
Early Experience in Autologous Chondrocyte Transplantation: A Report of 2 Cases

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ABSTRACT

Autologous chondrocyte transplantation has proven to be successful since its introduction in 1987. In this case report of two patients who underwent autologous chondrocyte transplantation, the early outcome has been excellent, as evidenced by improvement in IKDC score, Oxford Knee Score and American Knee Society Score at 9 months postoperatively. Magnetic resonance imaging at 6 months postoperatively demonstrated complete filling of repaired chondral defects with repair tissue. However, larger patient numbers, longer follow-up and further postoperative evaluation is needed so that we may determine the long-term survivability and success of this procedure in Malaysia.

INTRODUCTION

Articular cartilage has poor regenerative capability. Although the true longitudinal natural history of chondral injuries has not been well delineated, it is widely accepted that chondral injuries in a weight-bearing portion of the knee may progress to osteoarthritis.⁽¹⁾ Chondral injuries are frequently symptomatic with complaints of pain, swelling and clicking being common presenting symptoms, but it may also be found incidentally at arthroscopy for meniscal or ligamentous injuries.

There are different modalities of treatment of chondral defects. Arthroscopic debridement, microfracture, osteochondral autograft transplantation and autologous chondrocyte transplantation have all been used for the treatment of symptomatic defects. Whilst the former two procedures result in fibrocartilage repair tissue, the latter two results in hyaline repair tissue which has

been shown to be structurally superior to fibrocartilage.⁽²⁾

Autologous chondrocyte transplantation was first performed in 1987 and reported in 1994 by Brittberg et al.⁽²⁾ It is a two stage procedure – the first stage involves cartilage harvest via arthroscopy, and the second stage involves implantation of the cultured chondrocytes into the chondral defect. It is indicated in patients younger than 55 years with symptomatic Outerbridge⁽³⁾ or ICRS⁽⁴⁾ Grade III to IV chondral defects of the knee⁽⁵⁾ with a diameter larger than 20 mm.⁽⁶⁾ The location of the defect should be on the femoral or patellar articular surface and should be accessible for transplantation via open arthrotomy.⁽⁵⁾ Background factors such as instability, patellar maltracking and varus/valgus malalignment, which may have caused or may affect tissue repair, should be addressed prior to or at the same time as the transplantation procedure.

We report on our early experience with autologous chondrocyte transplantation in 2 patients.

METHODS

The study was approved by the ethics committee of the Medical Faculty, University of Malaya. In accordance with Malaysian law, patients were informed of the nature of the study and gave their written consent. Patients had cartilage defects down to, but not through, the subchondral bone, on a load-bearing surface of the femoral condyle or the patellar facet, with disabling symptoms of the knee, including localized pain, swelling, and retropatellar crepitus. Preoperative assessments included 2000 IKDC Subjective Knee Evaluation Forms,⁽⁴⁾ Oxford Knee

Score (OKS),⁽⁷⁾ American Knee Society Score (AKSS),⁽⁸⁾ anteroposterior and lateral knee radiographs, magnetic resonance imaging (MRI) and, in cases of patellar chondral defects, CT of the knee in 0°, 10°, 20° and 30° of flexion to detect patellar maltracking. The technique of ACT as described by Brittberg et. al.⁽²⁾ was performed (Figure 1).

ISOLATION AND CULTURE OF CHONDROCYTES

With the patients under general anaesthesia, diagnostic arthroscopy was performed in a tourniquet-controlled, bloodless field. Cartilage slices were obtained through an arthroscope from the intercondylar notch of the affected knee.

Chondrocyte cultures were performed in a tissue culture laboratory in Faculty of Medicine, University Malaya. Harvested tissue is then digested using collagenase for 24 hours. Cells released from the harvested tissue are then collected and cultured on to a mixture of DMEM and HAM-12 culture media. Cultures are stored in a CO₂ incubator at 5% concentration. The amounts of cell growth are calculated using a cell counter performed every 2 days. This observation is continued until confluence is reached after which the culture is trypsinized to release cells for further passage. This continues until expected cell numbers of between 2 to 5 million cells is achieved which usually takes approximately 4 to 6 weeks from the start of the culture process. (Figure 2)

