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SmallAnimal

Nonsurgical perspectives on CCL disease

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Exclusive CCL Series
This is part three of a four-part series on approaches to cranial cruciate ligament tears.

The road to nonsurgical canine cruciate management is paved with modalities and tools ready to assist with repair and recovery.

Part one of this series discussed managing owner expectations, strategies to protect the sound cruciate, diagnosing ligament and meniscal damage, and joint irrigation/visualization. In this continuing series on nonsurgical management of the injured cruciate, I will begin by discussing joint injectates.

What to inject?

Injection of the nonsurgical stifle joint takes place while the patient is sedated. Options of injectates include platelet-rich plasma (PRP), mesenchymal stem cells (MSC), hyaluronate, steroids, and autologous conditioned serum/plasma (ACS/ACP).

If the stifle appears to have stability (either through being a partial tear only [versus a full tear]), significant joint inflammation, or joint fibrosis, or alternatively, if there is question as to whether this is cruciate disease, then **PRP** is a reasonable injectate carrying minimal chance of deleterious effect. Its transforming growth factor beta ability will increase collagen, recruit progenitor cells, and reduce COX-2. Expect to repeat this at least once or twice in a four- to six-week period. Multiple leukoreduced PRP injections improved range of motion and decreased pain for four to six months in a model of experimental cruciate ligament transection in dogs (Cook et al. 2016). A single intra-articular (IA) injection of autologous platelets resulted in significant improvements at 12 weeks in dogs with natural osteoarthritis (OA) in the stifle and other joint (Fahie t al. 2013). Benefit was found in a group of dogs with acute cruciate injury treated with a single PRP injection despite continued OA (Bozynski et al. 2016).

Not many studies have shown superiority of stem cells over PRP in either human or veterinary patients. Multiple joint OA may be better addressed with stem cell therapy, but variation in products derived from whole blood or stem cell sources is quite high (Bogers 2018). The cost usually exceeds that of PRP procurement and reinjection because of the harvesting and initial invasiveness required.

IA injection of **MSC** had profound effects on reducing inflammation in contralateral stable partial cruciate canine tears (Muir et al. 2016). A recent study evaluating 36 dogs treated with PRP and bone marrow aspirate concentrate or adipose-derived stem cells found that both improved gait analysis and quality of life compared to controls (Canapp et al. 2016). Though these studies exist, justifying the cost of MSC without the volume of literature comparable to PRP puts stem cells on the back burner at this time.

Hyaluronic acid (HA) is added or injected solo for anatomically challenged cases (such as very straight or conformationally challenged hind limbs), those with known meniscal damage, or those with bone-on-bone contact, where a viscosupplement may help. But I also will use this as an anti-inflammatory for initial or low-grade inflammation when PRP is not available or is unaffordable. It induces chondrocyte proliferation, inhibits inflammatory mediators, and exerts an anti-apoptotic effect on chondrocytes (Keiichi et al. 2002). In a study assessing efficacy of IA HA, dogs with experimentally transected ligaments treated with HA were significantly clinically, though not histologically, improved compared to controls (Paschuck et al. 2016). Different forms/brands are available; theoretically, products that have a 1.5 to 2 million D molecular weight may have a more beneficial effect. Six months of pain relief was observed with IA compared to oral carprofen (Hellstrom et al. 2003). Polyglycan SA (ArthroDynamic Technologies Inc.) is a form of hyaluronate coupled with chondroitin and glucosamine that produces particularly good outcomes in inflamed joints.

Steroid injections are used for end-stage OA joints, patients with severe financial limitations, or when immediate improvements in very inflamed/swollen joints are required. The two most commonly used injectable IA steroids include methylprednisolone acetate and triamcinolone. Few studies exist on the use of IA steroids in canine patients. Positive outcomes were noted in a prospective randomized trial of hyaluronate with methylprednisone administered to dogs with elbow OA (Franklin et al. 2014). The *in-vivo* effects of corticosteroids (triamcinolone) on lesions was examined in 12 dogs with Pond-Nuki model of OA, and found it to be 100 percent effective in preventing cartilage erosions. The anti-inflammatory effect is immediate (24 hours) and lasts for months. Human chronic OA patients have this approach typically repeated three to four times per year. For many joints, I inject either triamcinolone or methylpred acetate when acute inflammation is present, and if there is significant improvement in the next week, discuss the more natural approach of PRP injections as a follow-up to the IA steroid. Early IA steroids have been shown to mitigate injury-induced changes in collagen fragmentation after experimental transection of ACL in pigs (Sieker 2016).

