CASE REPORT

2-Year Postoperative Evaluation of a Patient with a Symptomatic Full-Thickness Patellar Cartilage Defect Repaired with Particulated Juvenile Cartilage Tissue

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ABSTRACT

This case report describes the early results of a 36-year-old man who underwent repair of a symptomatic full-thickness patellar cartilage defect with transplanted particulated juvenile articular cartilage. At 2 years postoperatively, the patient has experienced substantial clinical improvement in both pain and function when evaluated with both International Knee Documentation Committee subjective evaluation and Knee Injury and Osteoarthritis Outcome Score outcome measures. Two-year postoperative magnetic resonance imaging demonstrates fill of the defect with repair tissue and near complete resolution of preoperative subchondral bone edema. To the best of the authors' knowledge, this case report is the first to report clinical results of this new technique at 2 years postoperatively.

KEYWORDS: Cartilage, knee, juvenile, particulated, clinical

Although many chondral lesions are asymptomatic, others cause significant disability in relatively young patients in whom joint arthroplasty is not desirable. Current clinical treatment options to repair symptomatic articular cartilage defects of the knee include debridement/chondroplasty,[1] marrow stimulation,[2,3] autograft transplantation (mosaicplasty/autologous osteochondral transfer procedure [OATS]),[4,5] autologous chondrocyte implantation,[6,7] and osteochondral allograft transplantation.[8,9] Treatment algorithms have been proposed utilizing these options, which take into account both patient- and lesion-specific factors.[10,11] However, there is also significant variation and controversy in the literature regarding the outcomes and resultant repair tissue generated with some of these procedures.[12–16]

In the present case report, we investigated the clinical outcome of a new cartilage repair technique with transplantation of juvenile particulated cartilage allograft tissue, which is fixed into the cartilage defect with fibrin glue. The rationale for the use of juvenile cartilage is based upon the unique properties of younger cartilage. Young articular cartilage tissue has a significantly higher cell density than adult articular cartilage.[17] Young chondrocytes have superior capabilities of producing extracellular matrix than mature chondrocytes.[18] There is some evidence that young cartilage may have better repair capacity than adult articular cartilage.[19,20]

To the best of the authors' knowledge, this is the first report on the use of particulated juvenile cartilage allograft for the repair of a full-thickness symptomatic

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cartilage defect at 2 years postoperatively. Data were collected with Institutional Review Board approval and patient consent.

CASE REPORT

A 36-year-old otherwise healthy man was referred for a workman's compensation–related injury to his right knee. He denied any history of prior injury or preexisting pain. The patient complained of retropatellar pain in his right knee, which was exacerbated with squatting and stair climbing. The pain limited his function as a recreational athlete. He desired to eventually return to moderate to strenuous activities, including recreational sports, without any pain. On examination, his knee was tender over the medial parapatellar region with mild palpable crepitation. There was no associated maltracking and his range of motion was not appreciably decreased. He was initially treated conservatively including the use of nonsteroidal anti-inflammatory drugs, but his pain persisted. Magnetic resonance imaging (MRI) was obtained, which revealed a full-thickness chondral defect of the patella with underlying edema and early subchondral cyst formation (Fig. 1). On the MRI, the lesion measured 10 mm by 11 mm in diameter and was located from the apex going into the medial facet.

Various treatment options were discussed with the patient including continued nonoperative treatment, arthroscopic chondroplasty, OATS, autologous chondrocyte implantation (ACI), fresh osteochondral allograft transplantation, and implantation of particulated juvenile allograft articular cartilage tissue (DeNovo® NT Natural Tissue Graft, Zimmer, Inc., Warsaw, IN). It was disclosed and explained to the patient that the surgeon (K.F.B.) was on the development team for this technology and had a financial interest in the technology. There was no financial incentive for the patient to choose one procedure over the others. The patient elected to proceed with implantation of the particulated juvenile allograft articular cartilage tissue through a small medial parapatellar arthrotomy.

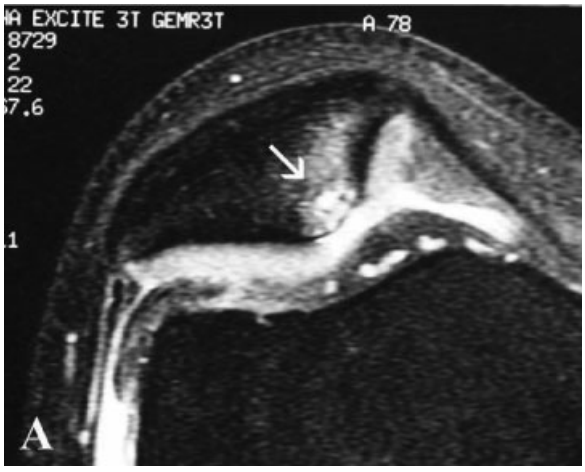

Figure 1 Preoperative magnetic resonance imaging demonstrating a full-thickness chondral defect of the patella with underlying bone edema and early subchondral cyst formation (indicated by the arrow).

