Adipose Derived Stem Cell Therapy in the Treatment of Canine Degenerative Joint Disease Secondary to Conformational Abnormalities

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- Chronic degenerative joint disease raises many challenges to the practitioner
- Long term NSAID administration can induce unwanted secondary side effects
- Autologous adipose derived stem cell therapy offers an effective option in treating canine DJD without requiring daily treatment.

A 4 year 9 month old 6.8kg (15 lb) intact male Rat Terrier named "Harley Blue" presented with a history of chronic lameness in both hind legs, a 6 month duration of refusal to go up steps, stiffness after rising from a laying position, and difficulty stretching. The dog also preferred lying to sitting. The lameness had persisted since 6 months of age. Previous diagnostic testing by the referring veterinarian included radiographs. Interpretation of those films revealed conformational abnormalities in both femurs and tibia. Management of this problem had included exercise restriction and NSAID therapy utilizing 25mg Rimadyl® (carprofen) once daily orally. The owner presented "Harley" because of gastrointestinal upset that had recently developed after administration of the NSAID. Pain was elicited upon flexion and extension of both hips and stifles which manifested as vocalization and an attempt at biting the examiner. "Harley" was radiographed under sedation with intravenous Propoflo (Propofol) and bilateral hip dysplasia, conformational abnormalities of the femurs and tibia, and stifle degenerative joint disease was evident. Rimadyl ® (carprofen) was discontinued and the owner was advised to temporarily

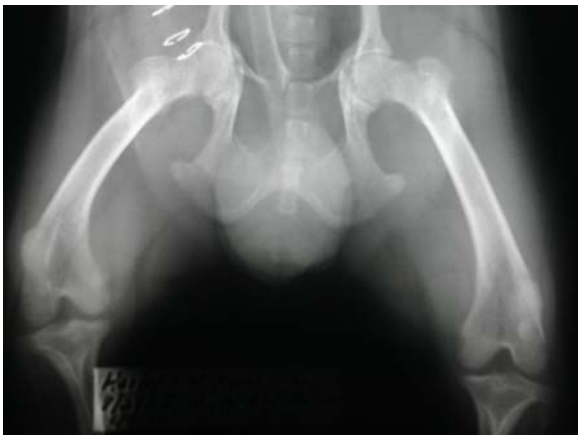

Figure 1: Bilateral femoral conformational abnormalities

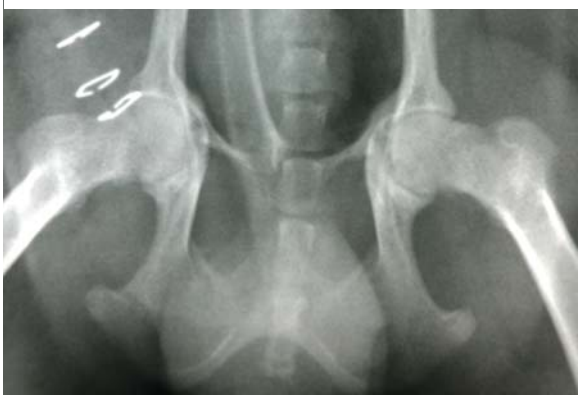

Figure 2: Hip Dysplasia

feed a modified diet. One week later, the patient re-presented to have an adipose tissue collection performed for intra-articular stem cell therapy. A pre-anesthetic panel revealed: ALT= 62 (10-100); ALKP 94 (23-212); TP 8(5.2-8.2); GLUC= 128

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(77-125); BUN= 16(7-27); CREA= 1.1 (.50-1.8); PCV=42%.

A 2O gauge l inch catheter was placed in the right cephalic vein and induction with 90mg (.9cc) ketamine/ 4.6mg (.9cc) diazepam intravenously was followed by direct intubation and maintenance with isoflourane and oxygen. The patient was placed in dorsal recumbency and the surgical site was clipped, prepped and draped in standard fashion. The patient was monitored by pulse oximetry, continuous ECG and blood pressure. A 5cm linear incision was made over the right inguinal fat pad. The subcutaneous tissues were separated using blunt dissection and 15 grams of adipose tissue was obtained. The tissue was directly placed into the collection vile and shipped overnight to the Vet-Stem™ laboratory in Poway, California.

