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The effects of low-dose radiotherapy on fresh osteochondral allografts: An experimental study in rabbits

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ABSTRACT

Objective: The aim of this study was to investigate the effects of low-dose fractionated radiotherapy on cartilage degeneration after distal femoral fresh massive osteochondral allograft transplantation.
Methods: Twenty-four New Zealand White rabbits were divided into three groups of 8 rabbits each. All rabbits underwent distal femoral medial condyle fresh massive osteochondral allograft transplantation from California rabbits. The group 1 underwent transplantation without any preliminary process. The group 2 underwent fractionated local radiotherapy of 100 cGy for five days starting on the transplantation day. The group 3 included the rabbits to which the grafts transplanted after radiating in vitro by a single dose radiation of 1500 cGy. The hosts were sacrificed twelve weeks later. Anteroposterior and lateral radiographs were taken. Synovial tissue, cartilaginous tissue, and subchondral bone were assessed histopathologically.
Results: Nonunion was present in three cases of group 2 and one of group 3 in which cartilage degeneration was more severe. Synovial hypertrophy and pannus formation were more obvious in non-radiated rabbits. Hypocellularity and necrosis of the subchondral bone were rare in group 2. More cartilage tissue impairment was present in group 3 compared to group 1.
Conclusion: In osteochondral massive allograft transplantations, the immune reaction of the host could be precluded with radiotherapy, and the side-effects can be prevented by low-dose fractionated regimen. The total dose of fractionated radiotherapy for an immune suppression should be adjusted not to damage the cartilage tissue, but to avoid articular degeneration in the long term.

Introduction

Osteochondral allografts (OCA) are used as biological implants in reconstruction following bone tumor resection, osteonecrosis, osteochondritis dissecans, osteoarthritis, and post-traumatic cartilage defects.[1–3] Complications following OCA application include fracture in the graft, nonunion, subchondral collapse, and osteoarthritis. These complications are usually thought to be secondary to immune response to the bony component of the graft. Cartilage viability is important for the success of OCA. Freezing and freeze-drying methods used to suppress immunity in bony allografts cause chondrocyte death in OCA. Even use of cryoprotectants such as glycerol and dimethyl sulfoxide is unable to provide chondrocyte survival in more than 50% of cases.[4,5] In response, fresh application of OCA without preservation has become more popular.

Fractionated low-dose radiotherapy has been used as a painkiller in some degenerative joint diseases, although the mechanism is still unknown.[6,7] An experimental model has been used to investigate the anti-inflammatory effects of fractionated low-dose radiotherapy on osteoarthritis. This model had a similar pathway to osteoarthritis developed after OCA transplantation.[8] Correspondingly, the present study was designed to reveal whether fractionated low-dose radiotherapy can prevent articular degeneration following fresh massive OCA transplantation.

Materials and methods

The present study was performed in an experimental and medical research laboratory, and the samples harvested for

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histopathological investigation were assessed by the Gazi University School of Medicine Department of Pathology. Radiotherapy applications were performed by members of the Hacettepe University School of Medicine Department of Radiation Oncology. Grafts were received by 4-month-old female New Zealand White rabbits weighing 2700–3200 g each. Donors were equally weighted California rabbits of the same age.

Twenty-four New Zealand White rabbits who underwent massive OCA transplantation had been divided into 3 groups. Group 1 underwent transplantation without preliminary process. Group 2 underwent fractionated radiotherapy for 5 days, beginning on the day of transplantation. Group 3 included rabbits that received grafts following in vitro, single-dose radiation.

Surgical technique

Rabbits were fasted 6 h prior to surgery, and were anesthetized by intramuscular injection of 50 mg/kg ketamine hydrochloride (Ketalar®; Pfizer, Inc., New York City, NY, USA) and 10 mg/kg xylazine hydrochloride (Rompun®; Bayer, Inc., Leverkusen, Germany). Infection prophylaxis (25 mg/kg cefazolin sodium; Sefazol®; Mustafa Nevzat, Inc., İstanbul, Turkey) was administered immediately prior to surgery. After the fur was shaved, the skin was sterilized with gauze pads soaked in 7.5% povidone iodine (Polyod®; Droğsan, Inc., Ankara, Turkey).