The DeNovo® NT cartilage allograft was recovered from a juvenile (3-year-old female) donor knee joint within 48 hours after the death of the donor. The donor whose tissue was used to process DeNovo® NT met all eligibility requirements. A series of screening tests were performed, including anti-human immune-deficiency virus (HIV) type 1 and type 2, HIV nucleic acid test, hepatitis B surface antigen, anti-hepatitis B core antigen, anti-hepatitis C virus, hepatitis C nucleic acid test, anti-human T-lymphotropic virus type I and II, syphilis, Epstein-Barr virus, cytomegalovirus, and West Nile virus. In addition, microorganism sampling testing and cell viability testing based on the standard live-dead assay were performed. Both the tissue procurement organization and the tissue processing organization (ISTO Technologies, Inc., St. Louis, MO) are accredited by American Association of Tissue Banks. The implantation of the particulated juvenile cartilage tissue was performed on day 46 after the death of the donor. Prior to the implantation, the cartilage tissue fragments were preserved in a nutrient medium within a sterile blister package at a controlled temperature. The patient completed International Knee Documentation Committee (IKDC) subjective evaluation and Knee Injury and Osteoarthritis Outcome Score (KOOS) clinical data forms, according to the relevant guidelines.[21,22] His knee function at this time is reported in Table 1.

An arthroscopy was performed and the full-thickness lesion was confirmed (Fig. 2A). No other significant intra-articular pathology was found. A 6-cm medial parapatellar arthrotomy was performed and the patella was everted. The chondral defect was debrided to a healthy cartilage rim (Fig. 2B). The lesion was well contained and measured 12 mm by 14 mm postdebridement (larger than initially indicated on MRI). The lesion was debrided to the calcified cartilage layer except where

Table 1 IKDC and KOOS Scores Preoperatively and 2 Years Postoperatively

	Preoperative	2 Years Postoperative
IKDC subjective evaluation	32	85
KOOS pain	67	94
KOOS other symptoms	75	96
KOOS activities of daily living	62	94
KOOS sports/recreation activities	5	75
KOOS quality of life	13	75

IKDC, International Knee Documentation Committee Subjective Evaluation; KOOS, Knee Injury and Osteoarthritis Outcome Score.

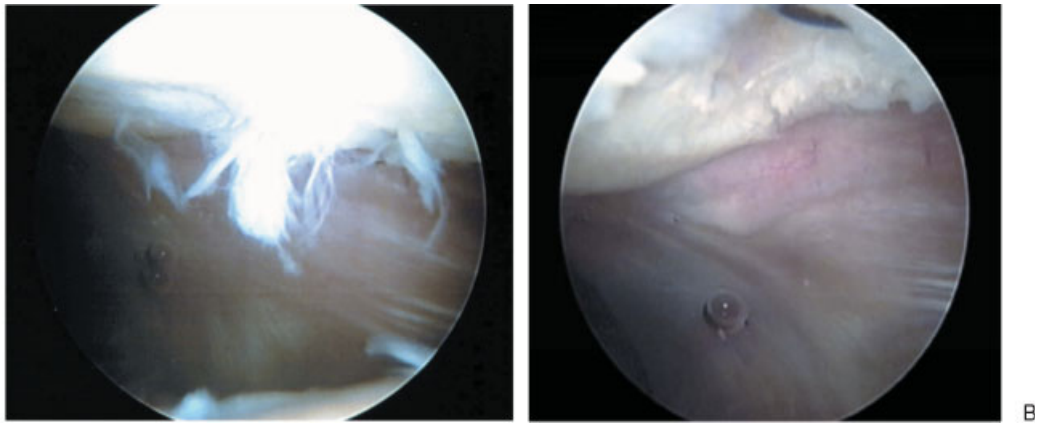

Figure 2 Scope images of the defect. (A) Predebridement; (B) postdebridement.

the cyst had developed. The fibrous tissue was removed from the cyst. The defect was ~8 to 9 mm deep in the area of the cyst. The juvenile allograft tissue (~0.1 cm^3) was manually dispersed as evenly as possible on the floor of the defect to try to obtain a homogeneous filling of the defect but staying just below (less than 1 mm) the adjacent cartilage surface. The juvenile allograft tissue was fixed within the defect with a fibrin adhesive (Fig. 3). Once the fibrin glue had set (~10 minutes), the knee joint was cycled to check stability and fixation of the graft. The tourniquet was not let down until the fibrin glue had set. The procedure was completed without complications.