TRANSPLANTATION

Prophylactic antibiotics (Cefuroxime sodium, 750 mg) were given intravenously in three doses over a 24-hour period during and after the surgery. The method of transplantation was as described by Brittberg et. al.⁽²⁾ With the patients under general anaesthesia, a medial or lateral parapatellar arthrotomy was performed in a tourniquet-controlled, bloodless field. The chondral lesion was excised as far as the normal surrounding cartilage but not as far as the subchondral bone plate. With the cambium layer facing the inside of the bone of the defect, a periosteal flap taken from the supracondylar region of the femur of the affected knee was used to cover the cartilage defect. The flap was sutured to the surrounding rim of the normal cartilage with interrupted 6-0 Vicryl® sutures leaving an opening in the upper part of the defect for insertion of cultured chondrocytes. The intervals between the sutures were sealed with fibrin glue and the patch was tested for water tightness by injecting saline into the defect and checking for leakage. The cultured

chondrocytes were inserted beneath the periosteal flap and the opening was closed with suture and fibrin glue. The joint capsule, retinaculum layer, and skin were sutured in separate layers, except in the case of patellar maltracking whereby the lateral parapatellar joint capsule was not repaired. The knee was covered with a small elastic bandage.

POSTOPERATIVE PROTOCOLS

Continuous passive motion was initiated within 6 hours postoperatively with the range of flexion limited to 30°. This was continued until patients were able to mobilize the knee independently. Quadriceps strengthening exercises were encouraged during the recovery period. Active movement of the knee without weight bearing was initiated two to three days after surgery. Patients were discharged with a protective knee brace which limited flexion to 45°. Once discharged, patients attended outpatient physiotherapy twice weekly initially for 12 weeks and then, subject to their progress, once weekly. Weight bearing was gradually introduced and, along with knee flexion, increased to the full extent, with isometric quadriceps training, during the first eight weeks after surgery.

FOLLOW-UP

Patients were evaluated at 2 weeks, 6 weeks, 3 months postoperatively, and at 3 monthly intervals thereafter. Evaluation with 2000 IKDC Subjective Knee Evaluation Forms, Oxford Knee Score, American Knee Society Score was performed at 3 monthly intervals, and a MRI 6 months postoperatively.

CASE REPORTS

Case 1

A 33 year old female presented with complaints of intermittent left knee pain and swelling of 1 year duration. Her symptoms were aggravated 1 month prior to presentation. She had increasing difficulty walking and was not able to kneel or squat. Her occupation involved frequent travelling. She used to jog and bowl prior to the onset of symptoms. However, since the aggravation of her symptoms, she has found great difficulty travelling due to pain, swelling and stiffness, and has not been able to continue with her sporting activities. Her preoperative IKDC Score was 34.5, OKS was 22, and AKSS was 90. Preoperative MRI showed a chondral defect which involved the lateral and medial facets of the patella (Figure 3A). CT scans of the knee demonstrated patellar maltracking (Figure

3B). She underwent ACT with lateral parapatellar release. Intraoperatively, the lesion measured 4 x 2 cm. Postoperatively, her outpatient physiotherapy was delayed by 2 weeks due to infection with *varicella zoster* (chicken pox). Her OKS and AKSS scores were 12 and 100 respectively by the 3rd month postoperatively and, at 9 months postoperatively, her IKDC Score was 79.3 A MRI at 6 months showed complete healing of the chondral defect of the patella (Figure 3C). Currently, she is pain free and able to kneel and squat.

Case 2

A 29 year old male presented with pain and instability of the right knee. The knee was swollen and he was not able to squat or run. He had a previous partial meniscectomy for a tear of the medial meniscus of the same knee. He was an avid soccer player and played competitively for his employers. His preoperative IKDC Score was 29.9, OKS 22 and AKSS 90. MRI showed a full-thickness chondral defect at the posterior medial femoral condyle of the right knee (Figure 4A). He underwent ACT of a chondral defect measuring 2 x 2 cm. He had an uncomplicated recovery period. His OKS and AKSS scores were 12 and 100 by the 6th week postoperatively, and IKDC score at 9 months postoperatively was 87.4. MRI at 6 months showed that the repaired chondral defect had healed (Figure 4B). He is able to jog and has resumed playing soccer albeit at a recreational level.

DISCUSSION

Since its introduction in 1994,⁽²⁾ autologous chondrocyte transplantation (ACT) has undergone considerable development. It has become an established form of treatment for symptomatic osteochondral defects in the knee.^(1,9,10) Recently, it has been adapted for use in the shoulder, elbow and ankle.^(11,12,13) ACT was first performed in Sweden in 1987 and the longest term results to date are from this original series of patients. Peterson et al reported good to excellent outcomes in 92% of patients with isolated femoral condyle and 65% of patients with patella chondral defects and .⁽¹⁴⁾ Since then, there have been other reports on the outcome of ACT which have also reflected good to excellent results.^(15,16,17) Although still early, we are encouraged by the excellent outcomes in our patients at 9 months postoperatively.

