Case Report

Autologous Chondrocyte Implantation for Traumatic Large Cartilage Defect

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Objective: *The authors report the immediate result (6 months) after Autologous Chondrocyte Implantation (ACI) in clinical and anatomic result with MRI. This is the first report of ACI that provides chondrocyte cells from a domestic lab.*
Material and Method: *ACI was done in a two-stage procedure, first stage via arthroscope to harvest cartilage and detect pathology. The authors found deep cartilage defect at grade 4 according ICRS, area 2.5 cm^2 and near total meniscus tear. Meniscal repair and cartilage shaving were done. Harvesting 300 mg of cartilage was done in this stage. Four weeks later, the second ACI was done. Lateral para-patellar was used. Periosteum was used as chondrocyte suspension and by suture to the healthy cartilage, using prolene interrupted suture in conjunction with fibrin glue to seal the pocket after injecting the cell. Range of motion exercise started on day 2, assisted with continuous passive motion machine. Running and jumping were restricted for 9 months.*
Results: *No complication was found, full range of motion and walking was done at 7-8 weeks post operative. Visual analogue scale improved from 3 points to 0 point. MRI shows evidence of 100% filling of the repair tissue in defect site associated with hypertrophy of the repair tissue above chondral surface.*
Conclusion: *Immediate result of ACI shows improvement in clinical and anatomic that present with MRI. Further follow up and case series is needed.*

Keywords: *Knee injury, Autologous chondrocyte implantation, Cartilage defect*

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The incidence of cartilage injury is high in young active men and women[1-5]. These patients are certain to have high-level activity and life long expectation. The long-term result is not good especially in deep large defect at the weight bearing area. Premature osteoarthritis can be expected[6,7].

Restoration of cartilage defect refers to healing or regeneration of the joint surface, including the hyaline articular cartilage and the subchondral bone. The conventional enhancement procedures of intrinsic healing capacity of cartilage (abrasion chondroplasty, microfracture, subchondral drilling) produce fibrocartilage via recruiting pluripotential cells from the bone marrow by penetrating to the subchondral bone[8]. Fibrocartilage lacks normal biomechanic properties to protect the underlying subchondral bone[9,10,11,14]. The exposure to the repetitive axial and shear forces can lead to progressive pain and disability, especially in a high demand patient[11].

ACI is the technique that used self-patient chondrocyte to duplicate cells *in vitro* until enough cells have been retrieved then re-implant into the defect and using a chondrocyte suspender (periosteum, collagen etc.) to hold in the defect[8,12,13,15].

This is the first case report of the clinical use of ACI technique in Thailand that provided cells by domestic laboratory. The authors present the immediate result of ACI in the treatment of large full thickness cartilage defect in clinical and MRI to represent anatomic resolve.

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Material and Method

A 16-year old high school volleyball athlete presented with knee pain for three months. One and a half years ago, he had non-contact injury at the right knee. After the injury, he had sudden swelling and could not put any weight on his right knee for about 2-3 weeks. The symptom was relieved by self-medication. The pain was worse especially after active activity movement in the last 3 months.

Physical examination: Thai male 185 cm height, weight 80 kg, limping gait, normal vulgus alignment, right thigh atrophy 2.0 cm, fluid shift +ve, lateral joint line pain. Range of motion: normal full extension but loss of 20 degree (120 degree) of flexion when compared to the contralateral knee. Anterior and posterior drawer test –ve, valgus, and varus stress test –ve. McMurray test cannot be done due to pain especially in the last 30 degree of flexion. The plain film of the right knee was within normal limit.

Surgical Technique

The ACI consisted of a two-stage procedure. First, the cartilage was arthroscopic harvested from the non-load bearing part of femoral condyle. After the chondrocyte isolation and incubation in the laboratory, the second procedure, chodrocyte re-implantation into the defect, was performed.