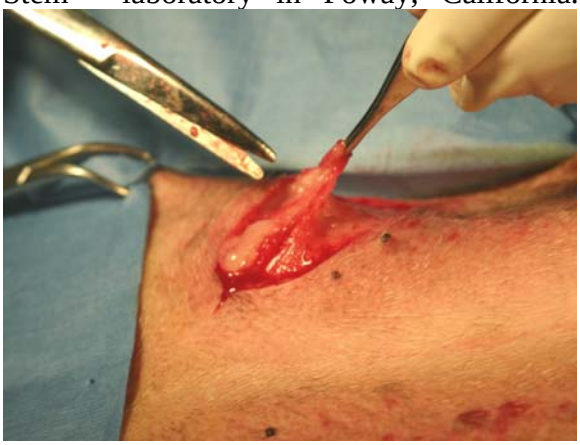

Figure 3 - Dissection of inguinal subcutaneous adipose tissue

The subcutaneous tissues were closed using 3-0 synthetic monofilament absorbable suture in a simple interrupted, bury the knot pattern minimizing dead space. The skin was closed with a subcuticular pattern and externally with stainless steel staples. The patient was administered 1mg (.3cc) Buprenex (buprenorphine) IV post-operatively. The recovery period was uneventful and the patient was discharged that afternoon.

Vet-Stem™ processing of the adipose sample yielded 81.3% viable cells with 420,000 cells per gram of tissue for a total viable cell yield of 5.6 million cells. The stem cells were returned via overnight courier within 48 hours of the original collection.

The patient was again induced with ketamine and diazepam via intravenous catheterization, intubated and maintained on isflourane and oxygen. The dorsolateral area over the left coxo-femoral joint and the cranial aspect of the left stifle was clipped and prepped in standard fashion. The previously mentioned patient monitoring parameters were again utilized. Using sterile technique each syringe was rolled similar to re-suspending insulin until a uniform consistency was attained. Using a 1 ½ inch 22 gauge needle, 1 cc of the cellular suspension (1.5 million cells) was injected into each joint in step-wise fashion so that sterile technique was not breached. The injection sites were covered with sterile 3x3 gauze and a trimmed piece of Elasticon. These bandages were allowed to remain on the patient throughout the remainder of the day. The process was repeated in the right coxo-femoral joint and stifle. During recovery, 1mg (.3cc) Buprenex (buprenorphine) was administered intravenously. The patient was again discharged that afternoon.

A 2 week post-procedure recheck was performed during which time the stainless steel staples were removed and the inguinal incision was assessed. The patient had not had any NSAID therapy in 22 days. The owner reported 6 days after the procedure the patient was more active, showed interest in playing, and attempted to go up the stairs. By 13 days post-procedure, the patient was running in their yard, playing with his ball, going up the stairs and sitting up on his hind legs to beg for a treat. The owner even commented that their neighbor had noticed the dramatic improvement in the

dog's attitude and activity level. To date, "Harley" has not had to take any NSAIDS and his owners are more than pleased with the results.

Figure 4: Full extension of hips under no physical or chemical restraint one month post-procedure.

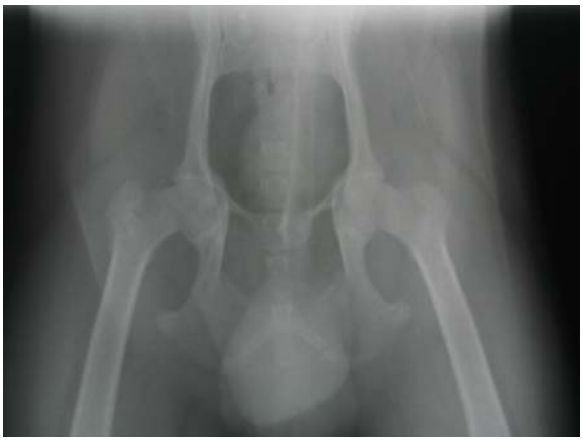

Figure 5: Radiographs under sedation one month post-procedure.

Intra-articular use of adipose derived stem cells has been documented to induce long-term pronounced clinical improvement in equine patients, improving lameness scores, minimizing or eliminating the need for palliative medical management, and increasing the rate of return to function. To date, this is the first documented clinical application of autologous adipose derived stem cell therapy in canine degenerative joint disease. Additional patient evaluation will be performed over the next months to quantify duration of pain relief and the presence, if any, of radiographically evident changes in the affected joints. Vet-Stem™ technology, utilizing the benefits of autologous adipose-derived stem cell therapy, can be an effective method in managing otherwise difficult cases of canine osteoarthritis and degenerative joint disease.

References:

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4. Fluorescently labeled mesenchymal stem cells (MSCs) maintain multilineage potential and can be detected following implantation into articular cartilage defects. Joseph Quintavallaa,*, Susan Uziel-Fusia, Jianyun Yinb, Ernst Boehnleina, Gary Pastora, Vincent Blancuzzia, Hem N. Singha, Karl H. Krausc, Elizabeth O'Byrnea, Theodore C. Pellasa, 2001 Elsevier Science Ltd.