Basic science studies show that implanted chondrocytes are present in repair tissue and express type II collagen.⁽¹⁾ ACT can produce hyaline-type repair

tissue which has the potential benefit of being a more durable and long-term solution for large chondral defects.^(2,18,19) Henderson et al used MRI to determine its usefulness in assessing autologous chondrocyte transplantation and concluded that it was a reasonable, non-invasive means of assessment of graft survival and cartilage maturation after ACT.⁽²⁰⁾ In this report, MRI of both patients at 6 months are indicative of good repair tissue fill but the question remains as to the quality of tissue repair. Confirmation of the production of normal hyaline articular cartilage can only be definitely assessed by second-look arthroscopy and biopsy of the repair tissue.

CONCLUSION

Autologous chondrocyte transplantation has proven to be successful since its introduction in 1987. In our early experience, the outcome of two patients at 9 months postoperatively has been excellent. However, larger patient numbers, longer follow-up and further postoperative evaluation, such as histological examination, is needed so that we may determine the long-term survivability and success of this procedure in Malaysia.

ACKNOWLEDGEMENTS

The authors acknowledge the excellent technical assistance of Ms AB Azera and Mrs J Khairussulhi. This study was made possible with a research grant from the National Biotech Directorate (NBD) and fundamental research grant of University of Malaya.

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Figure Legends

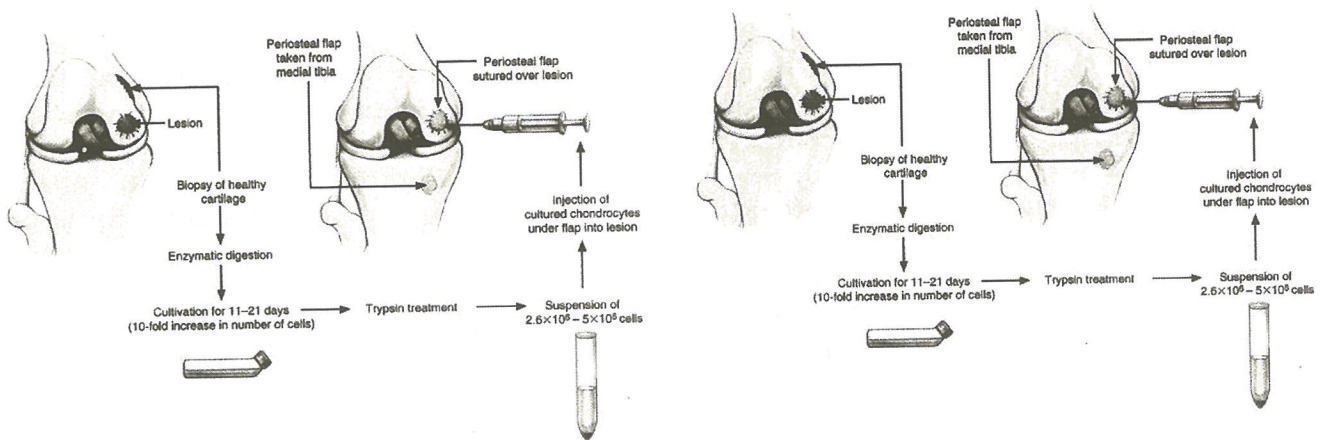


Fig. 1: Diagram of the autologous chondrocyte transplantation procedure⁽¹⁴⁾

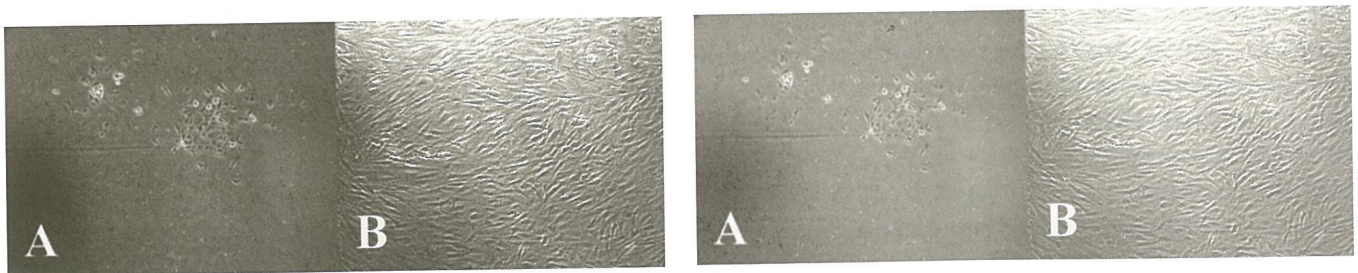


Fig. 2: (A) Microscopy after isolation of chondrocytes (B) Chondrocytes after confluence has been achieved