First stage

Knee arthroscopy was done through the anterolateral and anteromedial portal. Meniscus was reduced to its anatomic position, meniscal repair was

Fig. 1

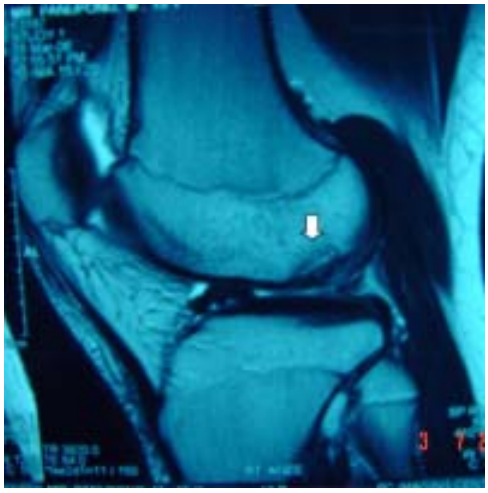

Fig. 2

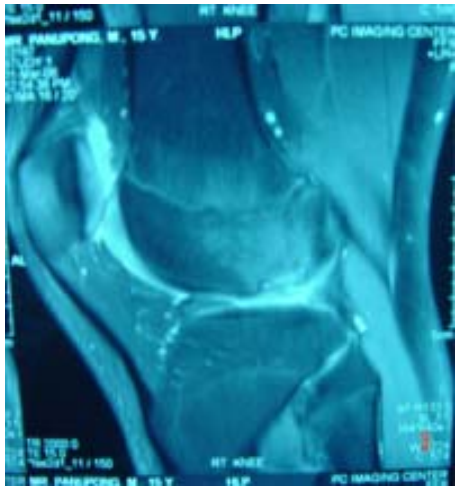

Fig. 3

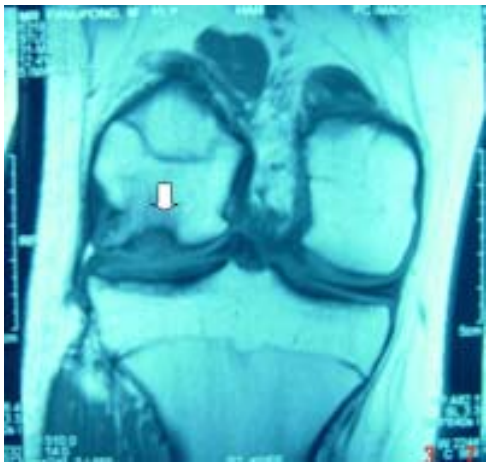

Fig. 4

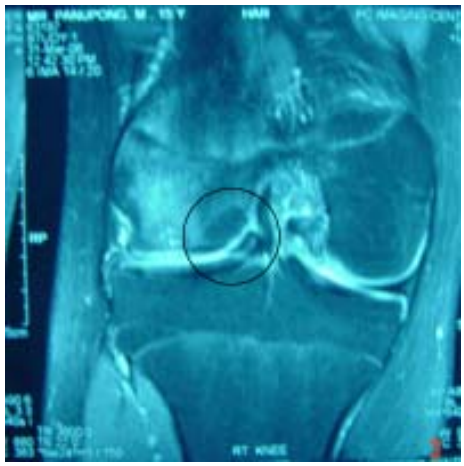

Fig. 1-4 MRI Finding: Saggital and coronal view show cartilage defect with changing signal of subchondral bone (arrow) and the whole meniscus was displaced into intercondylar area (circle)

done by starting from the posterior horn with used all inside suture (FAST-T-FIX, Smith & Nephew), then the medial horn was repaired by inside-out technique finally the anterior horn was fixed with outside-in technique. The cartilage defect was carefully shaved and unstable fragment removed. The chondral lesion was full thickness and can be classified as ICRS grade 4 (severe abnormal), length 1.8 cm and width 1.4 cm or area about 2.5 cm^2 (Fig. 7). Harvest small amount of cartilage slices (weight, 300 to 500 mg) were obtained from a non load-bearing area on the upper lateral femoral condyle of the injured knee. Then cartilages were minced in the media (DMEM; Gibco-BRL) and transferred to the laboratory in the cold chamber.

