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Histological and Gross Evaluation through Second-Look Arthroscopy of Osteochondral Lesions of the Talus after Failed Treatment with Particulated Juvenile Cartilage: A Case Series

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Learning Point for this Article:

Integration of particulated juvenile cartilage allograft with surrounding cartilage appears to be affected by biological and mechanical factors.

Abstract

Introduction: The treatment of osteochondral lesions of the talus (OLTs) recalcitrant to non-surgical interventions is challenging. Particulated juvenile cartilage allograft transplantation (PJCAT) has become a viable treatment option, obviating the need for an osteotomy or second-stage surgery and eliminating risk of donor site morbidity. Short-term outcomes have been promising, but failures associated with PJCAT have not been well described.

Case Report: Four patients with OLTs who had continued symptoms after PJCAT underwent a second-look arthroscopic evaluation. The quality of cartilage repair was evaluated using the international cartilage repair society (ICRS) score. Biopsy of the repair was taken for histological analysis. Two patients demonstrated a lack of integration of the allograft into the surrounding cartilage, and two had failures associated with impingement. Three patients' repairs were consistent with a Grade III ICRS score and one with a Grade II score. Histological examination demonstrated fibrotic repair tissue (Type 1 collagen) with depleted proteoglycans and Type II collagen.

Conclusion: There were no obvious patients or surgical factors associated with poor outcomes. Integration of PJCAT with surrounding cartilage appears to be affected by biological and mechanical factors. Further, understanding of factors influencing PJCAT integration will help develop more specific indications for use.

Keywords: Ankle, articular cartilage, DeNovo® NT Graft, juvenile allograft, particulated cartilage.

Introduction

Osteochondral lesions of the talus (OLTs) remain a difficult problem to treat. Failure to properly identify and treat an OLT can result in progressive degeneration of the articular cartilage, physical dysfunction, and osteoarthritis [1, 2]. The initial management of OLTs centers on non-surgical interventions, however, the intrinsic ability of the talar articular cartilage to heal is limited [3]. Non-operative treatment is successful in only 25–50% of patients [4, 5, 6, 7]. Therefore, in most cases, surgical intervention is necessary to treat symptomatic OLTs.

For symptomatic lesions refractory to non-surgical management, surgical intervention is used to either repair or replace the disrupted cartilage. Repair procedures involve marrow-stimulating techniques such as debridement, abrasion arthroplasty, subchondral drilling, and microfracture; fibrocartilage is produced through these procedures. Alternatively, restorative procedures have been developed in an effort to replace the affected articular cartilage with hyaline cartilage. These procedures include osteochondral autograft transfer, fresh allograft transplantation, and autologous chondrocyte implantation.

Particulated juvenile cartilage allograft transplantation

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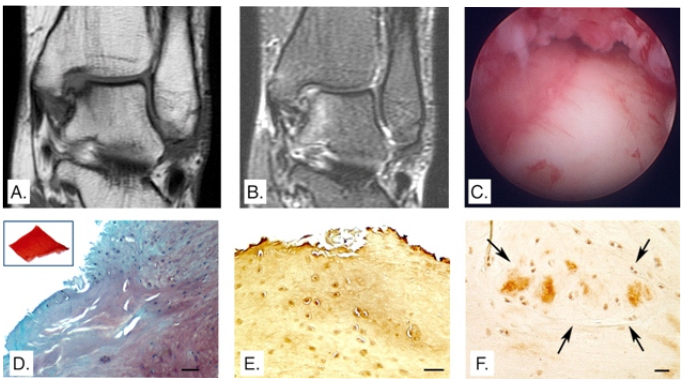

Figure 1: Patient 1 - coronal T1 (a) and T2-weighted (b) images performed 12 months after initial placement of particulated juvenile allograft placement demonstrating a heterogeneous signal with increased signal at the surface of the lesion suggestive of poor integration of the allograft. Second-look arthroscopic view (c) of the osteochondral defect demonstrated poor integration of the allograft tissue at the periphery of the lesion. Histological examination of the failed allograft repair. Safranin O staining of the repaired cartilage demonstrated severely depleted proteoglycans (d), compared with the DeNovo NT graft (d, inset). The majority of the cells in the repaired cartilage were positive for Type I collagen (e); there are small islands of Type II collagen (f, arrows), which are likely the residuals of the implanted particulated allograft.

(PJCAT) (DeNovo NT Natural Tissue Graft; Zimmer, Inc., Warsaw, IN) has emerged as a treatment option, in which allograft cartilage is harvested from deceased donors ranging in age from newborn to 13 years. PJCAT is an off-the-shelf option for the treatment of OLTs that eliminates the risk of morbidity associated with autograft donor sites and second-stage procedures [8,9].

