformity who had lateral compartment osteoarthritis.

Case presentation: Two middle-aged patients with lateral compartment osteoarthritis and valgus deformity were treated using DFO and hUCB-MSC implantation. They recovered sufficiently to perform moderate exercise one year after surgery. The International Knee Documentation Committee, visual analog scale, and Western Ontario and McMaster Universities Osteoarthritis Index scores showed continuous improvement after surgery. Cartilage regeneration of International Cartilage Repair Society Grade 1, which was similar to normal, was observed in both patients through second-look arthroscopy. With time, the modified two-dimensional magnetic resonance observation of cartilage repair tissue scores also increased in both cases.

Conclusion: This is the first case report detailing the results of treating lateral compartment osteoarthritis using hUCB-MSCs and DFO. In conclusion, this can be considered a new treatment option for such cases.

1. Introduction

Patients with valgus deformity of the knee often have pain and are eventually diagnosed with osteoarthritis (OA) due to the constant loading pressure on the lateral compartment of the knee [1–4]. Lateral compartment involvement with valgus deformity

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is much less common than medial compartment involvement with varus deformity in the knee joint. In order to treat lateral compartment OA caused by valgus deformity, partial or total knee joint arthroplasty is recommended [5]. However, in young patients, joint preservation surgery such as distal femoral varus osteotomy (DFO), which shifts the mechanical axis from the lateral side to the medial side, can be an alternative treatment because of the limitations of arthroplasty, such as prosthesis wearing [3].

Numerous cases have shown that patients with valgus deformity have improved clinical results after their mechanical axis is shifted through DFO [3–6]. However, in DFO, although the mechanical axis of the knee joint is shifted to the medial compartment, the cartilage defect in the lateral compartment cannot be repaired.

No studies have investigated cases of lateral compartment OA with valgus deformity treated by correction of the mechanical alignment by DFO and regeneration of the cartilage defect by using human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSCs). This paper describes two cases of lateral compartment OA treated by correction of the mechanical alignment by DFO and regeneration of the cartilage defect by using hUCB-MSCs.

1.1. Case reports

1.1.1. Case 1

A 50-year-old female patient with left knee pain visited the outpatient department after visiting another hospital. The x-ray obtained from the previous hospital showed valgus deformity (tibiofemoral angle: 3.5°), and magnetic resonance imaging (MRI) showed a lateral meniscus tear and defects of the lateral femoral condyle (LFC) and lateral tibial condyle (LTC) cartilage. She had undergone lateral meniscectomy 17 months ago but had no improvement of symptoms. She complained of left knee pain when weight-bearing and aggravated pain when walking down stairs. The follow-up x-ray obtained at the current hospital showed an increased valgus tibiofemoral angle of 5.5°, and follow-up MRI showed additional cartilage damage of the patella and trochlea. The treatment plan was to correct the valgus deformity by performing DFO and repair the cartilage defects by using hUCB-MSCs. The DFO was performed by using a lateral open wedge technique, and the plate was fixed with a Tomofix plate (Depuy Synthes, Raynham, MA, USA).

The patient used a knee brace for eight weeks post operation with nonweight-bearing crutches. From eight to 12 weeks, she was allowed to walk with a partial-weight-bearing crutch. The patient regularly participated in range of motion exercises with a continuous passive motion machine and quadriceps strengthening exercises, and used ankle pumps from four days to 12 weeks post operation.

