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Case report

# Repair of large full-thickness cartilage defect by activating endogenous peripheral blood stem cells and autologous periosteum flap transplantation combined with patellofemoral realignment

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ABSTRACT

Minimal-invasive procedure and one-step surgery offer autologous mesenchymal stem cells derived from peripheral blood (PB-MSCs) a promising prospective in the field of cartilage regeneration. We report a case of a 19-year-old male athlete of kickboxing with ICRS grade IV chondral lesions at the 60° region of lateral femoral trochlea, which was repaired by activating endogenous PB-MSCs plus autologous periosteum flap transplantation combined with correcting the patellofemoral malalignment. After a 7.5 year follow-up, the result showed that the patient returned to competitive kickboxing. Second-look under arthroscopy showed a smooth surface at 8 months postoperation. The IKDC 2000 subjective score, Lysholm score and Tegner score were 95, 98 and 9 respectively at the final follow up. CT and MRI evaluations showed a significant improvement compared with those of pre-operation.



## 1. Introduction

Articular cartilage is an avascular and aneural tissue, and the treatment of cartilage lesions is challenging because of its inherently poor healing ability. Current clinical treatments for large full-thickness cartilage lesions could lead to several problems, such as the donor site morbidity with mosaicplasty [1], the possibility of transmitted diseases and the inferior integration of allogeneic osteochondral transplantation [2], two operations for autologous chondrocyte implantation (ACI) procedure [3], dedifferentiation upon expansion and fibrocartilage repair following the transplantation using ACI and matrix-associated autologous chondrocyte implantation (MACI) [4], which are difficult to achieve a complete hyaline cartilage repair [5]. Nevertheless, stem cell-based therapy with a new kind of seeded cell will bring a new hope for those problems. Recently mesenchymal stem cells (MSCs) are an alternative for cartilage repair because of their ample sources, strong proliferation ability and differentiation potential compared to terminally differentiated chondrocytes. Generally, bone marrow (BM) is the main and traditional source of MSCs, but BM-MSCs have their own problems, in terms of limited number and highly-invasive procedures. Minimal-invasive procedure and one-step surgery make mobilized MSCs derived from peripheral blood (PB-MSCs) a promising candidate in the field of cartilage regeneration. Here we report a case of using mobilized endogenous PB-MSCs combined with autologous periosteum flap transplantation and patellofemoral realignment to repair large full-thickness articular cartilage defect of a patient with satisfactory result.

## 2. Case report

A 19-year-old male athlete of kickboxing presented with a five-year history of right knee sprain, and buckling at extension position during training 20 days ago, followed by the pain at the anterior knee, swelling and limited range of motion (ROM). Physical therapy and drug treatment failed to relieve his symptoms. Physical examination revealed that the knee alignment was normal, ROM was limited for flexion (120°), atrophy of the right quadriceps (the diameter was 43 cm on the right and 47 cm on the left), patellofemoral compression pain positive, patellofemoral crepitus positive, J sign positive, and knee extension pain with resistance was positive at 60°. The clinical signs of meniscal and cruciate ligament were negative. Plain radiographs showed subchondral defect at lateral trochlea of the femur and subchondral bone sclerosis around the defect. Laurin view from the X-ray plates showed subluxation of the patella in 30°, 60° and 90° flexion. The CT measurements showed that tibial tubercle–trochlear groove (TT–TG) distance was 20 mm, patellofemoral angle and patella congruence angle were all abnormal. Preoperative MRI showed that cartilage and subchondral bone injury at the trochlea, and the defect area measured as approximately 4 $cm^2$ on T2-weighted images in the sagittal, coronal, and axial planes.

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### 3. Mobilization and collection of PB stem cells

Currently, the full-thickness cartilage lesion was too large to be repaired by microfracture and mosaicplasty procedures routinely used in our hospital. There is no lab that has been certified by the State Food and Drug Administration of China (SFDA) to culture chondrocytes derived from patient's cartilage and then be transferred to the same patient, therefore, there's no legal-cultured chondrocytes from the lab that could be obtained to repair the large chondral lesion. After a comprehensive preoperative evaluation was performed in the Inpatient Department of Sports Medicine, the patient was transferred to the Inpatient Department of Hematology for PB stem cell collection where the patients' PB stem cells could be legally collected and autologously transplanted to the patients. In general, PB stem cells were mobilized by recombinant human granulocyte colony-stimulating factor (rhG-CSF, Granocyte, Chugai Pharmaceutical Co. Ltd., Japan). After conventional laboratory tests, the BM aspiration biopsies were carried out from the right posterior superior iliac spine for cytological examination, and the result of which showed normal. Then the patient was administered rhG-CSF 250 μg subcutaneously once a day to stimulate stem cells into PB. After 5 days, the number of blood leukocytes was monitored daily to assess the effect of the mobilization. The number of blood leukocytes was not rising until on the 7th day, it reached the desired level ($34.96 \times 10^9$/L), PB stem cells were collected with a CS 3000-PLUS blood cell separator (Baxter, USA). Then the patient and collected cells were transferred back to the Inpatient Department of Sports Medicine again for cartilage repair operation.