While the use of PJCAT has become more widespread with promising short-term clinical results [9], the treatment failures associated with its use have not been well described, and no

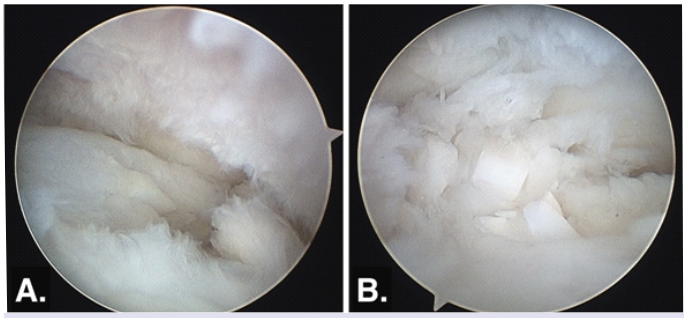

Figure 2: Second-look arthroscopic view of the osteochondral defect of Patient 2 after particulated juvenile allograft placement demonstrated fibrillation of the cartilage repair tissue. The anteromedial edge of the allograft repaired tissue appeared friable and lifted off of the subchondral surface (a). Within the area of unincorporated allograft, there appeared to be cubes of DeNovo NT that did not integrate into the surrounding normal cartilage (b).

studies have assessed the repaired cartilage quality in OLTs after PJCAT. We aimed to identify the characteristics of failure in these grafts through revision, second-look arthroscopy, and histological analysis of the failed grafts.

Case Report

Between February 2010 and January 2015, 69 patients underwent PJCAT for the treatment of an OLT at a single institution by a single surgeon. Among these patients, four patients subsequently underwent a second-look arthroscopic evaluation for continued symptoms. Informed consent was obtained from these patients before evaluation. The quality of cartilage repair was evaluated using the International Cartilage Repair Society (ICRS) score. Biopsy of the repair was taken for histological analysis in three cases.

A summary of clinical details and findings of the four patients is presented in Table 1. There were two men and two women with

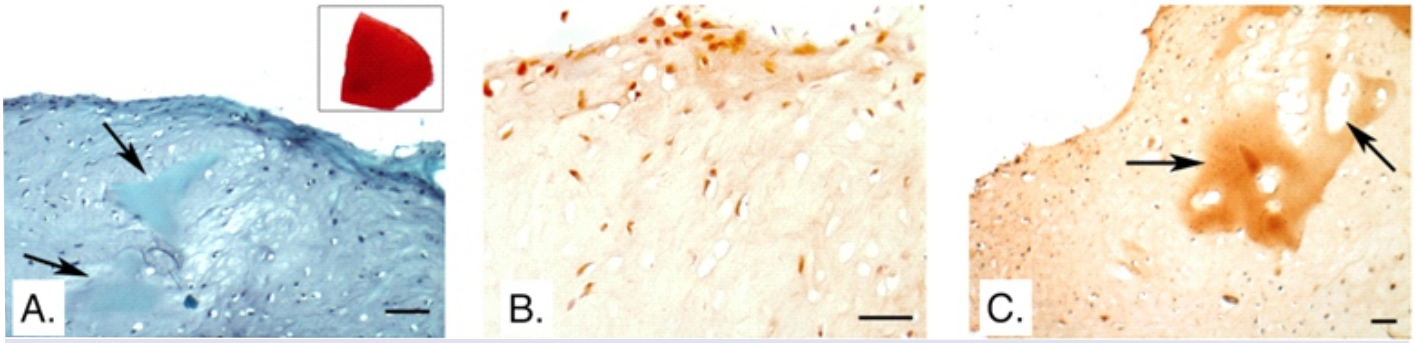

Figure 3: Histological examination of the failed allograft repair of Patient 3. Safranin O staining of the repaired cartilage demonstrated mostly fibrous tissue with severely depletion of proteoglycans (a), compared with the DeNovo NT graft (a, inset). Residual particulated juvenile cartilage cubes were seen within the fibrous cartilage (a, arrows). The majority of the cells in the repaired cartilage were positive for Type I collagen (b). While the most part of the repaired cartilage was depleted of Type II collagen (c), the residual DeNovo NT cubes were Type II collagen positive (c, arrows).

a mean age of 36.25 years (range, 15–44 years). None of the patients' past medical histories were remarkable for vascular, endocrine, inflammatory diseases, or disorders that are commonly associated with healing difficulties. All patients were previously diagnosed with an osteochondral defect of the talus that was initially treated with ankle arthroscopy with debridement and microfracture of the lesion. The average size of the OLT was 16.5 mm × 10.75 mm (range, 15–20 mm × 9–14 mm), and the mechanism of injury was traumatic in two patients and of chronic, unknown origin in two. One patient underwent lateral ankle ligament reconstruction and excision of a Haglund's deformity at the time of arthroscopy and microfracture of the OLT. Another patient underwent an additional procedure for osteochondral allograft transfer and lateral ankle ligament reconstruction before particulated juvenile cartilage allograft to the residual OLT. All patients had either minimal improvement of symptoms or recurrence of ankle pain. The average time between microfracture and placement of the particulated juvenile cartilage allograft for continued symptoms was 22 months (range, 3–62 months).

