WHAT IS YOUR DIAGNOSIS?

An eight-year old male neutered Cocker Spaniel was presented to the R(D)SVS Internal Medicine service for investigation of polyuria/polydipsia of seven weeks’ duration and neurological clinical signs (one seizure and intermittent circling) of three weeks’ duration. The neurological clinical signs were associated with episodes of hypoglycaemia, as confirmed by blood glucose measurements at the referring veterinary practice, and they would resolve after feeding.

The dog was up-to-date with vaccinations and worming, and had never travelled outside of Scotland. Physical examination was unremarkable, except for a bilateral systolic heart murmur grade III/VI.

1) What are your differential diagnoses for this dog’s problem list?
   2) How would you evaluate this case further?
   3) How would you treat and monitor this dog?

1) Problem List and Differential Diagnosis

   a) Hypoglycaemia (leading to neurological clinical signs)
      • Liver dysfunction or portosystemic shunt
      • Hypoadrenocorticism
      • Insulinoma
      • Other neoplasia

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- Polycythaemia
- Toxicosis (xylitol)
- Glycogen storage disease
- Insulin overdose (in diabetic patients)
- Sepsis (would present acutely)
- Toy breed and puppy hypoglycaemia

b) Polyuria/polydipsia
- Liver disease
- Renal disease (acute or chronic), pyelonephritis, Fanconi syndrome
- Hypercalcaemia, hypokalaemia
- Hypoadrenocorticism
- Hyperadrenocorticism
- Medications
- Polycythaemia
- Diabetes mellitus
- Pyometra (in females)
- Central and nephrogenic diabetes insipidus
- Psychogenic polydipsia

c) Heart murmur
- Structural heart disease (mitral valve disease, dilated cardiomyopathy, congenital heart disease, endocarditis)
- Abnormal blood viscosity (anaemia, polycythaemia)

2) Further Evaluation
Haematology showed severe polycythaemia (PCV 83%); serum biochemistry showed hypoglycaemia and was otherwise unremarkable. Urine analysis revealed isosthenuric urine (USG 1.010), proteinuria (UPC 2.7) and a marked number of red blood cells in the sediment (the haematuria was not macroscopic). A basal cortisol higher than 55 nmol/l ruled out hypoadrenocorticism. Blood insulin levels (taken at the same time as hypoglycaemia) were low, which is an appropriate response to hypoglycaemia, and not compatible with insulinoma. Systemic blood pressure was normal. Thoracic radiographs showed mild cardiomegaly and no evidence of respiratory disease. Echocardiography showed mild left atrium enlargement. Abdominal CT (figure 1) revealed a mass in the right kidney, and was otherwise unremarkable. Fine needle aspirates of this mass were consistent with a round cell tumour; fine needle aspirates of the liver and spleen did not reveal neoplastic infiltration of these organs. Immunocytochemistry to further characterise the round cell tumour (main differential diagnosis: lymphoma, histiocytic sarcoma, or plasma cell tumour) was non-diagnostic.
In summary, whilst the list of differential diagnosis for hypoglycaemia and, especially, for polyuria/polydipsia are quite extensive, the list of differential diagnosis for polycythaemia is not. Finding severe polycythaemia on initial blood work allowed the clinician to focus on the pursuit of aberrant erythropoietin production (renal neoplasia or neoplasia in other organs), tissue hypoxia (severe cardiac or respiratory disease) or polycythaemia vera.

3) Treatment and Monitoring
The combination of history and diagnostic investigations led to a definitive diagnosis of renal neoplasia; the mass was likely producing excessive erythropoietin. The hypoglycaemia was likely paraneoplastic and/or due to increased utilisation by the excessive number of red blood cells. The neurological clinical signs were caused by hypoglycaemia and probably also by increased blood viscosity in the brain.

Renal biopsies were discussed with the owner. As the owner decided he would not pursue chemotherapy or surgery, the patient received palliative treatment with phlebotomies, as frequently as required to ameliorate clinical signs. In each phlebotomy, 20 ml/kg of blood are withdrawn under sedation, and the same volume of blood was replaced with a crystalloid solution supplemented with glucose. Oral hydroxyurea, usually used in patients with polycythaemia vera, was started. Its use
has not been described in paraneoplastic polycythaemia in dogs; however, based on reports in humans with secondary forms of polycythaemia, it was felt reasonable to try this medication, in an attempt to reduce the frequency of phlebotomies. The renal proteinuria (likely associated with the renal tumour) was treated with enalapril (an angiotensin-converting-enzyme inhibitor). The patient was also started on pimobendan, since he met the criteria established by the “EPIC study”, which showed a delay in the onset of congestive heart failure in dogs with myxomatous valve disease receiving this drug. The patient is currently well, the polycythaemia and hypoglycaemia have resolved and he is seeing his veterinarian monthly (or as soon as clinical signs are noted) for haematology, blood glucose, and blood pressure.

References


Snead EC. A case of bilateral renal lymphosarcoma with secondary polycythaemia and paraneoplastic syndromes of hypoglycaemia and uveitis in an English Springer Spaniel. Vet Comp Oncol. 2005 Sep;3(3):139-4