Postoperatively, the patient was weight-bearing as tolerated with a knee brace locked in extension. He was immediately started on a continuous passive motion machine, 0 to 45 degrees, and was asked to increase flexion as tolerated. The brace was discontinued at 6 weeks postoperatively.

RESULTS

The patient reported that his preoperative pain was improved by 7 weeks postoperatively. By 7 months, the patient's range of motion was at 0 to 140 degrees, and he reported a considerable subjective improvement in pain from his presurgical baseline. He was able to participate in sports and perform squatting activities. A postoperative MRI at 21 months demonstrated full defect filling and nearly complete resolution of the preoperative subchondral bone edema (Fig. 4). At 2 years postprocedure, his IKDC and KOOS improved substantially. Table 1 shows the pain and function scores, quality of life, and return to sports/recreation activities preoperatively and 2 years postoperatively.[23,24]

DISCUSSION

Each of the alternative treatment options in this case has potential benefits but also inherent limitations. Arthroscopic debridement is a minimally invasive procedure that can remove unstable cartilage fragments and provide symptomatic relief for a subset of patients.

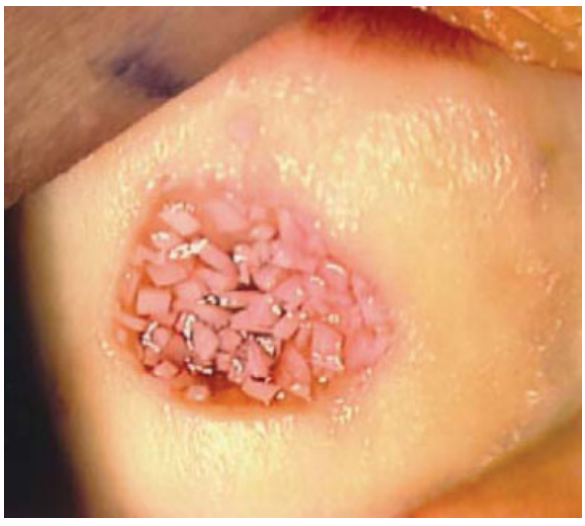

Figure 3 Full-thickness patellar chondral defect following placement of the DeNovo® NT graft which is secured with fibrin glue.

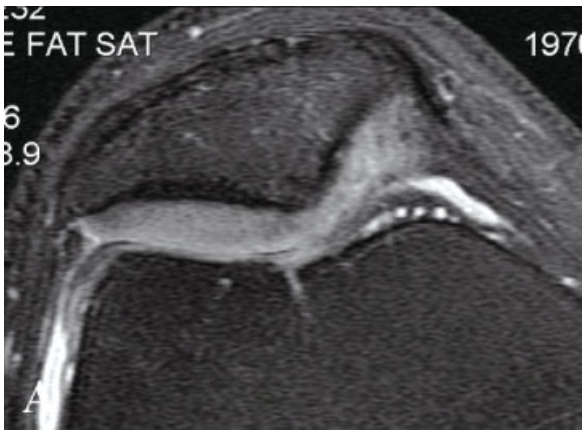

Figure 4 Postoperative magnetic resonance imaging at 21 months reveals near resolution of the bone edema and repair tissue within the previous defect site.

However, the efficacy of pain relief is controversial[1] and no repair tissue is created, which often limits its effectiveness in younger, active patients with full-thickness defects. Although marrow stimulation (microfracture/drilling/abrasion) is often performed by the senior author (K.F.B.) for other anatomic locations in an effort to generate fibrocartilage, it is not typically utilized clinically for the patella.[2,3] OATS/mosaicplasty is also used to treat cartilage defects by transplanting single or multiple osteochondral plugs from the low-weight-bearing donor sites of the patient's joint to the high-weight-bearing recipient sites.[4,5] This technique is commonly utilized with very good success for smaller femoral condylar lesions.[25] Although a recent report showed that this procedure may be effective for patellar defects, the senior author has had more variable success for lesions requiring more than a single plug.[26] Also, donor side morbidity is being increasingly recognized as a source of persistent knee symptoms following OATS procedure.[27] ACI has been used to repair chondral defects[6] by transplanting in vitro expanded chondrocytes isolated from a cartilage biopsy from the first stage of the procedure to the defect site in the second stage of the procedure. This technique has been used for chondral defects with reasonably good medium- and long-term clinical success. However, this technique has several limitations. ACI requires multiple operations (typically a two-stage procedure with 30% of cases requiring an additional third stage to debride hypertrophy of the periosteal flap used to cover the defect during the cell implantation).[7,28] Second, the clinical advantages of ACI over simpler/cheaper microfracture and mosaicplasty for small and medium defect sites are controversial. Additionally, Carticel® (Genzyme, Inc., Cambridge, MA), although used with some success for the patella, is currently approved by the FDA only for treating defects on the femoral condyles and trochlea.