Particulated juvenile cartilage allograft was placed according to the standard surgical technique provided by the manufacturer and was performed by a single surgeon. For each patient, all sites of possible impingement were addressed, and one patient underwent lateral ankle ligament reconstruction at the time of PJCAT. All patients were non-weight-bearing for 6 weeks and then started progressive weight-bearing and physical therapy. High-impact activities were not allowed for at least 6 months postoperatively.

Second-look arthroscopic evaluation

Second-look arthroscopy was performed at a mean of 14 months (range, 8–28 months) after PJCAT allograft. The quality of cartilage repair was evaluated using the ICRS score. The ICRS grading has been previously used to macroscopically evaluate the cartilage repair after microfracture or autologous chondrocyte implantation [10]. Delaminated and friable cartilage at the periphery of the lesion was debrided and sent for histological examination. Additional procedures were performed including debridement of soft tissue or bony impingement or microfracture. Biopsy of the repair was taken for histological analysis.

Results

In this series, second-look arthroscopies demonstrated different degrees of incorporation of the allograft into the OLT. Each OLT was originally a large lesion (≥15 mm in diameter). In two patients, the failure of the allograft appeared to result from a failure of biology (Patients 1 and 4). Arthroscopic examination in these patients identified irregular and fibrotic repair tissue with little to no integration with the surrounding articular cartilage. In contrast, mechanical factors may have had an influence on the outcomes of the remaining two patients (Patients 2 and 3), which were associated with sites of bony and soft tissue impingement. Histological examination consistently demonstrated deposition of degenerative Type I fibrocartilage with minimal evidence of Type II hyaline cartilage formation. Proteoglycans within the repaired defect were severely depleted.

Patients 1 and 4 demonstrated similar findings with a lack of integration of the allograft into the surrounding cartilage. Magnetic resonance imaging findings of the failed PJCAT demonstrated increased edema along the talar surface and body at the lesion and a heterogeneous signal with increased signal at the surface of the lesion suggestive of poor integration of the allograft (Fig. 1a and b). On arthroscopic evaluation in these patients, the particulated juvenile cartilage allograft tissue appeared soft at the surface with poor integration at the periphery of the lesion (Fig. 1c). The tissue at the junction of the lesion and allograft appeared hypertrophied, fibrotic, and irregular. The findings were consistent with a Grade III ICRS repair scores (abnormal). On histological examination of Patient 1, the repaired cartilage was fibrillated on the surface and had lost regular zonal organization. The matrix was severely depleted of proteoglycans when compared with fresh cartilage allograft (Fig. 1d). The majority of the cells in the repaired cartilage were positive for Type I collagen (Fig. 1e). Type II collagen was almost absent from the repaired cartilage; however, islands of Type II collagen were found, possibly residual implanted particulated allograft (Fig. 1f).

During arthroscopic examination of Patients 2 and 3, bony and soft tissue impingements were noted in the incompletely repaired areas of the lesions. Patient 2 demonstrated fibrillation of the cartilage surface of the previous allograft defect (ICRS Grade I). Overall, the majority of the defect had been successfully treated with good appearance and incorporation of the particulated allograft. With further probing at the site of the previous OLT, the anteromedial edge of the allograft appeared incompletely healed and mechanically unstable. The tissue was friable and lifted off of the subchondral surface (Fig. 2a). The findings were consistent with a Grade III ICRS repair score (abnormal). In Patient 3, the bulk of the cartilage graft appeared to be intact with good incorporation of the cartilage allograft cubes into the surrounding matrix. Areas over the surface of the lesion appeared fibrillated with a small peripheral edge of the allograft that was not incorporated with the native cartilage. The

findings were consistent with a Grade II ICRS repair score (nearly normal). Both of these patients demonstrated areas of unincorporated allograft in which there were cubes of particulated juvenile cartilage allograft that had not integrated within the lesion and surrounding healthy cartilage (Fig. 2b). Again on histological examination, the removed cartilage was fibrous and completely depleted of proteoglycans (Fig. 3a). The residual particulated juvenile cartilage cubes noted on arthroscopy were seen within the fibrous cartilage. Immunohistochemistry demonstrated that most of the cells expressed Type I collagen (Fig. 3b). While the most part of the repaired cartilage was depleted of Type II collagen, the residual allograft cubes were Type II collagen positive (Fig. 3c).