Chondrocyte culture

The chondrocyte isolation was initiated not later than 6 hours after the operation. The cartilage was washed twice in Ham's F-12 medium (Gibco BRL, Paisley, Scotland) supplemented with gentamicin sulfate (50 mm/mL), amphotericin B (2 mm/mL), and L-acorbic acid (50 mm/mL). The minced cartilage was digested 16-20 hours with clostridial collagenase (0.8 mm/mL, catalog no. C-9407, >1200 IU/mg; Sigma, Freehold, New Jersey) and deoxyribonu-clease (0.1 mm/mL, catalog no. D-5025; Sigma). The isolated cells were resuspended in culture medium containing DMEM/F12 1:1 (Gibco BRL) with 10% serum and gentamicin sulfate (50 mm/mL), amphotericin B (2 mm/mL), L-acorbic acid (50 mm/mL), and L-glutamine (Gibco BRL). The chondrocytes were incubated in 7% Co_2, in air at 37°C (Fig. 8). After one week, the chondrocytes were trypsinized (trypsin-ethylene diaminetetraacetic acid 0.125%) and re-suspended. The 3-4 weeks incubation was needed for an adequate number of chondrocytes (5 x 10^6). The quality-control procedures consisted of photographic recording of cell morphology and SDS-PAGE for collagen type II production. The transplanted chondrocytes were trypsinized and suspended in 0.5 ml. of medium in a cold sterile package.

Second stage

The knee arthroscopy was performed. The arthroscopic finding of the repaired meniscus showed stable repaired meniscus and remodel conforming in tibiofemoral joint.

Lateral parapatellar arthrotomy was done. The chondral lesion was prepared using a sharp scalpel and small curettage to remove unstable cartilage until reaching the stable and healthy cartilage. The subchondral bone plate must be carefully preserved (Fig. 11).

