

Case Report

The Treatment of Hyperadrenocorticism in a Canine using Chinese Herbal Medicine

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Case History and Clinical Signs

An eleven year old female shih tzu, weighing 7.7kg, presented having been diagnosed elsewhere with hyperadrenocorticism (Cushing's disease). Her owners were seeking alternatives to conventional treatment protocols.

Cushing's Disease is a combination of symptoms associated with overproduction of endogenous cortisone, either due to a benign functioning tumour of the pituitary gland, or a malignant tumour of the adrenal gland. Older dogs are most frequently affected, and owners often confuse the signs with: "getting old". Symptoms include: sluggish behaviour and panting, weight gains, tendency to develop arthritis, cardiac disease, skin disease, urinary tract infections, diarrhoea, enlarged livers, excessive thirst or appetite (but not often both). More serious consequences include thromboembolism, acute pancreatitis, immune effects and possibly diabetes mellitus.

Two treatment options had been offered by her original vet. One was to use mitotane, which is the most commonly used treatment for Cushing's disease in dogs. Up to 25% dogs can suffer adverse effects during induction, and up to 30% of dogs during maintenance therapy with mitotane. These are usually the result of rapidly lowering levels of cortisone resulting in hypoadrenocorticism. Other side effects include gastrointestinal signs and neurological signs (Braddock 2005). The second option, Trilostane, is currently only available at specialist veterinary centres in Australia due import requirements of the drug. A trial conducted at the University of Sydney showed no adverse side effects. Availability and cost are a factor; however, with the total cost possibly triple that of mitotane treatment (Braddock 2003).

A friend had suggested homeopathic treatment, and the owners had sought out a non veterinary homeopath. After a two month trial, the dog developed diarrhoea, and was treated by her local vet with antibiotics.

When she presented to our surgery, her owners reported that she was always acted profoundly hungry, and had gained weight. She was not, however drinking excessively, and she did not always eat all food offered. Her owners said she had a nervous disposition and could be snappy. She barked constantly at food time, (in the evening) and when left alone. On examination she had profound dental disease. Her heart rate was 120, and no abnormal heart sounds were heard. She panted constantly through the initial exam (one hour). Her skin had a few hot spots on her skin, and she was recovering from otitis externa (an ear infection).

Her diet consisted of: cooked human grade meat, commercial canned food, rice, pasta and a small amount of commercial dry food. Her owners said she was fussy. TCM exam revealed a thick swollen pink tongue. The pulse character was not reported. Her owners remarked that she really "felt the heat."

Her owners had a good understanding of conventional approaches, and the risks of non treatment of Cushing's disease in dogs. They elected to try alternative approaches for three months, and if there were not sufficient improvement, to reconsider conventional options.

Treatment Plan

1: A change to a low glycaemic index diet with no carbohydrates

2: A Chinese Herbal Formula: Si Miao San (Four Marvel's Powder) 30g total, dose: 1/3 teaspoon BID.

A follow up call one week after the initial visit and the owners reported she was taking the powdered herbs with no problems. Her owners reported she seemed drowsy.

At a follow up visit three weeks later her owners reported that she seemed calmer during the daytime than before, and panted less. She had lost weight (now 7.2kg). Where before she had been agitated from 6am onwards, she now seemed calm until 9pm (evening meal time). The patient was taking the herbs, and eating more vegetables in her diet. There was no change in her drinking and urinating, and she still seemed hungry. At this time there was no change in her treatment.

She was reassessed by her usual vet 6 weeks later. She now weighed 6.9kg, and had lost a total of 800g since her treatment began. Blood tests, however, showed similar levels to those taken before treatment with the herbs, and her vet assessed that her condition was unchanged. Despite this her owner was convinced the patient had definitely improved.

We examined her at our clinic another month later; exactly 3 months after herbal treatment had been initiated. Her weight was now 6.7kg, a total of 1kg weight loss (12.9% body weight) since treatment began. Her owners reported she had more energy. She was calmer and quieter during the day, and less agitated at feeding time. Her owners also reported much less panting. They said she was still consistently more stressed in the evening, TCM exam showed a tongue which was slightly pale and swollen, and her pulses seemed slippery. Oral exam showed she still had profound dental disease, with dental calculus, gingivitis and gingival recession.

The dose of Si Miao San (Four Marvel's Powder) was increased at this point to 1/2 teaspoon BID. At last telephone update, her owners were pleased with her progress, feeling that she was even calmer with the increased dose and they were not considering conventional options at this stage.