ACS/ACP or interleukin receptor antagonist protein (IRAP) has been used as a treatment for OA in humans and horses for many years. Current evidence supporting the efficacy of ACS in canine OA patients is lacking. Processing results in the concentration of IL-1RA and other healing factors without undesirable increases in IL-1B (Stief et al. 2011); however, the efficacy of such efforts in the clinical treatment of OA or ligament disease is lacking (Saunders et al. 2018). In a

prospective, randomized, double-blinded trial comparing outcomes in dogs with bilateral elbow OA treated with hyaluronan plus methylprednisolone or ACP, lameness, activity, and pain were evaluated, and both treatments found to have beneficial effects for dogs with bilateral elbow OA (Franklin and Cook 2013).

"Surgery may not be an option for many canine patients due to family economics, the pet's age weighed against investment, the patient's comorbidities, including obesity and other joint arthritis, or even postoperative care issues (*e.g.* time and financial investment, patient restraint and altered lifestyle, and environmental concerns)."

Stability

Once instability has been diagnosed in the cranial cruciate deficient stifle, a means of providing external stabilization is required for successful nonsurgical management. Some orthoses manufacturers require "molding" or "casting" of the brace while the patient is sedated; others prefer the same to be done while the patient is awake and standing. Functional bracing can offer enhanced proprioception, relaxation, controlled motion, and reduced fatigue, in addition to providing mechanical protection via limiting anterior translation of the joint. Stiffness of the hinge greatly influences joint mechanics. A recent retrospective study examining CCL-deficient dogs treated with an orthoses showed improved pressure index or weight bearing even in one patient with meniscal damage (Carr 2016). It is important to ensure appropriate break in, continued modification of activity, and regular (daily) exams for rub sores/soft tissue iatrogenic injury. Custom-made orthoses can help reduce these problems, but even so, owners should be made aware of the complication and patient intolerance possibility (Hart 2016).

While custom-made orthoses (Hero, K-9 Orthotics and Prosthetics Inc., OrthoPets) have historically fit best, these devices still require much time of the owner and patient for casting, fitting, and training, as well as application/accommodation of the device to the limb. Noncustom- and semicustom-made devices do exist, such as A-traC Dynamic Brace, Ortocanis, Caerus CCL Brace; they're slowly progressing in quality, durability, waterproof nature, and cost. If a custom model is sought, carefully follow company guidelines on casting; wait on casting until swelling has subsided to avoid fitting issues. One study showed owner satisfaction for stifle bracing was quite high (Hart 2016). While not yet scientifically proven, it's well accepted that a rehabilitation program will improve the success of the device.

Prolotherapy is the injection of substances (usually dextrose, sterile water, or saline) into the joint capsule or degenerative ligament to cause inflammation, which in turn increases circulation and stimulates tissue repair. Though veterinary evidence is lacking, human knee OA prolotherapy improves function, reduces pain, and increases quality of life; a recent medical systematic review showed it is supported for treatment of tendinopathies, knee and finger joint OA especially where instability exists, and spinal/pelvic pain due to ligament dysfunction. As prolotherapy's goal is increased inflammation to aide healing, it is most reasonably used without anti-inflammatories and with specific localization/imaging guiding injection.

Exercise restriction

Nonsurgical management of cruciate injury requires strict rules of no running, jumping, or using stairs. This doesn't mean crating though, as movement is important, and prevention of psoas, hamstring, and quadricep overactivity/tie up is critical. In the house, confinement can consist of room/barrier gates, etc. Outside, leash restraint and small pens predominate for a minimum six to 10 weeks (normally a total of three to six months), depending on the degree of injury; smaller breeds may require less restriction time. Slow, gradual activity (*i.e.* extended leash return to off-leash/uncontrolled activity in the four- to 12-month period) must follow the period of strict control. Because we are always on the lookout for meniscal injury, caution is advised even for up to a year after injury is first noted. To assist owners in this lengthy period, devices such as Help 'Em Up, HandicappedPets Walkin' Rear Lift Harness, or the Walkabout Harness support the injured limb from the pelvic floor versus the abdomen, thus alleviating further psoas and lumbar pain in a cruciate-deficient patient.

