Osteochondral defects of the talus treated by mesenchymal stem cell implantation - early results

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Abstract

The purpose of this study was to present early results of talus cartilage defects treatment with autologous mesenchymal stem cells CD34+ implantation technique. Nine (9) patients were treated, due to IV degree chondromalation (by ICRS). The applied standard procedure included: clinical examination, AP and lateral x - ray, MRI, preoperative, as well as during control examination. The surgical procedure consisted of the defect's debridement, harvesting and fixation of the periosteal flap and CD34+ implantation. Clinical results were assessed after 6 months to 3 years by clinical examination, Magee score and MRI. Good and very good clinical results were obtained and confirmed by MRI in 8 cases. In one case, cartilage hypertrophy was noted. There were no delamination and infection signs.

Key words: mesenchymal stem cells, cartilage repairs, osteochondral talus defects.

Introduction

Osteochondral defects with painful failure of the talocrural joint cause inconvenience for patients and decrease their vital activity. Joint cartilage defect is a cause of pain and swelling in lower limb, regardless whether loaded, or at rest. A limited potential for osteochondral defect healing may lead to ankle arthrosis. Usually, in talar chondral defects, the subchondral bone is involved, and either osteosclerotical or cystic lesions make natural healing processes impossible. Joint resurfacing by osteochondral autografts is limited to smaller defects of 2 - 4 cm^2 [1] and the potential donor site morbidity is discussed [2]. Allografts, although successful with some surgeons, impose limitations of donor availability and are associated with disease transmission. Autologous chondrocyte implantation (ACI) is currently indicated for focal, isolated defects [3, 4]. ACI-regenerated hyaline tissue is, sometimes, not properly integrated with the subchondral bone and with healthy chondral defect margins. In large, full thickness defects, delamination of regenerated tissue is frequent.

The new and promising direction of repairing cartilage defects by chondrogenic induction is the autologous mesenchymal stem cell implantation. Mesenchymal stem cells are a rare population of undifferentiated cells, isolated in adults from different tissue sources and differentiating into mesodermal lineages, like: bone, fat, muscles, cartilage, tendons and marrow stroma. Stem cells are multipotential with multidirectional lineage, stimulated by local intrinsic and extrinsic factors. Local environment interactions and tissue signalling molecules provide stimulation to the differentiation of a new line of cells and proper cartilage formation, rebuilding and integration [5, 6]. As for the physiology of healing processes in cartilage defects, the restitution of joint surfaces by hyaline cartilage, as well as subchondral bone reconstruction are of paramount importance, as they warrant normal biomechanical and biochemical properties and a good integration of regenerated tissues.

Materials and Methods

The authors assessed 9 patients, treated by the mesenchymal stem cell implantation technique. All the patients were treated, due to IV degree chondromalation (by ICRS). The standard procedure was: a clinical examination, AP and lateral x - ray and MRI, performed preoperatively, as well as during control assessment. The average defect was 0.5x0.7 cm with 0.5 - 1.0 cm

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Figure 1. Ankle MRI with osteochondral defect in talus medial site.

Figure 2. Intraoperative view - osteochondral defect.

Figure 3. Intraoperative view - implantation of cells

depth. In deep lesions (more than 0.5 cm), with subchondral bone involvement, autologous cancellous bone grafting (sandwich technique) was performed in all the cases. The defects as well as the operative solutions were photographically documented. The

Figure 4. MRI after 9 months from the operation.

patients were stimulated by growth factor G-CSF (0,3 mg subcutaneously per seven days). Cytometric assessment of patient blood and leukocytes and reticulocyte assessment were performed 3 times during the stimulation period. Mesenchymal stem cells were harvested from patient blood by cell separators on the day of the surgery. Cell suspension was measured in a flow haemocytometer and the quantity of cells with membrane CD34+ marker was counted (cell/cm^3 suspension).

The surgery procedure consisted of resection of damaged tissues, harvesting of the periosteal flap from anteromedial surface of the tibia, flap fixation by suturing and fibrin glue and, finally, an injection of CD34+ cell suspension. Surgical exposure to the talus was either anterior or by ankle osteotomy - medial and lateral. The site of osteotomy was fixed with screws. Clinical and radiological results were assessed after 3 months to 3 years after surgery. Ankle function was evaluated, both clinically and by the Magee 10-point score (patient subjective gait assessment [7].

Magee score:	
without limitation	10 points
pain after long distance	8
mild compliance	6
moderate compliance	4
walking with crutches	2

In MRI (T1, T2 and STIR sequences), major attention was paid to good defect reconstruction, rebuilding of subchondral bone, proper integration of regenerated cartilage with bone and intact defect margins.

Results

In all the cases, good wound healing was observed. No bacterial infections were observed in any of the patients. In 8 cases, gait assessment after operation (Magee score) improved and the patients, after three months, had not limitations in walking. We observed one case with longer bone healing at the site of ankle

osteotomy. In MRI (T1, T2 and STIR sequences), it was observed in all the patients that the defects were well refilled with tissue with signal the same as that from normal cartilage. In two cases, fibrotic changes in margin parts of regenerated tissue and the periosteal flap were found. In one patient, hypertrophic tissues of the reconstructed area were shown. Neither swelling, nor locking nor pain was observed after 3 months from the operation. Delamination of repaired cartilage was not observed in any of the cases. Furthermore, proper integration of regenerated cartilage with rebuilt subchondral bone and MRI confirmed intact defect margins. The examples of good results, confirmed by MRI, are shown in Fig. 1. - Fig. 4.

Discussion

The obtained early clinical results of talus resurfacing with mesenchymal stem cell CD34+ implantation provide promising operative prospects in talar chondromalatia. It is very important to confirm such early observations after 6-7 and more years from the surgery. An annual assessment and MRI control seems to be a valuable procedure for graft rebuilding, and biomechanics evaluation. In deep cystic osteochondral lesions, cancellous bone grafting was necessary for the restoration of normal bone stock to stem cell CD34+ implantation. This is also very important, due to the restoration of talus mechanical function in the ankle joint. The presented autologous stem cell implantation technique is, together with ACI, one of the valuable repair procedures, as it offers possibilities of defect refilling with hyaline or hyaline-like cartilage. Experimental studies [6] presented morphological, histological and histochemical rebuilding of stem cell grafts in animal models. Hyaline or hyaline-like cartilage were the final result of cell transplantation. Multidirectional potential of stem cell differentiation, stimulated by local environment factors, such as the transforming growth - factor - beta family or bone morphogenetic proteins [5, 8], gives possibilities of implant conversion to chondrocytes and revascularised subchondral bone. An important observation in this study was the proper refilling of large, full thickness defects with tissues, well integrated with the subchondral part. Delamination was not observed, due to possible rebuilding of subchondral bone with good revascularisation [6]. By contrast to the autologous chondrocyte implantation technique, bone bleeding predicts better subchondral healing and good integration of regenerated hyaline cartilage. Final MRI assessment in all the cases showed subchondral restoring and satisfactory integration of grafts, which may have good long-term results.

Conclusions

The stem cell CD34+ implantation technique is a valuable procedure in large, full thickness talus cartilage repair. Bone grafting must be performed in all cases of deep osteochondral defect to obtain bone stock restoration and proper chondral integration.

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