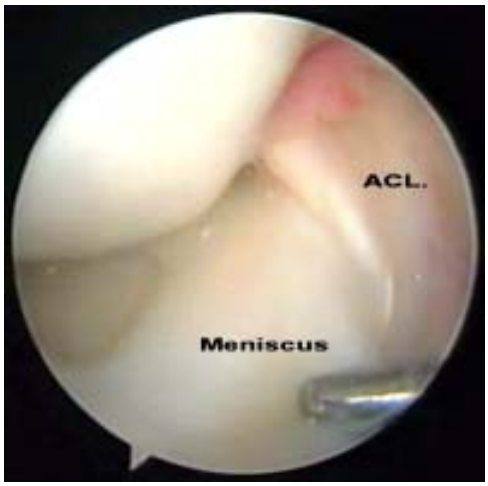

Fig. 5

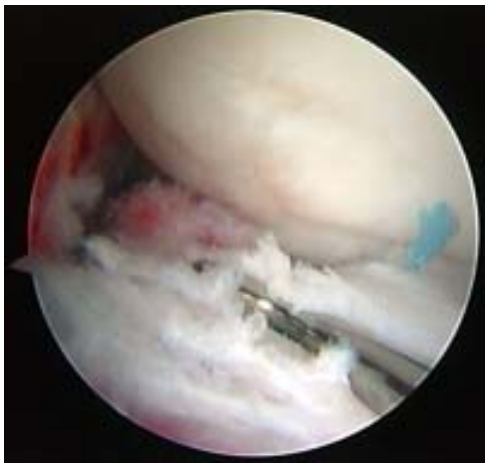

Fig. 6

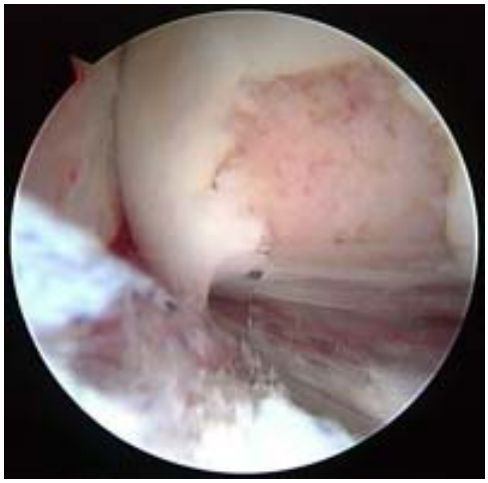

Fig. 7

Fig. 5-7 Arthroscopic finding displaced bucket-handle meniscal tear
The whole thickness chondral flap before and after shaving

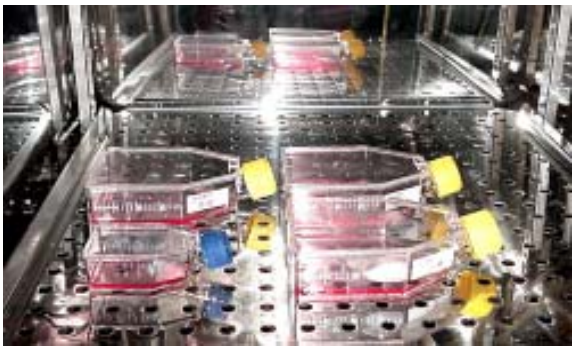

Fig. 8 Shows incubation station

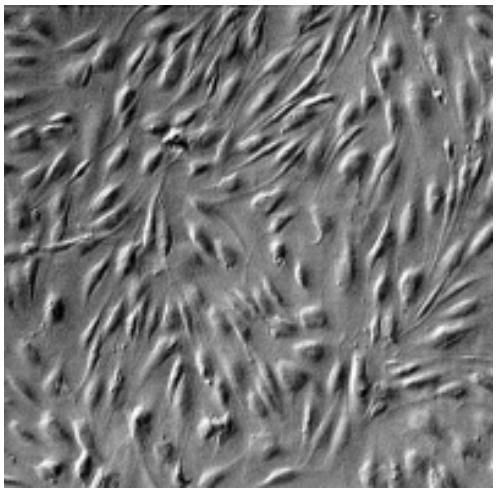

Fig. 9

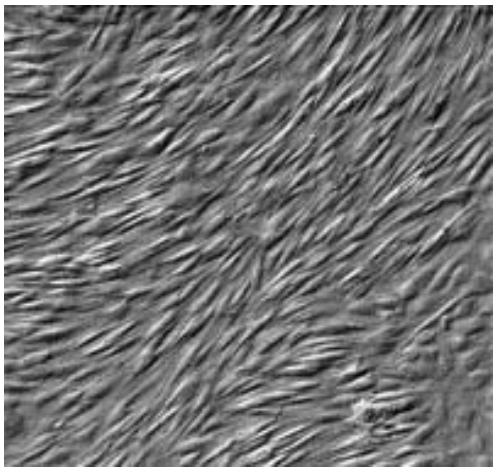

Fig. 10

Fig. 9-10 Progression of chondrocyte cell in quality and quantity were monitor with photography

The anteromedial incision of proximaltibia was exposed, for periosteum harve sting that to be the chondral suspensor.

The periosteum graft was placed into the chondral defect. The cambium layer side faced to the defect and then sutured in watertight fashion with interrupted sutures (Prolene 6-0). The fibrin glue was used to make a water-seal pocket. The small upper edge was left open for the chondrocyte injection (Fig. 12).

Chondrocyte that was already prepared in an insulin syringe with angiocatheter (Fig. 12) was injected into the periosteum pocket and then closed with interrupted sutures. Fibrin glue was used to seal the periosteum. (Fig. 13, 14) No drain was needed and the wound was closed layer by layer. The compression bandage was applied.