Physical rehabilitation and exercise therapy

All physical rehab exercises and procedures are accomplished with the patient on leash or in an enclosed area for control. Because of the reciprocal apparatus, early passive range of motion focused on the hock (versus stifle) and massage of the gastric, hamstrings, quads, gluteals, and epaxials can truly help reduce inflammation via facilitating movement of joint fluid. Early neuromuscular health returns via a combination of initial relaxation flexion and massage-induced extension, three-legged stands, circle walking, withdrawal stimulation, weight shifting, and balance exercises. During the postinflammatory strength training period, slow obstacles, uphill walking, sitting square exercises, backward walking, and weights can ensure protection with strengthening. As the stifle continues to heal, neuromuscular electrical stimulation (NMES) with sitting and weight shifting, increased duration and mileage of walks, slow controlled trotting, spotted stairs, uneven or zigzag surface maneuvers, and cavalettis are included. Underwater treadmill activity is used for early edema reduction and joint unloading, resistance, and improved strengthening as recovery progresses; appropriate water depth and speed are dependent on progress. Late in the rehab process, swimming activity can begin, but joint stability is imperative during it and other rehab exercises. Regular therapeutic ultrasound, NMES, and manual joint compressions and mobilizations often are included in all phases of exercise therapy.

Photobiomodulation

Low-level light therapy or laser therapy can reduce inflammation, stimulate tissue metabolism, modulate pain signaling, and accelerate MSC proliferation. Human knee OA patients treated with light therapy exhibited improved microcirculation and reduced pain when treatments were delivered twice weekly during a four-week period (Hegadus et al. 2009). A recent study compared laser therapy to sham laser therapy in treating canine elbow OA during a six-week period and found improved quality of life and reduced lameness, and reduced need for NSAIDs in treated patients (Looney et al. 2018). Doses of 10-20 J/cm^2 (higher than previously published doses) initially delivered more frequently may be required for treatment of chronic CCL disease. In early injury, lower energy and longer treatment times (class IIIb) may allow for better treatment of synovitis, although depth of penetration for most CCLs and the inherent chronicity of cruciate disease process make class IV lasers instruments of choice. Enhancement of PRP therapy with photobiomodulation can be better focused on medial compartment, meniscus, and flexed open joint when the patient is sedated.

Weight reduction, dietary changes

In an older but significant study, body weights of dogs with ruptured CCL were significantly greater than those of control dogs (Duvall 1999). Prevalence and risk factors for primary diagnosis of CCL injury were reviewed in canine patients; increasing body weight within breeds was associated with increased odds of cruciate pathology (Taylor Brown et al. 2015). In a more recent study, the severity of cruciate ligament degeneration was significantly correlated with dogs' age and body weight (Doring 2018). Suffice to say, weight loss and nonsurgical cruciate disease management go hand in hand.

Higher protein, lower carb, reduced fat diets can assist with preserving lean muscle; adding fresh vegetables (beans and peas), eggs, and fat-free chicken to a dog's diet can build tissue strength and rehab energy. Of all macronutrients, protein plays an essential role in all stages of wound healing and is essential to collagen synthesis, angiogenesis, fibroblast proliferation, immune modulation, and tissue remodeling. During healing, the value of fresh water/different water sources to not only enhance circulation and provide hydration, but also to improve satiety and aide weight loss, cannot be underestimated.

Anti-inflammation

Any joint can become a battleground once inflammation starts. To reduce the complex cycle of destructive joint pathology stemming from frayed ligament fibers and stretched joint capsules (upregulation and release of inflammatory mediators and degradative enzymes, proliferation of cells, recruitment of inflammatory and immune cells, and production of anticollagen antibodies), get on the anti-inflammatory wagon as soon as possible. NSAIDs should be included initially in management, except when prolotherapy, PRP, or MSC has been injected into the joint. Other means of reducing acute inflammation include parenteral polysulphated glycosaminoglycans and arnica preparations, topical NSAIDs (diclofenac) and penetrable lidocaine gels/creams, and cryotherapy. Cold compression therapy was found to decrease signs of pain, swelling, and lameness and increase stifle joint range of motion in dogs during the first 24 hours after TPLO (Drygas 2012); this modality is used regularly in patients without surgical intervention to reduce inflammation as well, especially postrehab exercises.