Discussion

The initial treatment for the patient consisted of the TCM formula Si Miao San (Four Marvel's Powder): which is made up of:

- Cang Zhu (Atractylodes Rhizome)
- Huai Niu Xi (Achyranthes root)

- Yi Yi Ren (Coix seed)
- Huang Bai (Phellodendron bark)

The primary action of this formula is to drain Damp, and its secondary functions are to clear Heat, move and tonify.

This formula was chosen initially because in Chinese medicine Cushing's disease is due to an accumulation of Damp Heat. In small animal medicine Damp Heat results from Spleen Deficiency due to inappropriate diet, (either too much food or excessive carbohydrate loads). Instead of producing the useful Fundamental Substances, the Spleen produces a useless fluid which is seen as exudates, oily skin or mucus. If the body can't eliminate this Damp, over time it forms excess body fat, oedema, ascites, abdominal distension, and benign growths such as warts or lipomas (Marsden 2006). The patient's diet was unbalanced (consisting primarily of protein and carbohydrate) and she was overweight.

There is research to suggest that functional pituitary (and maybe adrenal tumours) can be associated with insulin resistance (Elliott *et al*, 2000), so the patient also started a low glycaemic diet. This addressed both the conventional aspects of treatment (a low carbohydrate diet to reduce insulin resistance) and TCM aspects (i.e. no longer overloading the spleen with too many carbohydrates, and therefore improving Spleen function).

Damp Heat also seemed to be an appropriate pattern from the history as described by her owners: with increased appetite but not thirst, weight gain, and her agitated restless behaviour, and the effect heat had on her. Her swollen red tongue was also consistent with Damp Heat.

In the Liver, Damp accumulation results in hepatomegaly, and elevations in liver enzymes such as ALP. Accumulations in the head result in a wet swollen tongue. As Damp continues to accumulate, the normal circulation of Qi and Blood is reduced, and the resulting stasis causes accumulation of Heat. Heat signs include red tongues, and increases in either appetite or thirst. Patients usually avoid hot places.

Damp heat can add to Liver Yang, causing it to rise and flare as anger or aggression. Heat accumulation in the Upper Burner agitates the Heart Yang resulting in restlessness and hyperexcitability.

At her second reassessment her tongue, although still swollen, appeared less red. Her anxious behaviour had reduced. Both these signs are consistent with Cooling down or less Heat. Her blood pressure had only been measured once, but was within normal limits. Hypertension would have been consistent with excess Damp. Her tongue still appeared swollen at the last examination, and so the dose of Si Miao San (Four Marvel's Powder) was increased.

Si Miao San

Cang zhu, or red atractylodes root, is a warm spicy bitter herb. It tonifies the Spleen, and drains Damp. In conventional medicine, Cang Zhu has been shown to reduce weight and improve glucose tolerance in senile obese patients (Shi *et al*, 2006).

Huai Niu Xi or achyranthes root acts as a blood mover, and relaxes the sinews of the lower back, which enables the formula to be used in patient with not only acute inflammatory conditions, but also more chronic ones. It has been shown to contain triterpinoid saponins. In Western Herbal medicine it is antispasmodic, astringent and diuretic, and the root is used for: dropsy, rheumatism, stomach problems, skin diseases and rabies (Plants for a Future). In Chinese medicine, triterpinoid saponins are often included to enhance absorption of other herbs (Wynn and Fougere 2007).

Yi Yi Ren or Coix seed is a cool sweet bland herb which has an affinity for the Spleen, Stomach and Lung. Its primary function is to drain Damp, but it also clears heat and provides some support for the Spleen. In conventional medicine it has been shown to reduce obesity through neuroendocrine mechanisms (Kim *et al*, 2007). It has also been shown to reduce production of steroids in the zona grannulosa of the adrenal gland (Hsai *et al*, 2006) and has been shown to reduce plasma lipids. Regular ingestion has also been shown to inhibit neoplastic cells.

Huang Bai or Phellodendron bark is a cold bitter herb with an affinity for Kidneys, Bladder and Large Intestine. Its primary action is to clear Damp Heat from the Lower Burner, and it also acts to clear Heat Toxins. The bark is antibacterial, antirheumatic, aphrodisiac, bitter stomachic, cholagogue, diuretic, expectorant, febrifuge, hypoglycaemic, opthalmic and a tonic (Plants for a Future database).

Phellodendron contains berberine an isoquinoline alkaloid, which has been shown to have antibiotic activity (Yu *et al*, 2005), and also to reduce insulin intolerance (Lee *et al*, 2006). Berberines also have antioxidant properties, and have been shown to induce apoptosis in cancer cells. Beta-sitosterol helps normalise adrenal cortisol output. Berberine has improved pancreatitis, a known possible complication of hyperadrenocorticism.