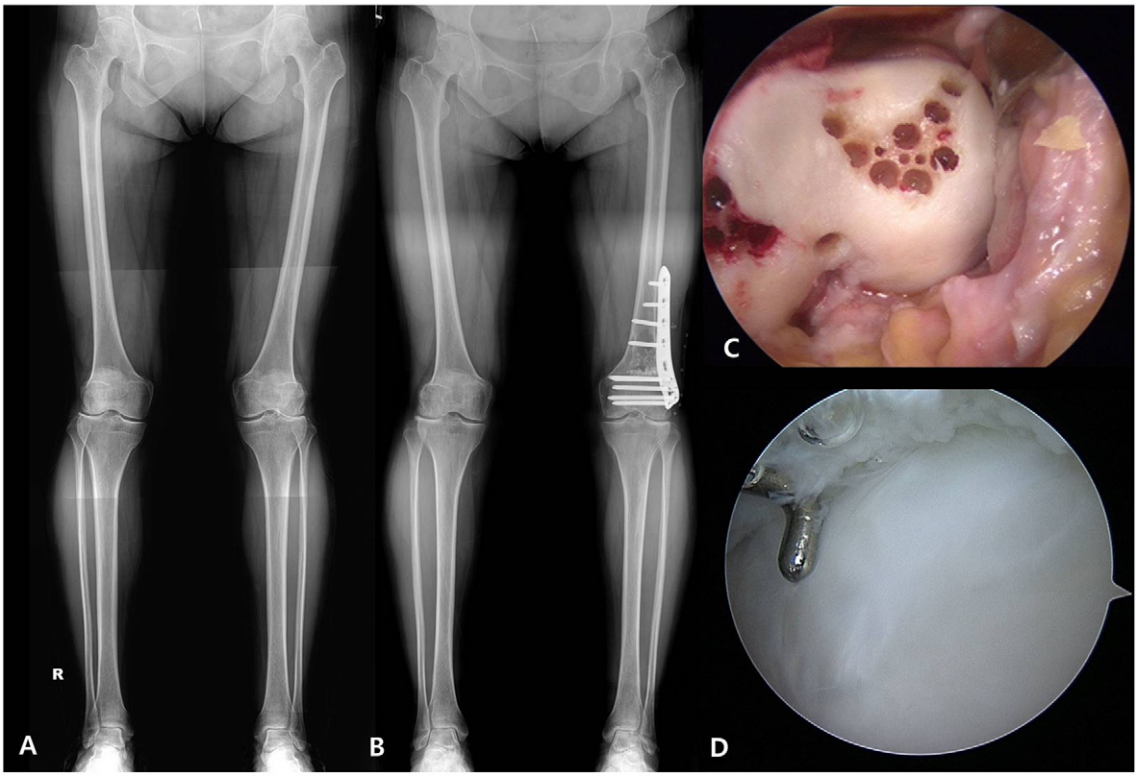

Figure 1. A. A 50-year-old female patient's pre-operative standing radiograph shows left knee valgus deformity (femorotibial angle: 5.5°). **B.** Postoperative standing radiograph shows left knee valgus deformity correction after distal femoral varus osteotomy. **C.** A mixture of sodium hyaluronate and human umbilical cord blood-derived mesenchymal stem cells was implanted in the holes of the left lateral femoral condyle. **D.** The second-look arthroscopic image at 18 months post operation demonstrates cartilage regeneration at the left lateral femoral condyle.

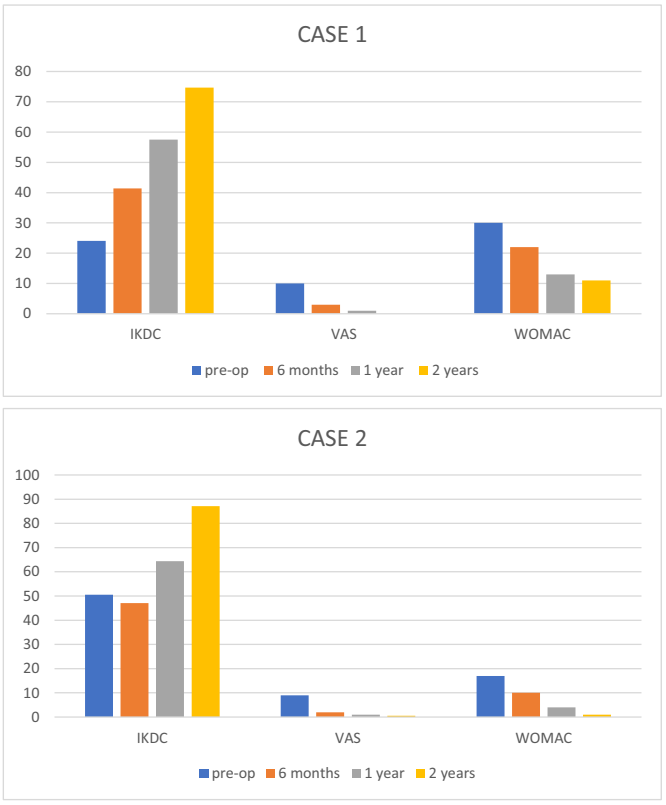

Figure 2. Clinical scores of the two cases. VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; IKDC, International Knee Documentation Committee score.