Post operative program

Pain was controlled with analgesic and NSAID IV form. CPM was started after removing the compression dressing about the second day post operative (> 24 hours), starting from 0-30 degree and then progressive to 90-0 degree within 2 weeks. After pain control success the active knee flexion was started as tolerated to get active flexion about 90 degrees within second weeks.

Isometric quadriceps muscle exercise and ankle exercise were started in the post operative day. Open chain training was restricted for 3 months.

The weight bearing was restricted for 6 weeks, and then the progressive weight bearing was encouraged. The presented patient could have weight bearing in seven weeks post operative. Jumping and running were not permitted for 6-9 months.

Results

The presented patient was discharged in the second week and had total stitch removal on the fourteenth day. Follow-up at the interval of four, eight, twelve weeks and then at sixth months was performed. No complications were detected. The full range of motion was achieved in eight weeks. The patient could have the full weight bearing without pain at the seventh week.

Visual analogue scale for pain was 3 points at pre-operative period, improved to 0 point at the sixth month follow-up. Regarding the authors' restricted post operative program, the knee score was not included at the time of follow-up.

Physical examination at the sixth month; the circumference of the right thigh was 48.5 cm, compared

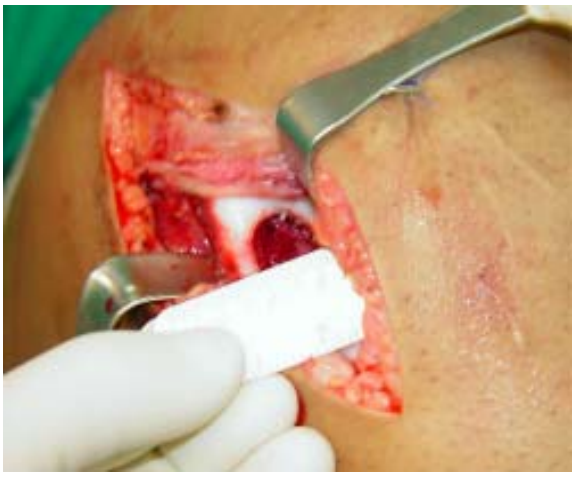

Fig. 11 Sizing of lesion

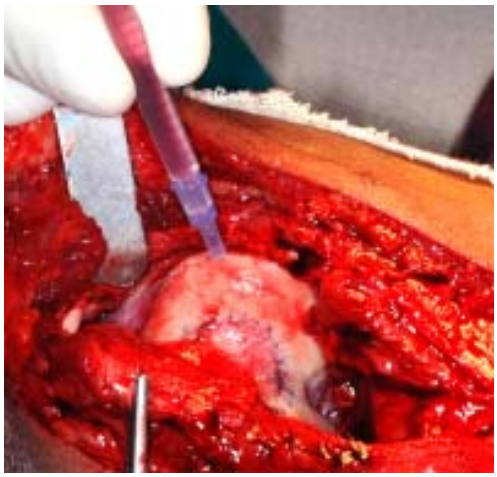

Fig. 12 This show same technique that injected cell in to pocket (picture from the other case)