Si Miao San (Four Marvel's Powder) is used when there are overt signs of Heat and Damp accumulation, combined with Spleen deficiency. Heat symptoms may include: red tongue, itch, increase in either thirst or appetite, but not usually both, intolerance to heat and seeking cool, hyperexcitability and inflammation. Heat is caused by accumulation of Damp, signs of which may be: polyuria, straining to defecate or urinate, lipomas, tendency to gain weight, elevations in ALP, mucoid discharges, rounded abdomen and halitosis.

In Si Miao San (Four Marvel's Powder), red atractylodes tonifies Spleen and dispels Damp. Phellodendron dries Damp and clears Heat from the Lower Jiao. Coix drains Damp and clears Heat, while giving support to the Spleen. Achyranthes harmonises the formula by moving blood and enabling the other herbs to be absorbed, and providing an astringing effect on fluid loss which balances the drying effect of the other three herbs.

It is regarded as a strong but safe anti-inflammatory formula (Marsden 2006). It is also used for: fungal otitis externa, moist pyoderma, allergic dermatitis, seborrhoea oleosa, anal sacculitis, degenerative myelopathy, immune mediated thrombocytopaenia, epilepsy; lymphoma, vestibular disease, osteoarthritis, recurrent pancreatitis, glomerulonephritis colitis and cystitis where TCM signs are appropriate.

The patient began to show signs of improvement as soon as she started the formula. Her owners complained of a sedative effect, which may have been a reduction in Heat and Liver Yang, therefore reducing her restlessness and excitability. The reduced panting at home also reflects reduced Heat. At the outset, her agitation would begin at 6-7am, which on the Circadian clock coincides with the Stomach meridian. After treatment with Si Miao San (Four Marvel's Powder), her excitement only becomes apparent at 9pm, which is the Triple Burner. If this sign persists, her herbal prescription should be reassessed, depending on her other signs.

Her increased energy levels and mobility can be attributed to Heat and Damp reduction, manifesting mainly as fat loss. Interestingly, despite the reduction in calories, her pestering for food reduced. Once again this can be attributed to reduction in Damp Heat (increased appetite but not thirst), as well as the individual herb's effects on her glucose tolerance and insulin levels. The low glycaemic index diet also had a part to play in the reduction of weight and appetite.

Her ACTH stimulation result remained unchanged after three months of herbal treatment, although no worse. There may be many reasons for this. One to consider is the ongoing profound dental disease, which probably caused chronic low grade stress and immunosuppression. This may have resulted in continued stimulation of her adrenal glands to produce cortisone. Although her owners were disappointed the results did not reflect the improved clinical picture, they were happy with her progress. Their aim had been to make her feel better without risk or extra stress, and through the herbs and diet they had achieved this. Her usual vets were also pleased with her progress.

Conclusion

Although not reflected in her follow up blood tests, the patient is a much better and happier dog after treatment with Si Miao San (Four Marvel's Powder) and her diet. The low glycaemic diet alone would have probably helped weight loss and improved energy levels, but not as quickly as when combined with the herbs. Although we could not say there are no risks of adverse events associated with the continued cortisone levels, many of the risk factors e.g. blood pressure, weight, stress on the pancreas are being controlled.

Overall, the diet supported the action of Si Miao San (Four Marvel's Powder), gently aided by the liquid herbs, with no side effects to the patient. Therefore, with appropriate supporting signs, Si Miao San (Four Marvel's Powder) and low glycaemic diet would seem to be a viable alternative for treatment of Hyperadrenocorticism in patients who do not wish to proceed with more risky and expensive conventional options.

Her treatment plan reflects our philosophy in small animal medicine, which is to consider the patient as a whole, and gently address the underlying imbalance, and allow the body the time and space to heal. The goal of treatment is improved quality of life, not necessarily improved blood test results.

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Appendix A

Low Glycaemic Index Diet for the Patient:

- 300g lean beef raw
- 25g raw beef liver pinch iodised salt
- 1 cup leafy green vegetables finely grated or chopped

Above quantity of food to last 5 days

Supplements: 1/4 teaspoon flax oil daily Multivitamin tablet daily

Biography

Dr Karen Goldrick was born in Sydney, Australia. She gained her veterinary degree from the University of Sydney in 1987. After graduation, she spent some time traveling and doing locum work in the UK for a few years before returning to Australia. After ten years in private small animal practice, Karen joined All Natural Vet Care in Sydney in 2005, where she practices to this day. She was certified in Acupuncture by IVAS, has studied Chinese Herbal Medicine at the Sydney College of Traditional Chinese Medicine and Western Herbal Medicine at the Sydney College of Natural Therapies. She recently completed CIVT's Graduate Diploma of Veterinary Chinese Herbal Medicine course.

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