WHAT IS YOUR DIAGNOSIS?

A 6 year old female neutered Boxer dog was presented with a several week history of lethargy and inappetance. Her owners reported that she was dull, withdrawn and appeared uninterested in her surroundings.

Physical examination revealed that the dog was very quiet and subdued. Her body condition was 4/9. Her heart rate was 60 beats per minute with a regular rhythm, no murmurs detected, and matching femoral pulses of good quality. Respiratory rate was 30 breaths per minute, with no associated effort and no abnormalities on thoracic auscultation or percussion. Abdominal palpation was unremarkable and no organomegaly, fluid thrill or abdominal masses were detected. Her peripheral lymph nodes were within normal limits. Her rectal temperature was 38.0°C.

1) What are your differential diagnoses for this case?

2) How would you evaluate the case further?
1) Differential diagnosis

The differential diagnoses for lethargy, dullness and subdued behaviour include:

a) Metabolic eg hypoglycaemia, hypocalcaemia, hepatic encephalopathy
b) Endocrine eg hypoadrenocorticism, hypothyroidism
c) Neurological eg intracranial mass
d) Haematological eg anaemia, polycythaemia
e) Neuroromuscular eg myasthenia gravis
f) Neoplasia
g) Cardiovascular eg pericardial effusion, arrhythmia
h) Respiratory eg laryngeal paralysis
i) Musculoskeletal eg hip dysplasia, bilateral cruciate rupture

The differential diagnoses for inappetance include:

a) Inflammatory diseases eg bacterial, viral, fungal or protozoal infections, immune mediated diseases, pancreatitis
b) Gastrointestinal diseases
c) Metabolic diseases eg kidney, liver, adrenal or heart disease, hypercalcaemia, diabetes mellitus, hypoadrenocorticism
d) Neoplasia
e) Central nervous system disease
f) Psychological causes
g) Fever

2) Evaluation

Given the lengthy list of potential differential diagnoses in this case, the initial diagnostic tests undertaken were haematology, biochemistry and urinalysis tests. This allowed us to screen for a wide range of metabolic and haematological disorders which could be the cause of the dog’s clinical signs. The haematology profile was generally unremarkable apart from a mild neutropenia (2.9x10^9/l, ref range 3.6 – 12.0). The biochemistry profile was also generally unremarkable revealing only a mild increase in ALT (146 IU/l, ref. range 21-102). Urinalysis revealed a urine specific gravity of 1.015. No abnormalities were detected on urinalysis and sediment examination of urine was unremarkable.

An orthopaedic examination was performed by colleagues in the orthopaedic service. There was no clear evidence of neck pain although pain was elicited following palpation of her lumbosacral spine and tail. Pain was present on maximal extension of both stifle joints although neither was considered to be unstable. A neurological evaluation was then performed which did not reveal any abnormalities in her proprioception and cranial nerves. The spinal reflexes, anal reflex and cutaneous trunici reflex were also within normal limits. A basal cortisol concentration was measured and was within normal limits (116nmol/l, ref. range 20-230), making the diagnosis of hypoadrenocorticism unlikely. Serum creatine kinase concentration was also within the reference range. Systolic blood pressure was also measured and was within the reference range and retinal examination was unremarkable.

Whilst the orthopaedic examination revealed minor abnormalities such as discomfort on extension of stifles and palpation of lumbosacral spine and tail, these abnormalities were
considered to be an unlikely explanation for the historical signs reported by the owner. Since the haematology and biochemistry tests did not reveal any significant abnormalities, additional diagnostic tests were then performed, namely thoracic radiographs and abdominal ultrasonography. Again, these investigations failed to reveal any significant abnormalities.

During the hospitalisation period, the dog was very subdued and depressed. Whilst the neurological examination was unremarkable, the lack of abnormalities in the initial screening tests and her persistently depressed state made us concerned that an intra-cranial lesion could be the cause of her clinical signs. Consequently, an MRI was then performed which revealed a large pituitary macroadenoma. This lesion was considered to be clinically significant and so the dog was immediately treated with mannitol and dexamethasone in an attempt to reduce the intracranial pressure. Although pituitary tumours can cause endocrine disorders such as hyperadrenocorticism, they can also cause non specific signs such as lethargy, subdued behaviour and inappetance\(^2\). In this case, radiotherapy was considered to be the therapy of choice to treat the pituitary mass. A pre-treatment CT scan confirmed the presence of a markedly contrast enhancing, lobulated soft tissue attenuating mass located within the pituitary fossa (figure 1). Our colleagues in the oncology service prescribed a radiotherapy course of 40 Gy delivered in 2 Gy fractions (figures 2 and 3). This treatment was remarkably effective as the dog's clinical signs had vastly improved by the end of the radiotherapy course.

**Discussion**

Dogs with pituitary tumours can present with clinical signs related to excessive hormone production, which occurs in pituitary dependent hyperadrenocorticism, and/or due to the space occupying effects of the mass. The neurological signs attributed to pituitary masses in dogs are wide ranging and include changes in behaviour, inappetance, apparent blindness, seizures and aggressiveness. MRI and CT imaging are the only non invasive methods for determining the size and presence of pituitary masses. Radiotherapy is the most widely used treatment for pituitary tumours in dogs which are causing significant clinical signs due to the space occupying effects of the mass\(^2,3\). A wide variety of radiotherapy regimens have been reported and the current hyperfractionated regime offered at HfSA is considered to be a gold standard treatment in terms of delivering a high cumulative dose of radiotherapy but split over a large number of treatment sessions in an effort to limit side effects. As in this case, radiotherapy can be highly effective at reducing clinical signs associated with pituitary tumours and a 2 year survival time of over 85% has been reported in a large case series of dogs with pituitary tumours treated by hyperfractionated radiotherapy\(^2\).

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Figure 1: CT image of brain showing pituitary mass (arrow)

Figure 2: Linear accelerator at HfSA

Figure 3: Image from radiotherapy planning process showing how pre-treatment CT images can be used to develop a focussed radiotherapy treatment plan.