### 4. Surgical procedures

During the operation, arthroscopic examination showed: $2 \times 2$ cm$^2$ ICRS grade IV chondral lesions at the 60° region of lateral femoral trochlea [6]. Ten centimeter curved incision was made at medial patella, then the patellar tendon and tibia tubercle were created and the patella was dislocated laterally. Cartilage lesion was debrided until minor bleeding was seen from subchondral bone (Fig. 1), the unstable cartilage was also taken away until a stable vertical cartilage rim appeared. The sterilized silver foil from the suture packaging was used to measure the size and shape of the defect. The autologous periosteum was harvested from the anteromedial side of the tibia tubercle. The silver foil was tailored as a template in the same size and shape of the defect, and the periosteal flap was cut out to fit the template, then, the periosteal flap was sutured to the normal cartilage's surface around the defect site with the germinal layer of the periosteum towards the outside using a 7-0 Vicryl suture. The rim of the suture site was sealed with fibrin glue. Two milliliter concentrated PB stem cell suspension was injected by using an 18-gauge needle under the periosteum flap whose rim-cartilage interface was sealed with fibrin glue (Fig. 2). In order to correct the abnormal TT–TG, patella congruence angle and patellofemoral angel, the tibia tubercle was transferred 1.5 cm medially and refixated to the new site with two cortical screws after the lateral patellar retinaculum was released and the medial retinaculum was shortened.

### 5. Post-operative rehabilitation

The patient was advised to follow strict rehabilitation program after the operation. Immediately after the operation, the knee was immobilized with hinged knee brace. Excessive intraarticular forces should be avoided to protect the graft during the early postoperative period. Continuous passive motion (CPM), isometric leg muscle strength training and gradually increased weight-bearing exercises should be the initial steps of the rehabilitation process. At the 8th week after operation the ROM was required to obtain normal movement as quickly as possible. Full weight bearing was allowed and the brace protection was not necessary at the end of the 8th week after operation. The patient could start to swim and jog at 3 months and return to the normal training at 6 months after surgery.

### 6. Follow-up and evaluation

MRI was evaluated for the involved knee 22 days after operation. The two screws for transferred tibia tubercle fixation were removed and the second-look arthroscopy was undertaken, the repaired site was evaluated 8 months after operation. The patient completely resumed training 9 months after surgery, the preoperative signs and symptoms disappeared. MRI was taken for the second time at 2.5 years after operation for the cartilage repaired knee. The final follow-up took place at 7.5 years after operation including: physical examination the same as pre-operation; X-rays, CT and MRI; Tegner, Lysholm and IKDC 2000 scores.

#### 7. Result

Second-look under direct arthroscopic visualization 8 months postoperation (Fig. 3): the repaired site showed a smooth surface without cracks, but slightly yellowish and shallow compared with the surrounding normal cartilage; the texture was not soft with probe; and some small blood vessels appeared surrounding the repair site. There was no evidence of abnormal calcification or necrosis. Physical examination revealed that the knee alignment was still normal as shown in the final follow-up; the ROM was normal compared with 120° flexion before operation; patellofemoral compression pain, patellofemoral crepitus, J sign and knee pain were all negative during resistance extension in the whole ROM. The IKDC 2000 subjective score, Lysholm score and Tegner score were 95, 98 and 9 respectively at final follow up. Compared CT images of pre-operation with 7.5 years

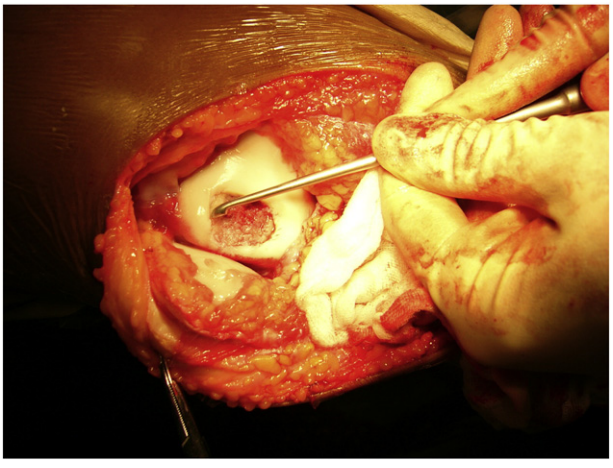

**Fig. 1.** Minor bleeding from the subchondral bone after the curette.

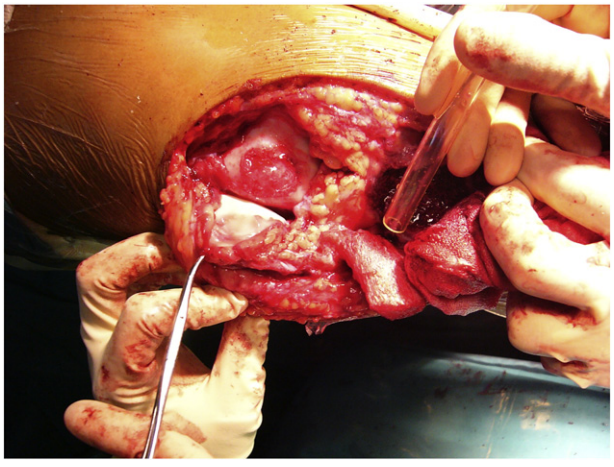

**Fig. 2.** Intraoperative photo of the repair site covered with periosteum flap after injection with PB-MSCs into the lesion.