Eighteen months after her operation, a second-look arthroscopy was performed with plate removal. Cartilage regeneration of the LFC, LTC, patella, and trochlea was International Cartilage Repair Society (ICRS) Grade 1 and showed similar hardness when pressed with the probe (Figure 1 A-D). The International Knee Documentation Committee (IKDC) score was 24.1 pre-operatively, 41.4 at six months post operation, 57.5 at one year post operation, and 74.7 at two years post operation. The visual analog scale (VAS) score was 10 pre-operatively, and it decreased to thee, one, and 0 after six months, one year, and two years post operation, respectively. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score was 30 pre-operatively, and it decreased to 22, 13, and 11 after six months, one year, and two years post operation, respectively (Figure 2). The tibiofemoral angle was corrected to 2.4° varus. Magnetic resonance imaging performed at five months and 16 months post operation showed that the two-dimensional magnetic resonance observation of cartilage repair tissue (2D MOCART) score increased from 30 to 60. No complications occurred at the site of DFO.

1.1.2. Case 2

A 48-year-old male patient complained of pain in the lateral aspect of his right knee and instability during descending sloped surfaces. The x-ray showed a valgus deformity (tibiofemoral angle: 10°), and MRI showed cartilage defects at the LFC, LTC, and trochlea, with rupture of the anterior cruciate ligament (ACL). The hUBC-MSCs were implanted at the LFC, LTC, patella, and trochlea, and DFO by medial closed wedge osteotomy was performed to correct the valgus deformity using an OhtoFix plate (Ohtomedical, Goyang, Korea).

The patient used a knee brace for eight weeks post operation with non-weight-bearing crutches. From eight to 12 weeks, he was allowed to walk with a partial-weight-bearing crutch. The patient regularly participated in range of motion exercises with a continuous passive motion machine and quadriceps strengthening exercises, and used ankle pumps from four days to 12 weeks post operation.

The ACL reconstruction was performed at 14 months after the first operation along with plate removal. Intraoperatively, the area of the previous cartilage defect was examined. The cartilage regeneration status was ICRS Grade 1, and hardness of the cartilage was similar to that of normal cartilage (Figure 3 A-D). The IKDC score was 50.5 pre-operatively, and it increased to 47.1, 64.4, and 78.1 at six months, one year, and two years post operation, respectively. The VAS score was nine pre-operatively, and it decreased to two, one, and 0.5 after six months, one year, and two years post operation, respectively. The WOMAC score was 17 pre-operatively, and it decreased to 10, four, and one after six months, one year, and two years post operation, respectively (Figure 2). The varus tibiofemoral angle was corrected to 1.3°. Magnetic resonance imaging was performed at five months