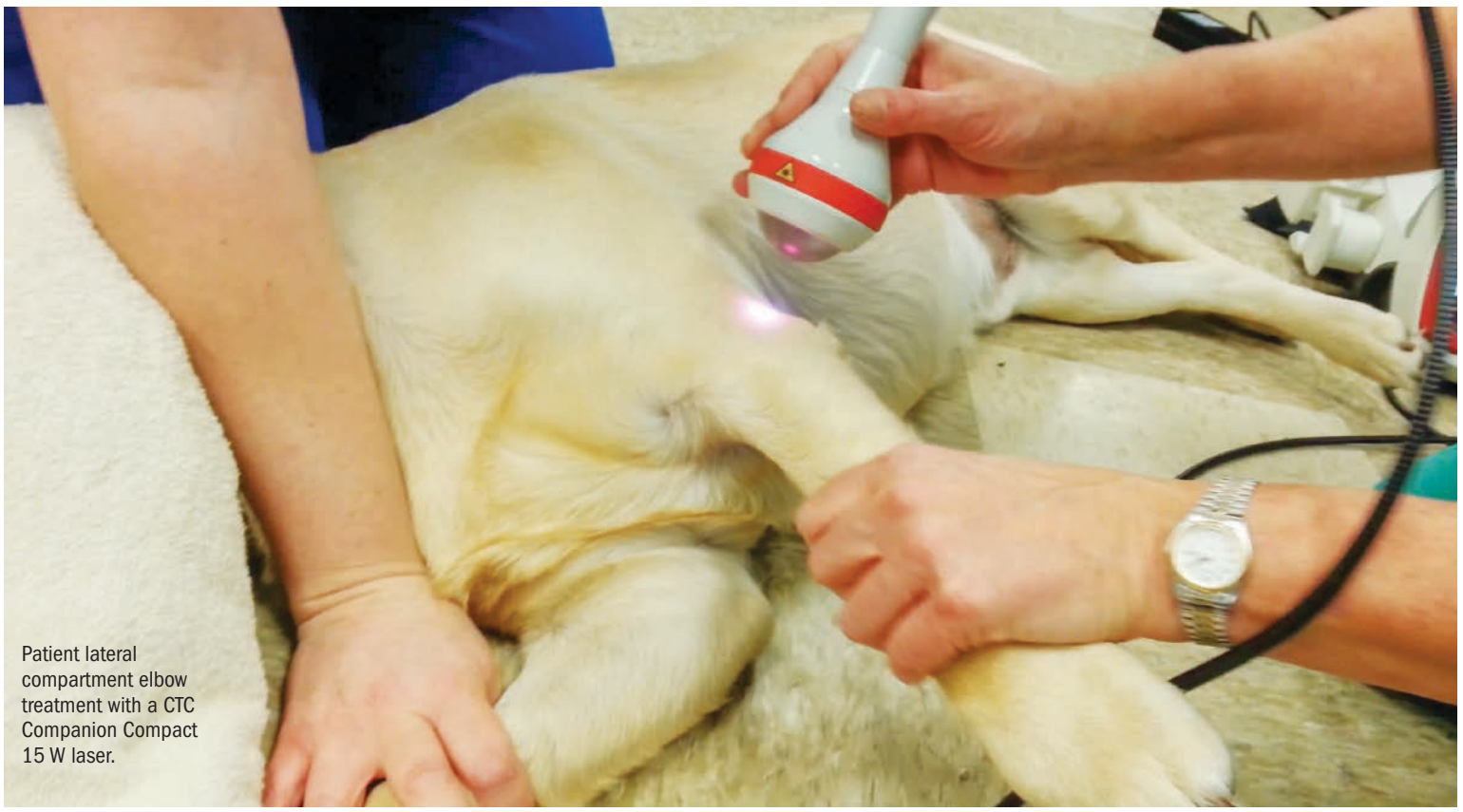
Sedation and analgesia

To maintain at least initial exercise changes and restraint, as well as assist the owner in beginning rehab therapy, trazadone, oral transmucosal (injectable) acepromazine dexmedetomidine (Sileo), acetaminophen, and gabapentin can provide sedation anxiolysis. Beyond the methods discussed above, some patients may also require a bit more analgesia. The goal is not to make the dog pain free, but to reduce compensatory muscle spasm, chronic pain neural signaling, and inhibitory feedback, which can limit the repair process. Toward that end, gabapentin, pregabalin, mexilitene, codeine, and hydrocodone all have been used to assist with initial analgesia. Along with its bitter distastefulness, dysphoric effects, and difficult dosing due to capsular sizes, oral tramadol appears ineffective for musculoskeletal pain (Davila 2013). A recent study showed

10 days of treatment with oral tramadol as administered (5 mg/kg, PO, q 8 h) provided no clinical benefit for dogs with osteoarthritis of the elbow or stifle joint (Budsberg 2018).

The road to nonsurgical canine cruciate management is paved with modalities and tools ready to assist with repair and recovery. Though lengthier than surgical repair, and certainly labor intensive at times on behalf of owner and patient, there exists a means to help those patients who cannot undergo surgical fixation. Science, technology, and innovative treatments continue to help us find means to work with this group of clients and patients. ●

For detailed information on this topic, watch an in-depth webinar at http://www.litecureinfo.com/CCLWebinar2.



Patient lateral compartment elbow treatment with a CTC Companion Compact 15 W laser.