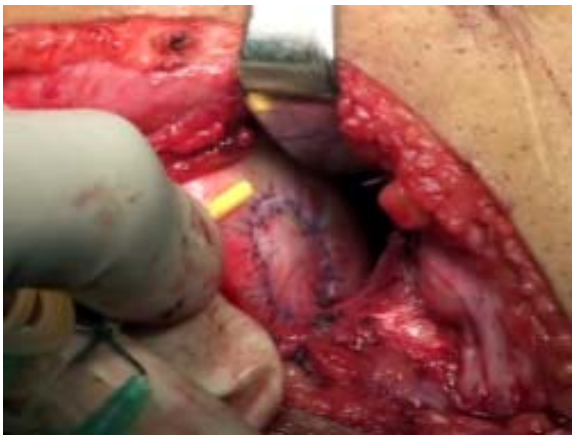

Fig. 13 Fibrin glue used to seal small pore

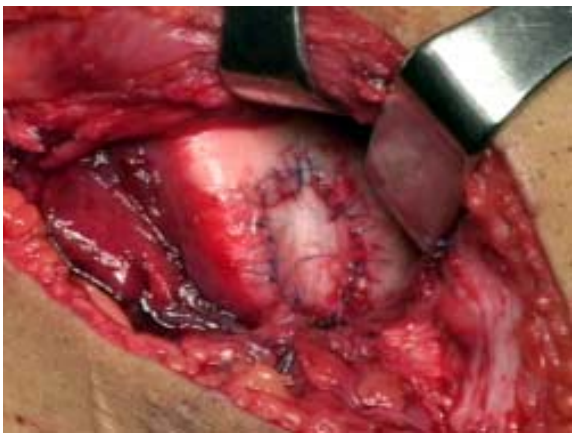

Fig. 14 The procedure was finished

to 46.5 cm of the left. The full range of motion was achieved, and there was no tenderness at the joint line. The McMurray test was –ve. There was no tenderness at the graft donor site. MRI finding: Autologous chondrocyte implantation of a chondral defect in posterior aspect of lateral femoral condyle was described following the ICRS guideline[13].

Sagittal T2-weighted, fast-spin-echo image (T2W) (TR: 3000, TE: 85) of lateral femoral condyle (Fig. 15) shows 100% filling of the repair tissue in defect site associated with hypertrophy of the repair tissue above the chondral surface. There is hypersignal T2W line in interface between native and the transplant cartilage. This bright signal could be either integrating repair tissue, which has fluid-like signal, or incomplete integration. No evidence of subchondral cyst formation beneath the interface is seen. Sagittal proton-density-weighted, fast-spin-echo image shows shallow subchondral bone marrow edema due to post operative change (Fig. 16).

Discussion

Strategy in the treatment of cartilage defect does not depend on which is the best procedure but on the detecting and treatment of an associated lesion, the controlling appropriate environment for cartilage repair e.g. mechanical overload correction by corrective osteotomy[13]. In the presented case, the anatomic repair of the meniscus is the important procedure.