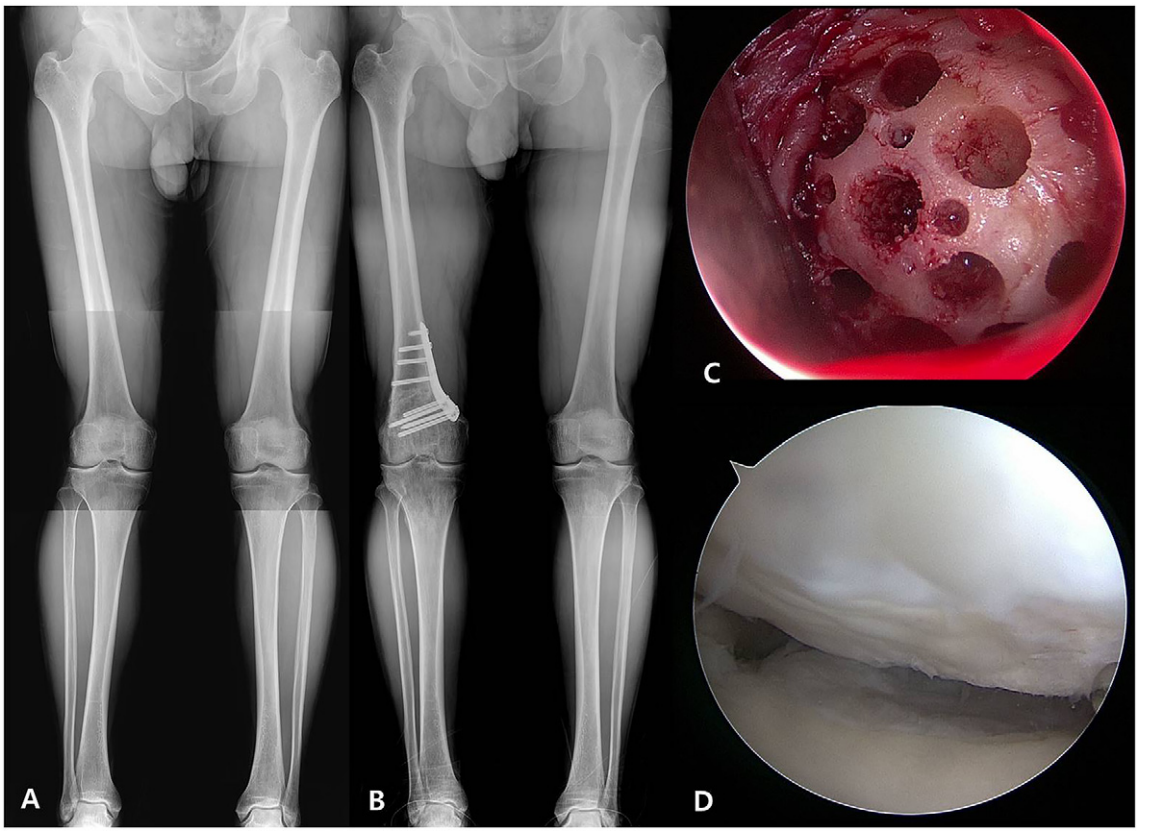

Figure 3. A. A 48-year-old male patient's pre-operative standing radiograph shows right knee valgus deformity (femorotibial angle: 10°). **B.** The postoperative radiograph shows right knee valgus deformity correction after distal femoral varus osteotomy. **C.** A mixture of sodium hyaluronate and human umbilical cord blood-derived mesenchymal stem cells was implanted in the holes of the right lateral femoral and tibial condyle. **D.** The second-look arthroscopic image at 26 months post operation demonstrates cartilage regeneration at the right lateral femoral and tibial condyle.

and 26 months post operation, and the 2D MOCART score improved from 30 to 80. There were no complications at the site of DFO. Screw removal was performed at one year after ACL reconstruction along with third-look arthroscopy. Cartilage regeneration and the ACL graft status were good.

1.2. Surgical technique

After the epidural block, routine skin preparation for orthopedic surgery was performed. A pneumatic tourniquet was inflated to 300 mmHg. After diagnostic arthroscopy, unstable cartilage at the lateral tibia was removed by performing curettage from the figure-four position, and it was microfractured using an awl.

The LFC was exposed by dissecting the lateral retinaculum and the capsule through a five-centimeter longitudinal incision just lateral to the patella. Unstable cartilage was removed, and the margin was debrided perpendicularly. By using a four-millimeter drill bit, holes were made every two millimeters. Between the holes, micro-drilling was performing using a 2.0-mm Kirschner (K)-wire. Water was removed from the joint by using suction and gauze. Finally, the hUCB-MSCs (Cartistem; Medipost, Seoul, Korea) mixed with sodium hyaluronate were implanted in the holes up to the articular surface, and the wound was closed with sutures.

A 15-cm longitudinal incision was made from the medial surface of the vastus medialis above the patella. Then, vastus medialis was dissected and retracted using a Bennet retractor. The periosteum was dissected to expose the femur. The K-wire was inserted from the osteotomy site to the lateral epicondyle under image intensification. A second K-wire was inserted parallel behind the first K-wire. The level of osteotomy was drawn on the bone, and each wire was inserted so their ends met. A cut was made on the bone between the K-wires, using an oscillating saw, and multiple drilling was performed to prevent fracture of the lateral femur. Varus force was carefully applied. Next, the alignment was evaluated by placing the metal rod in the middle of the femoral head and ankle. The OhtoFix plate (Ohtomedial) was placed on the femur and used to fix the distal part by locking it with screws.

