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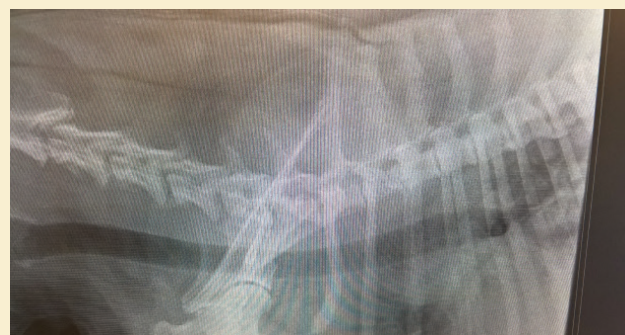
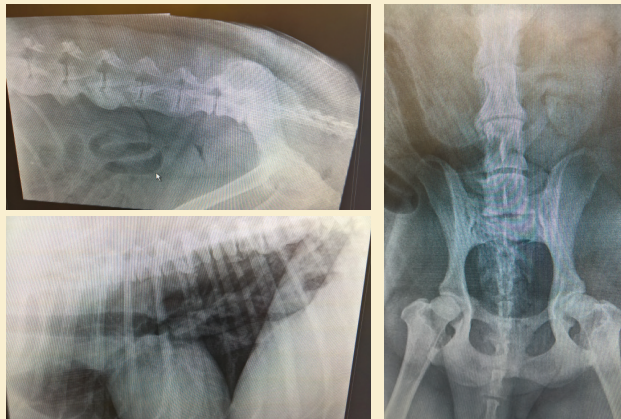
Lumbosacral disease treated with regenerative medicine

By Andrew Armitage, BSc, BVM&S, MRCVS
For The Education Center

Trudy, a 7-year-old female neutered bloodhound, presented at Greenside Veterinary Practice in Scotland, U.K., in May 2016 due to unwillingness to exercise, difficulty climbing stairs, inability to jump and lethargy.

On physical examination, Trudy was found to be overweight (body condition score 3/5) and had a marked loss of lumbar spine flexibility with areas of pain on palpation. There was an exaggerated cutaneous trunci reflex at the thoracolumbar and lumbosacral junctions on palpation. Neurological examination revealed mild proprioceptive deficits in both hind limbs during the paw-righting reflex. The patella reflex was normal. There was reduced muscle mass in both hind legs and pain on caudal extension of both hips with reduced range of motion. Stance analysis with the Companion Stance Analyzer revealed increased weight bearing on the thoracic limbs and a reduction in weight bearing on the pelvic limbs. A normal dog would bear 60 percent of its weight on the thoracic limbs (30 percent each) and 40 percent on its pelvic limbs (20 percent each). Trudy's values were left forelimb 34 percent, right forelimb 33 percent, left hindlimb 16 percent and right hindlimb 17 percent.

Trudy was admitted for further investigation, including radiography and digital thermal imaging.



Radiographs revealed evidence of severe lumbosacral disease with degeneration and mineralization of the lumbosacral disc.

The radiographs revealed severe bridging spondylosis from the caudal thoracic spine to the sacrum. There was also evidence of severe lumbosacral disease with degeneration and mineralization of the lumbosacral disc. The hips had moderate osteoarthritis (OA).

Digital thermal imaging revealed an increased heat signal from the lumbar spine and lumbosacral junction consistent with pain, inflammation and muscle spasm in this region.

A diagnosis of severe thoraco-lumbar spondylosis with severe lumbosacral disc disease and moderate hip OA was made on physical and radiographic findings.

Trudy was started on NSAIDs, gabapentin and tramadol medications. She was put on a calorie-restricted prescription diet (PVD OM) and restricted exercise. A course of laser therapy was also started at this time. The hips and LS regions were clipped and a Companion CTX Class IV laser therapy unit was used to treat these areas. Trudy had six treatments over two weeks at a dose of 5,460 joules for each hip and 5,400 joules for the lumbar spine using 12 watts in continuous wave.

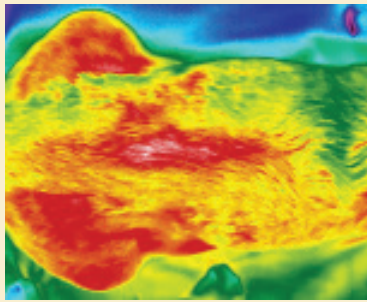
Trudy initially responded to treatment with reduced pain and increased mobility. But in June 2016, she became increasingly weak on her hind legs and became ataxic and uncoordinated. The proprioceptive deficits in both hind limbs were increasing, and she scuffed the nails of digits 3 and 4 when she walked. This video shows her ataxia and paraparesis at the time: www.youtube.com/watch?v=f6MXAU0dbG0.