Discussion

The biology of healing of particulated juvenile cartilage implants in cartilage repair remains unclear. When using particulated cartilage, the immediate effect of the minced cartilage is to fill the defect. However, the most important healing response hinges on the subsequent integration of the particulated cartilage with the surrounding host cartilage. The success of this integration is determined by the complex interplay between biological and mechanical factors [11]. Biologically, the allograft tissue coupled with the disruption of the subchondral plate provides the scaffold and mesenchymal stem cells, respectively, needed for the production of hyaline cartilage. However, mechanical factors are also important, influencing the growth, differentiation, and distribution of the cells and subsequent tissues.

While the marrow-stimulating techniques incite the local release of chondrocytes, the restorative techniques have focused on providing a scaffold for cartilage repair. The newest of these techniques is the use of PJCAT. In the largest cohort using PJCAT in the treatment of OLTs, Coetzee et al. [9] demonstrated good to excellent results in 78% of patients (18/23) with an average lesion size of 125 mm [2]. At an average follow-up of 16.2 months, the average American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score was 85 ± 18. In moderate-sized lesions (10–15 mm in length), 92% of patients (12/13) had an AOFAS score >80. However, in large-sized lesions (≥15 mm in length), only 56% of patients (5/9) had AOFAS scores >80. At 16 months, one patient with a large lesion failed PJCAT treatment, developing approximately 25% delamination of the graft. Despite its good short to mid-term results, the failures associated with particulated juvenile cartilage allograft have not been previously characterized in the foot and ankle literature.

The results of second-look arthroscopy after other treatment options of OLTs have been previously reported. Lee et al. reported results from 20 ankles treated with arthroscopic microfracture [12]. Arthroscopy performed 12 months after surgery demonstrated incomplete healing in 7 of 20 ankles, with fibrotic scars in 7 of 20 ankles and synovitis in 2 ankles. In terms of ICRS overall repair grades, 40% demonstrated abnormal cartilage. Furthermore, complete integration was found in only 30% of lesions. Kim et al. evaluated 52 ankles that were previously treated with osteochondral autograft transfer [13]. On repeat arthroscopy, pathological lesions including fibrous adhesions, synovitis, graft incongruence, and uncovered areas between the grafts were observed. Of these, only the presence of uncovered area between the graft plugs (filled with fibrous cartilage, unstable fibrous cartilage, or no coverage) was associated with worse outcomes. Kwak et al. performed second-look arthroscopic surgery in 25 of 29 patients with OLT treated with autologous chondrocyte implantation [14]. 11 ankles demonstrated periosteal hypertrophy while three were found to have abnormally firm cartilage (ICRS Grade III + IV). However, there was no correlation between the arthroscopic cartilage findings and clinical outcomes.

Conclusion

In this case series, we identified characteristics of failure in the grafts of these four patients through second-look arthroscopy and histological analysis of the failed grafts. Two patients had failures associated with lack of allograft integration with the surrounding native cartilage, and two patient's failures were associated with mechanical impingement. The findings support previous identification of biological and mechanical factors as critical to the successful treatment of OLTs with particulated juvenile cartilage allograft. Understanding these mechanisms will further help to determine the best indications for the use of PJCAT.

Clinical Message

When treating refractory OLTs, patient-specific factors, as well as size and depth of the lesion, may significantly influence the effectiveness of an intervention. In these cases, all patients had a large lesion (≥15 mm in diameter) that was initially treated with microfracture. No additional patient or operative factors associated with poor outcomes were identified. As long-term follow-up data for the use of PJCAT becomes available, the success of this treatment versus other surgical treatment options for OLTs will become more apparent. Determining which patients are ideal candidates for PJCAT will be important to maximal functional outcomes.

Table 1: Clinical details and findings of patients.

Case	Gender	Age	Mechanism	OLT size (mm)	OLT location	Time to PJCAT (months)*	Time to second look (months)**
1	F	42	Atraumatic	20×14	Medial, middle-third	8	28
2	M	15	Traumatic	15×10×8	Posterior medial	62	9
3	M	44	Traumatic	16×10×3	Medial, middle-third	3	8
4	F	44	Atraumatic	15×9×3	Medial, middle-third	15	11

*Time from original ankle arthroscopy and microfracture surgery to time of PJCAT, **time from PJCAT to second-look ankle arthroscopy, OLTs: Osteochondral lesions of the talus, PJCAT: Particulated juvenile cartilage allograft transplantation

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