In the case of lateral open wedge DFO, after hUCB-MSCs were implanted, as described earlier, a 15-cm longitudinal incision was made. Then, the iliotibial band was cut to elevate the vastus lateralis. Next, the lateral intermuscular septum was dissected to expose the lateral distal femoral shaft.

Under fluoroscopic guidance, a K-wire was inserted proximally, three centimeters distally from the lateral femoral epicondyle, and pushed further in the direction of the base of the metaphyseal flare of the proximal medial epicondyle. Another K-wire was inserted parallel to the already inserted K-wire. Under guidance of the inserted K-wire, osteotomy was performed with an oscillating saw until it reached one centimeter before the medial cortex. Then, using laminar spreaders, the opening wedge was made at the osteotomy site according to the pre-operative plan. In order to assess alignment, a metal rod was placed in the middle of the femoral head and the ankle. The locking Tomofix plate (Depuy Synthes) was placed at the osteotomy site to fix the distal part using locking screws and, finally, proximal fixation was completed.

2. Discussion

Many clinical researchers have proven that DFO is effective in treating patients with valgus deformity of the knee with lateral compartment OA [2–4]. Finkelstein et al. reported that the 10-year survival rate was 64% in 20 patients with valgus deformity of the knee with lateral compartment OA after undergoing DFO [1]. Backstein et al. reported that after 123 months of follow-up in 38 patients; 60% of them showed good or excellent results, and the 10-year survival rate was 82% [6]. Wang et al. reported that the 10-year survival rate was 87% in 30 patients [4].

Shifting the mechanical axis through DFO does not repair the cartilage defect caused by lateral compartment OA. Additionally, in the case of varus deformity of the knee with medial compartment OA, shifting the mechanical axis laterally through high tibial osteotomy (HTO) does not repair cartilage defects. However, one report showed that a cartilage defect was replaced by fibrous cartilage after HTO [7]. Compared with HTO alone, HTO with cartilage regeneration showed better results in many research studies [7,8]. Therefore, in Case 1, it was assumed that DFO with cartilage repair would have a better result than DFO alone, even though total lateral meniscectomy is a contraindication of cartilage repair.

The hUCB-MSCs rarely cause an immune reaction, have high cell activity, are not affected by the patient's age, and can be extracted at any time in any quantity [9]. Park et al. reported the results after a seven-year follow-up of repaired cartilage defects with hUCB-MSCs, and they showed good cartilage regeneration with improved clinical results without any severe complications [10].

In the two presented cases, lateral open wedge technique and medial closed wedge distal femur varus osteotomy were used to correct the valgus deformity, and hUCB-MSCs was implanted in the cartilage with defects. After the follow-up periods, second-look arthroscopy was performed to determine whether the cartilage regeneration was ICRS Grade 1. The 2D MOCART score was measured by MRI, and the score was higher based on the last follow-up image than based on the first follow-up image. The WOMAC, IKDC, and VAS scores were measured after six months, one year, and two years post operation, and they improved within a timely manner.

In Case 2, ACL reconstruction was performed at 14 months after cartilage reconstruction. In order to treat the patient's complex problems, distal femoral osteotomy, cartilage repair, and ACL reconstruction could have been performed simultaneously. However, there were several risks to consider (i.e., prolonged operative time, interrupted ACL tunnel placement, possibility of another cartilage repair failure, and postoperative knee joint stiffness) [11]. It was believed that after osteotomy, protected weight-bearing could reduce the instability-related problem, and osteotomy and cartilage repair were performed first.

In this case series, DFO together with cartilage repair for the treatment of lateral compartment OA with knee valgus deformity improved the clinical results. However, as this is a report of only two cases, further research is necessary to prove that DFO with cartilage repair is superior to DFO alone.

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Declarations of competing interest

None.

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Data statement

All data included in the manuscript are available upon request.

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