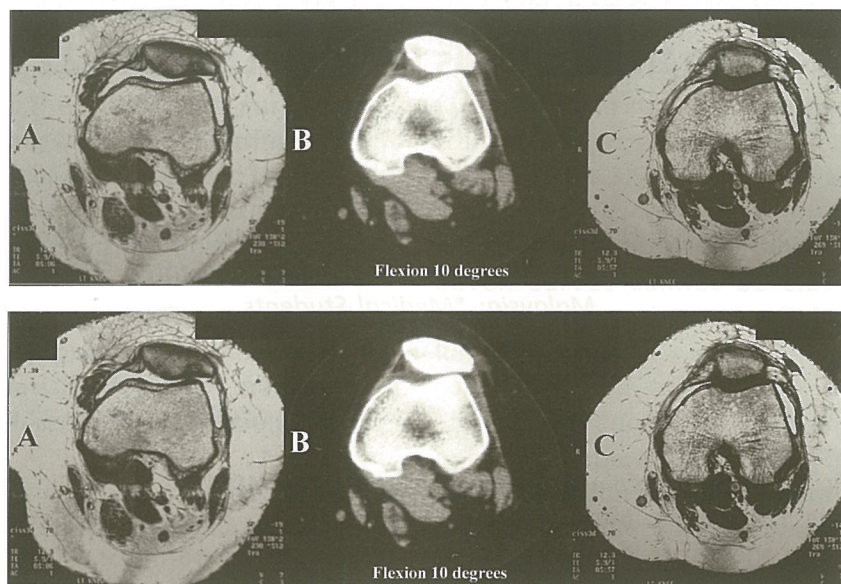


Fig. 3: (A) Preoperative MRI showing effusion and thinning of articular cartilage of medial and lateral facets of the patella. (B) CT scan with the knee in 10° of flexion demonstrating patellar maltracking. (C) Postoperative MRI at 6 months showing good filling of the previous defect with repair tissue

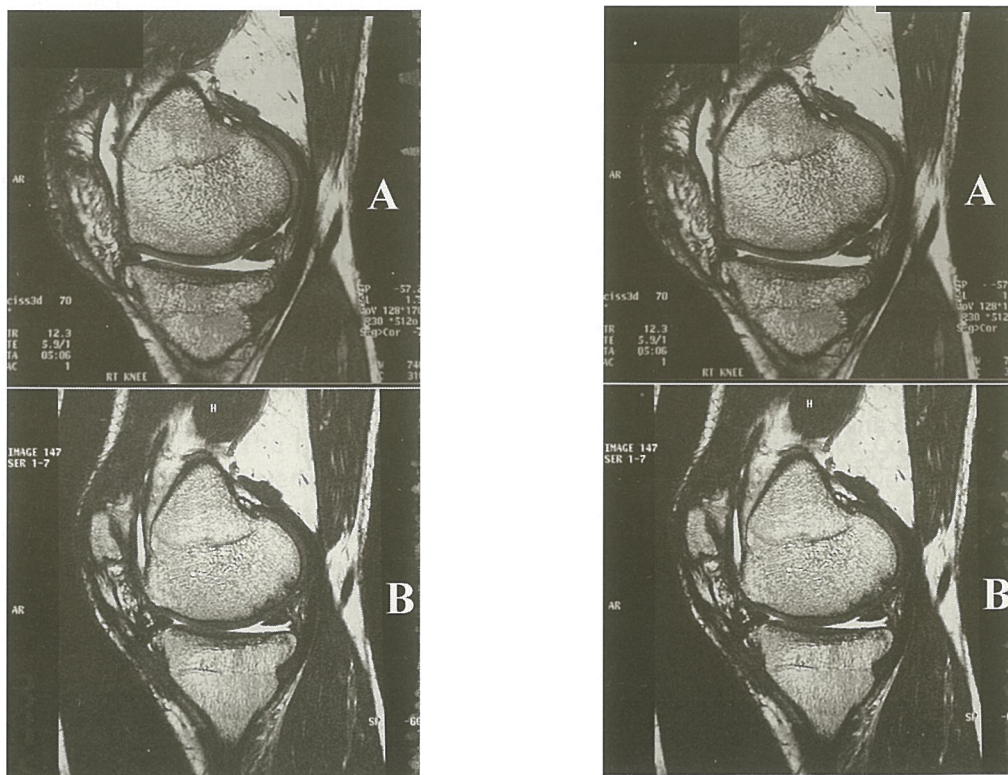


Fig. 4: (A) Preoperative MRI showing full-thickness chondral defect in the posterior aspect of the medial femoral condyle. (B) MRI 6 months postoperatively showing complete filling of the defect with repair tissue