Combination Therapy of Mesenchymal Stem Cells with Matrigel for Meniscal Injury in a Dog

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Abstract: A 6-year-old castrated male Miniature Pinscher weighing 3.5 kg was presented with left hind limb non-weight bearing, knee pain and lack of extension of the knee joint. Due to the same symptoms, the dog had previously undergone surgery for patellar luxation and cruciate ligaments injury at 8 month ago in another animal hospital. Following radiographic and magnetic resonance imaging (MRI), the problem was diagnosed as a lateral meniscus injury. Surgical resection of injured meniscus and transplantation of mesenchymal stem cells with matrigel resolved all symptoms.

Key words: Dog %Meniscus Injury %Mesenchymal Stem Cells %Matrigel

INTRODUCTION

The meniscus is a wedge-shaped semilunar fibrocartilage that lies between the weight bearing joint surface of the femur and the tibia. The overriding problem with a meniscal injury is the limited capacity the meniscus has to heal itself effectively [1, 2]. Tears located within the avascular region are larger and more complex and have been shown to have a limited capacity for repair, particularly with the presence of associated joint instability [3, 4]. For symptomatic meniscus injury, the majority of meniscal surgeries involve a partial resection of injured meniscus, leaving the joint deficient in meniscal function. Moreover, loss of meniscal tissue frequently leads to long term degenerative joint changes, articular cartilage degeneration and osteoarthritis [5].

The meniscus injury in our case was a persistent left hind limb non-weight bearing and knee pain in a dog that formed after surgical repair of the same symptoms. The following report described diagnosis, treatment and application of mesenchymal stem cells (MSCs) with matrigel as scaffold. This was a rare case of canine lateral meniscus injury and symptoms were improved by the combination of surgical procedure and stem cells.

MATERIALS AND METHODS

A 6-year-old castrated male Miniature Pinscher weighing 3.5 kg was presented to My Pet Animal Medical Center, South Korea with left hind limb non-weight bearing and knee pain. He had previously undergone a surgery at 8 month ago and had been on non-steroidal anti-inflammatory drug (NSAID) therapy in other animal hospital. According to the owner, the Miniature Pinscher had been operated on patellar luxation and cruciate ligaments repair. After the surgery, the symptoms did not improve and he pleaded the knee pain. The veterinarian who operated him removed pin used in tibial tuberosity transposition, but the owner also reported continuous non-weight bearing and knee pain.

When originally presented to our hospital, the dog pleaded pain when palpated and manipulated over the left hind limb. Physical examination revealed severe muscle
RESULTS

During the surgical procedure, we confirmed previously operated injured trochlear groove and intact cruciate ligaments (Fig. 3A). After lateral meniscectomy and debridement, the removed meniscus space was filled with MSCs [4, 6] and matrigel [7, 8] (from the Department of Veterinary Physiology, College of Veterinary Medicine, Seoul National University). The major components of matrigel are laminin, collagen and fibronectin. In addition, the matrigel is soluble and sterile extract of basement membrane proteins that form a three-dimensional (3D) gel at 37°C and has a rich store of growth factors as well as promotes the differentiation of many different cell types [9]. In addition, MSCs was injected directly into the stifle joint under sedation after one week from surgery. Postoperative care included administration of oral medication with antibiotics and NSAID for two weeks. Robert Jones Bandage was maintained for seven days. After two weeks from surgery, we performed rehabilitation including range of motion (ROM) and ice pack twice per day and swimming per 7 days during hospitalization. Then, he started occasional weight bearing of operated hind limb at the same time. In addition, survey radiographs showed widening of the lateral joint line and no progressed degenerative arthritis (Fig. 1C). After one month from surgery, weight bearing time of operated hind limb was increased as well as there was no pain during rehabilitation. Normal gait of operated hind limb has been observed in two months after the surgery.
DISCUSSION

Mesenchymal stem cells (MSCs) have been proposed as an exciting alternative in tissue and cellular regeneration [10]. MSCs have been shown to be useful in the regeneration of skin and bone defects in humans [10-14] and of many more different tissues in animals [14, 15]. In particular, recent evidence has shown that MSCs can help in the regeneration of meniscal defects [16-18]. In addition, the scaffold may provide a bridge to fill the gap between the cut ends of the defects and also as a vehicle to deliver cells and biomolecules for cell replacement or modification of the unfavorable microenvironment as inflammation [8, 19, 20]. Furthermore, a cell/scaffold combination could be a very promising alternative for repair of meniscal injury [15, 21, 22]. MSCs have been shown to help in the regeneration of meniscal defects using artificial scaffolds [23] or injected directly into the joint [24]. Therefore, we hypothesized a combination of complementary strategies aimed at enhancement of functional recovery after meniscal injury. Indeed, previous studies have shown that stem cell transplantation in combination with a complementary strategy provided improved therapeutic benefits as compared to stem cell administration alone. Also, these studies reported in the literature have provided histological evidence that combination therapy may be a good approach for treating meniscal cartilage lesions [15, 23, 25].

The mechanism of between MSCs and matrigel cannot be determined from our case report. However, our case showed a clear improvement in clinical signs in chronic lesions and indicated that combination of MSCs and matrigel show the possibility of treatment for meniscal injury in canine clinical application. Although our case was treated by surgery and stem cells with matrigel, more cases of treatment for meniscal injury are needed in the small animal practice.

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REFERENCES