She was admitted to the hospital for stem cell therapy to treat her spinal and disc degeneration and hip OA. She was pre-medicated with acepromazine and morphine, and anaesthesia was induced with propofol. She was maintained on gaseous anaesthesia (sevoflurane). Sixty ml of blood was drawn from the jugular vein and used to produce 4 ml of PRP with a platelet concentrating factor of 8.8 and virtual elimination of red blood cells and neutrophils (Post spin RBCC $0.28 \times 10^{12}/L$, Neutrophils $1.27 \times 10^9/L$, Lymphocytes $9.83 \times 10^9/L$). PRP was produced using the Companion CRT system.

The left hip was clipped and surgically prepared, and 30 ml of bone marrow was obtained from the femur using the Companion BMAC collection kit. The bone marrow was used to produce 3 ml of BMAC, and 0.7 ml of BMAC was combined with equal volumes of PRP and injected into the epidural space at the LS junction. A further two lots of 0.7 ml BMAC and PRP was injected into both hips. The remaining 0.9 ml of BMAC was placed into a sterile container and shipped to Cell Therapy Sciences Ltd by overnight courier. Approximately 20g of fat were harvested from the falciform ligament via a midline laparotomy. The adipose tissue was placed in sterile saline and was shipped along with the BMAC for cell culture.

The adipose tissue and BMAC was used to isolate and culture expand mesenchymal stem cells from the samples. Fifty million adipose-derived mesenchymal stem cells (ADMSCs) and 10 million bone marrow-derived mesenchymal stem cells (BMDMSCs) were produced in separate cultures and suspended in autologous serum. The cells were sterility tested, and then cryogenically frozen and shipped overnight to Greenside Veterinary Practice.

In July 2016, Trudy was given 50 million ADMSCs (1 million cells/kg bodyweight) by slow intravenous infusion. She was then sedated, and 10 million BMDMSCs were implanted into the epidural space at the LS junction. A course of laser therapy began immediately following implantation. This video shows Trudy at two weeks following her second treatment (six weeks from the first



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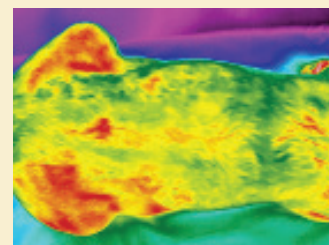
treatment): www.youtube.com/watch?v=ZBmzFbsM8hs.

At two weeks following her second treatment, Trudy showed no pain on palpation of her spine. She was still mildly ataxic, but she had regained strength and coordination in her hind limbs. She still received a NSAID (mavacoxib 2 mg/kg monthly) but the gabapentin and tramadol had been reduced and stopped without any deterioration in her pain or activity. There was still some proprioceptive delay in both hind limbs, but this had improved dramatically over the last six weeks.

By three months following stem cell treatment, Trudy was exercising normally again and not showing any signs of pain or lameness. Her placing reflexes were normal, and she no longer scuffed her nails during ambulation. Her NSAID was stopped at this time.

This video shows her after a 3-mile walk up into the hills: www.youtube.com/watch?v=9zN-o7jyE9U.

Six months after her initial treatment, Trudy continues to improve. She has gained muscle mass in both pelvic limbs (Gulick tape measurements of left and right thigh



After treatment, digital thermal imaging showed a more normal thermal image of the lumbar spine.

circumference had increased by 2.8 cm and 3 cm, respectively) and is not currently receiving any medication. She was found to be exercising normally without lameness or stiffness. Stance analysis revealed a normal weight distribution with 29 percent on the left fore-

limb, 30 percent on the right forelimb, and 21 percent and 20 percent on the left and right pelvic limbs, respectively. Digital thermal imaging showed a more normal thermal image of the lumbar spine.

Repeat radiographs showed a clearer lumbosacral disk, with a reduction of ventral spondylosis at L6-L7 and L7-S1.

A sample of Trudy's adipose-derived and bone-marrow-derived stem cells have been cryogenically frozen so that they can be used to culture more cells in the future (without having to perform a repeat harvest) in case she needs further treatments. ●

Dr. Andrew Armitage is a partner at Greenside Veterinary Practice in St. Boswells, Scotland. His special interests include advanced regenerative therapy techniques. He is particularly interested in investigating the use of Class IV laser therapy and regenerative medicine for acute and chronic conditions. Visit him at www.stemcellsscotland.co.uk.

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