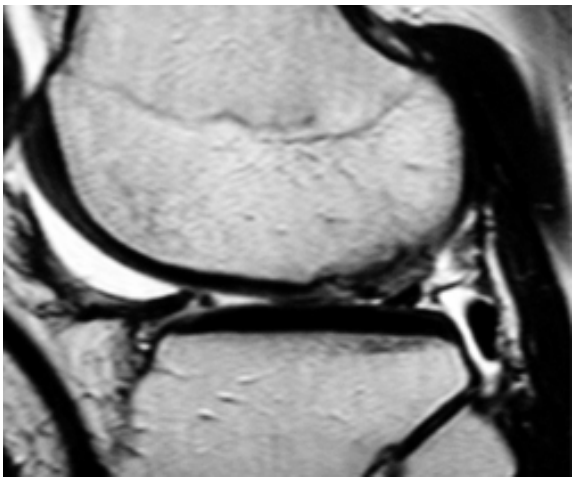

Fig. 15 Sagittal T2-weighted of lateral femoral condyle

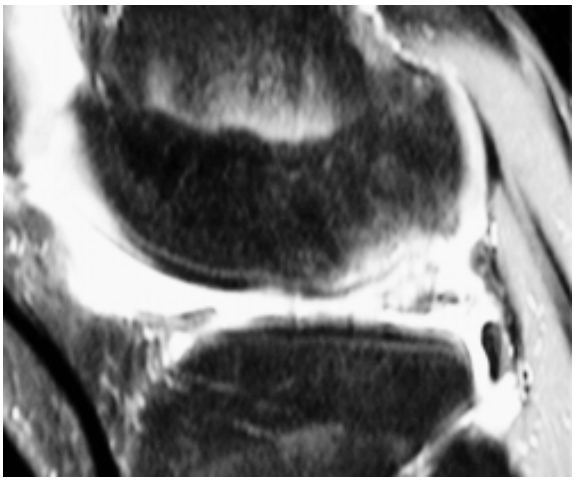

Fig. 16 Sagittal proton-density-weighted, fast-spin-echo

The restoration of hyaline cartilage is the goal for long-term success. The major problems are the procedure and the cost effectiveness of these expensive procedures. The cell therapy procedure especially ACI provides convincing results with high quality hyaline-like cartilage, even though some reports have shown no advantage in short-term result compared to the conventional procedures[20,21]. Further clinical improvements have been reported 1-2 years after the operation due to implant tissue maturation[18]. In the present case, the immediate clinical result and MRI showed improvement over the pre-operative period. The high quality hyaline-like cartilage would provide good prognosis in young, active patients. The long-term result will be followed. The domestic laboratory is capable of providing the cell therapy treatment for cartilage defect, which is the expensive imported technology. The ACI is the potential alternative option for the young patients who have cartilage injury. It can provide clinical improvement and prevention of early degenerative joint disease.

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การปลูกถ่ายเซลล์กระดูกอ่อนของผู้ป่วยเองในการรักษากระดูกอ่อนข้อเข่าบาดเจ็บจากอุบัติเหตุ

ชลวิช จันทร์ลลิต, ชาญณรงค์ เกษมกิจวัฒนา, วิทย์ วราวิทย์

รายงานฉบับนี้เป็นรายงานเบื้องต้นผู้ป่วยหนึ่งคนเป็นครั้งแรกที่ทำการปลูกถ่ายเซลล์กระดูกอ่อนของผู้ป่วยเอง (Autologous Chondrocyte Implantation / ACI) ซึ่งเตรียมเซลล์กระดูกอ่อนโดยห้องปฏิบัติการภายในประเทศ โดยรายงานผลการรักษาที่ 6 เดือน โดยดูกายวิภาคผ่าน MRI และอาการทางคลินิก

***วัสดุและวิธีการ**: ACI เป็นขั้นตอนการผ่าตัด 2 ครั้ง โดยครั้งแรกได้ทำการส่องกล้องข้อเข่าเพื่อตรวจพยาธิสภาพ โดยในผู้ป่วยรายนี้พบผิวกระดูกอ่อนข้อเข่าเสียลึกตลอดผิวข้อ (ICRS grade 4) ขนาด 2.5 ตารางเซนติเมตรและหมอนรองข้อเข่าฉีกขาด ซึ่งได้ทำการซ่อมผ่านทางการส่องกล้องร่วมกับทำการเก็บกระดูกอ่อนจำนวน 300 มิลลิกรัม*

ขั้นตอนที่ 2 คือการใส่เซลล์กระดูกอ่อนโดยห่างจากขั้นตอนแรก 4 สัปดาห์ โดยการผ่าตัดเปิดข้อเข่า ทำการเตรียมแผลผิวข้อกระดูกอ่อนและใช้เยื่อหุ้มกระดูกคลุมปิดรอยแผลโดยเย็บเป็นลักษณะกระเปาะใส่เซลล์ หลังจากนั้นฉีดเซลล์กระดูกอ่อนใต้เยื่อหุ้มกระดูก

***ผลการศึกษา**: ไม่พบภาวะแทรกซ้อน ผู้ป่วยสามารถเดินลงน้ำหนักเต็มไม่ปวด ในสัปดาห์ที่ 7 visual analogue scale ดีขึ้นจาก 3 คะแนน เป็น O คะแนนใน 6 เดือน MRI พบว่ารอยแผลเติมเต็มและมีการขยายเหนือแผลผิวข้อ*

***สรุป**: ผลการรักษาเบื้องต้นแสดงให้เห็นว่าการรักษาด้วย ACI สามารถทำให้อาการทางคลินิกดีขึ้นและทางกายวิภาคดีขึ้นโดยดูจาก MRI ในอนาคตคงต้องการการรายงานจำนวนผู้ป่วยที่มากขึ้นและติดตามระยะเวลานานขึ้นต่อไป*