Introduction

Meniscal injuries in human and veterinary patients result in a significant loss of function, and those occurring in the avascular zone of the meniscus will not heal spontaneously. Although most meniscal injuries are currently treated by partial meniscectomy, most research is now focused on methods for producing functional tissue in avascular meniscal defects. We have previously demonstrated the ability to induce meniscal-like tissue regeneration in large, avascular meniscal defects using porcine small intestinal submucosa (SIS). While the results of our previous work have been encouraging, complete regeneration of the meniscus with total protection of articular cartilage has not been realized in large (80%), avascular defects. Early biomechanical disruption of regenerating tissue has been proposed as a primary detriment to achieving complete regeneration. The purpose of this study was to determine the effects of biomechanical protection and fibrin clot augmentation on meniscal tissue-engineering using SIS grafts in dogs.

Methods

Twenty-four dogs underwent an interior subtotal (approximately 80%) meniscectomy within the avascular portion of the medial meniscus by means of a medial arthrotomy with medial collateral ligament (MCL) detachment via osteotomy. Dogs were randomly assigned to one of four groups: SIS graft alone (SIS), autogenous fibrin clot alone (Clot), SIS graft plus autogenous fibrin clot (SIS-C), or no graft (NG). Grafted dogs received a SIS graft that was configured to approximate the size and shape of the resected portion of meniscus and sutured into place using simple interrupted sutures of 5-0 prolene (Fig. 1). Clot and SIS-C dogs received an autogenous fibrin clot placed into the meniscal defect. A specially-designed, hinged transarticular external skeletal fixator (ESF) was placed on all dogs after MCL reattachment and closure. Dogs were confined to cage rest for the entire post-instrumentation period. The ESF was maintained for 5 weeks with 0° range of motion (ROM) for the first 3 weeks followed by 10° ROM for week 4 and 20° ROM for week 5.

The dogs were sacrificed 3 weeks (n=12) or 6 weeks (n=12) after instrumentation. The day prior to sacrifice the dogs were evaluated by lameness scoring, knee radiographs, and ultrasonographic determination of replacement tissue cross-sectional area (CSA). After sacrifice, dogs were evaluated for gross and histologic appearance of meniscal replacement tissue, amount of replacement tissue, articular cartilage damage (%ACD), and replacement tissue collagen content. All statistical analyses were performed using a computer software program. Significance was set at p<0.05.

Results

The only complications (n=6) noted were due to improper ESF placement resulting in secondary synovitis and articular cartilage pathology. The gross appearance of replacement tissue ranged from meniscal-like tissue covering the entire defect to no identifiable replacement tissue present. (Figure 2). At 3 and 6 weeks, the replacement tissue CSA was significantly (p<0.01) higher in groups SIS and SIS-C compared to groups Clot and NG (Figure 3). The central CSA of the replacement tissue was less than that at the anterior and posterior horns, but greater than what has been reported in previous studies. At 3 and 6 weeks, femoral and tibial %ACD were significantly (p<0.01) lower in groups SIS and SIS-C compared to groups Clot and NG (Figure 4). Histologically, replacement tissue ranged from meniscal-like tissue with excellent integration into remaining meniscus to no replacement tissue present (Figure 5). Subjectively, groups SIS and SIS-C demonstrated the most consistent and appropriate meniscal regeneration.

Discussion

Small intestinal submucosa has been shown to induce meniscal-like tissue regeneration in large, avascular defects of the canine meniscus. SIS meniscal grafts have consistently resulted in greater tissue regeneration and chondroprotection than partial meniscectomy. Previously, meniscal regeneration has been near normal at the anterior and posterior horns with poor central regeneration. Biomechanical forces placed on the SIS grafts during early tissue replacement were proposed to be the primary cause of this poor central regeneration. In the present study, significantly more meniscal replacement tissue was present in dogs receiving SIS grafts resulting in greater protection of the articular cartilage. In addition, early biomechanical protection of the grafts through the use of an ESF potentiated more appropriate regeneration in the central meniscus. The addition of autogenous fibrin clot did not augment meniscal regeneration in this model. These data further support the use of SIS as an appropriate biomaterial with which to produce a tissue-engineered meniscus.

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