The extremity was draped in a sterile fashion, and an anterior longitudinal incision was made. Joint approach was made by medial parapatellar capsular incision, and medial collateral ligament was horizontally incised in the center. Condyles were entirely exposed with the knee in flexion. The medial femoral condyle was osteotomized with an electric bone saw from the medial aspect of the intercondylar notch to the medial femoral cortex, 0.5 cm proximal to the attachment of the medial collateral ligament. Anterior cruciate ligament and medial meniscus were secured intact (Fig. 1a). Fresh and similarly dimensioned medial femoral condyle allograft harvested from a California rabbit, using the same technique, was orthotopically transplanted. Fixation of the grafts was established with 2 k wires (Fig. 1b, c). Transected stumps of the medial collateral ligament were repaired in an end-to-end fashion with 5-0 polypropylene (Prolene®; Ethicon, Inc., Edinburgh, Scotland). The joint capsule was then sutured in a continuous manner with 4-0 vicryl (Ethicon, Inc., Edinburgh, Scotland), as was the skin, with 4-0 catgut (Droğsan, Inc., Ankara, Turkey).

Implementation of radiotherapy

Group 2 underwent fractionated low-dose local radiotherapy with Cobalt-60 external beam radiation following surgery. Five times, 100 cGy exposure to radiotherapy was administered on a per-day basis. A total of 500 cGy was administered, with the first dose administered the evening following surgery. The animals were anesthetized with 10 mg/kg of ketamine hydrochloride prior to radiotherapy. In Group 3, the harvested grafts were placed in a sterile jar with 0.5% NaCl and wrapped with sterile drapes. Grafts were exposed to a single dose of 1500 cGy radiotherapy and were transplanted after 6 h.

Postoperative follow-up

Anteroposterior and lateral radiographs were postoperatively obtained. No immobilization was performed for the knees. The animals were allowed to move freely in cages under relative humidity of 55 ± 5% and temperature of 21 ± 3 °C. They were fed with standard rabbit granule ad libitum, with free access to water. Hosts were sacrificed after 12 weeks by injection of air into the heart. The femur and the tibia were osteotomized at mid-shaft level in order to obtain the entire joint.

Samples were fixed with 10% formalin solution after radiographs were obtained. Following macroscopic examination (Fig. 2), samples were decalcified in a 10% formic acid solution for 1 week. Samples were embedded in paraffin blocks and sagittally sectioned into 6-μm slices. Slices were stained with Hematoxylin and Eosin

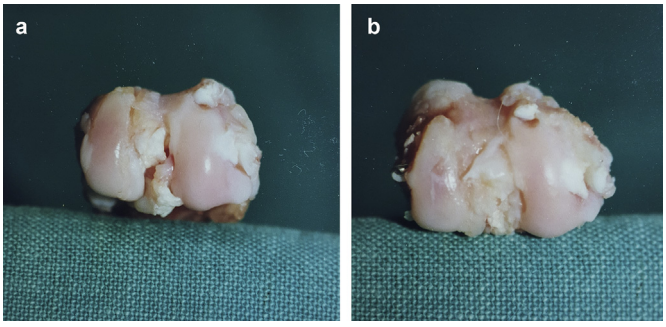

Fig. 2. Macroscopical evaluation of the articular surface of the osteochondral allograft. a. Normal articular cartilage of the graft. b. Degeneration of the articular cartilage of the graft.

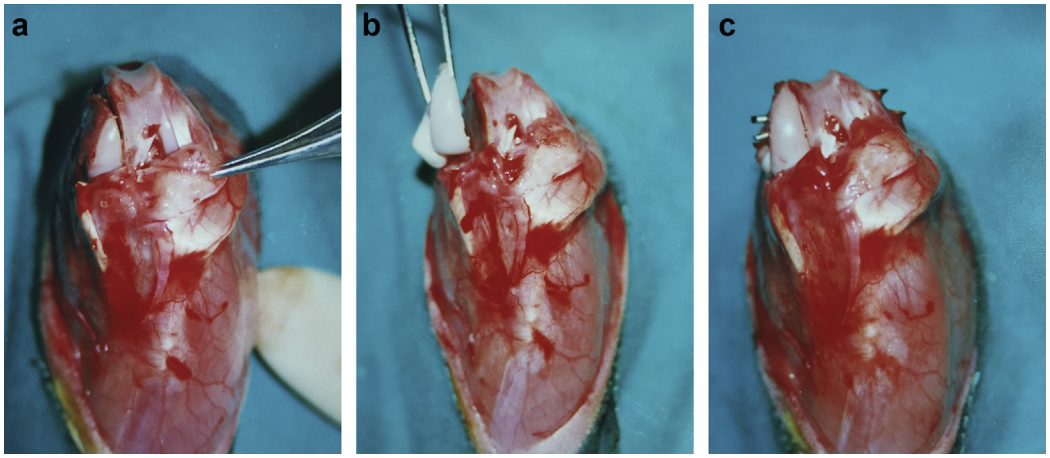

Fig. 1. Surgical technique of osteochondral allograft transplantation. a. Oblique osteotomy was performed between the medial aspect of the intercondylar notch and the medial femoral cortex, using an electric bone saw. b. Position of fresh osteochondral allograft. c. Fixation of the osteotomy with 2 k wires.