All the above treatments are essentially autologous-based. However, an allogeneic approach has also been adopted in clinical practice by transplanting osteochondral plugs or shell grafts taken from fresh donor joints to repair cartilage defects of the recipient joint. This technique has been successfully used in repairing chondral and osteochondral defects even with large defect sizes.[8,9,29] However, the availability of donor tissue limits its usage to ~2000 cases annually in the United States. Furthermore, matching and transplanting grafts for patellar defects can be much more challenging than for femoral or tibial defects and therefore is not commonly used in this setting.

The concept of using particulated cartilage tissue to repair cartilage defects was initially reported in a rabbit study.[30] Subsequently, a goat study[31] and a horse study[32] were reported in which autologous adult cartilage tissue pieces distributed onto a biodegradable synthetic membrane were implanted in cartilage defects. The membrane was secured with multiple resorbable staples inserted into subchondral bone. A horse study was also conducted (ISTO Technology, Inc., Technical Report, 2007) to evaluate an alternative concept where juvenile human cartilage pieces were implanted to repair cartilage defects. In this study, isolated cartilage pieces were secured in cartilage defects with autologous fibrin glue alone. No membrane coverage or bone-penetrating fixation device was used. The horses were sacrificed at 6 months postimplantation. The cartilage pieces were shown to undergo a remodeling process, and the surgically created cartilage defects were completely filled with new cartilage repair tissue. In addition, no bone necrotic changes or other significant bone remodeling took place. In contrast, control defects treated identically but without the implantation of juvenile cartilage pieces showed less filling, weaker staining for glycosaminoglycans (indicative of repair tissue of more fibrous nature), and significant subchondral bone necrosis. It is interesting to note that juvenile human articular cartilage does not elicit xenograft rejection when transplanted to repair cartilage defects in animals.[33] In addition to animal studies of cartilage repair with particulated cartilage pieces discussed above, short-term clinical success of the new cartilage repair technique with transplantation of juvenile cartilage tissue pieces was reported recently by Farr and colleagues.[34]

Potential benefits of this new technique include single-stage procedure, simplicity in the surgical technique, implantation of juvenile tissue, no donor site morbidity, and no periosteal flap hypertrophy issues. However, as with any living tissue transplantation procedures such as fresh osteochondral allograft transplantation, there is a risk of disease transmission. This risk can, to a large extent, be mitigated by adhering to rigorous donor screening, tissue recovery, and processing procedures according to current Good Tissue Practice[35] and microorganism sampling testing prior to the product release of each lot (one lot consists of multiple packages of particulated cartilage tissue from one single donor). Despite stringent donor screening, tissue recovery, tissue processing, and tissue postprocessing testing, as for any human tissue or organ transplantation, there exists a risk for disease transmission. In addition, as with any living tissue transplantation, there is a tissue availability constraint and logistic challenges such as a limited shelf life. The shelf-life consideration arises from the cell viability of tissue. Typically, fresh osteochondral allografts need to be implanted within around 30 days after the death of the donor due to decreasing cell viability over time.[36] Similarly, DeNovo® NT tissue, with ~80% average cell viability at time of packaging according to the standard live-dead assay performed at ISTO Technologies, Inc., needs to be implanted within 52 days after the packaging of the tissue into sterile packages.

An ongoing preliminary study is evaluating the potential mechanism(s) associated with the creation of defect-filling repair tissue (e.g., expansion of tissue piece volume). Certainly, more research is needed to understand better the underlying mechanism of this new cartilage repair technique. It does appear, however, that at 2-year follow-up, this technique was able to provide significant improvement in outcome scores as well as maintain repair tissue in this symptomatic patellar defect. The senior author (K.F.B.) has now performed seven of these procedures (with over 1-year follow-up) for patellar defects with encouraging subjective and MRI results.

CONCLUSION

The patient who is the focus of this report has thus far had a successful clinical outcome with over 2-year follow-up. Outcome scores showed significant improvement in both pain and function. Twenty-one-month postoperative follow-up MRI demonstrated defect filling with repair tissue and near-complete resolution of subchondral bone edema. Further follow-up is needed to evaluate the long-term outcome of the DeNovo® NT procedure and histological characterization of the repair tissue. The early results of this new technique have been promising for select patients.

DISCLOSURE

The senior author (K.F.B.) would like to disclose that he is a consultant for Zimmer, Inc. and receives royalties for the product that is the subject of this report.

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