

## INSULINOMA MANAGEMENT IN A GERIATRIC LOCAL DOG

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### SUMMARY

A 14-year-old, spayed female local dog was presented to University Veterinary Hospital-University Putra Malaysia (UVH-UPM) for the complaint of uncontrollable seizures. The intracranial neoplasia or trauma as a cause of seizures was ruled out based on magnetic resonance imaging conducted prior to presentation. Full diagnostic investigation inclusive of haematology, serum biochemistry, parasitology, thoracic and abdominal radiography and abdominal ultrasonography was conducted. A diagnosis of insulinoma was made from the persistent, low fasting blood glucose levels and the inappropriately high fasting insulin level, as well as the response to treatment with prednisolone.

Keywords: Insulinoma, Seizures, Canine

### INTRODUCTION

Insulinomas are functional beta-cell tumours of the pancreatic islet cells. The clinical signs are attributable to hypoglycaemia as a result of hyperinsulinaemia. It is uncommon in dogs and often undiagnosed (Garrett, 2003). Little is known about the survival times associated with the various medical treatments (Jaillardon *et al.*, 2011).

### CASE REPORT

A 14-year-old, spayed female local dog was referred to University Veterinary Hospital-Universiti Putra Malaysia (UVH-UPM) for seizures. Prior to presentation to UVH, an intracranial tumour or trauma as the cause of the seizures was ruled out by the referral practice based on magnetic resonance imaging of the brain, and the dog was treated with phenobarbitone 30 mg (1/4 tab, twice daily) for about one month with no clinical improvement. Physical examination revealed no remarkable findings except for bilateral immature cataracts. The following diagnostic tests were conducted: haematology and serum biochemistry, *Ehrlichia canis* IgG immunocomb test, as well as chest and abdominal radiography. A result of the complete blood count was normal while the serum biochemistry analysis results (Table 1) were non-specific and did not contribute towards determining the cause of seizures:

**Table 1. Abnormal serum biochemistry values for the dogs**

Biochemistry parameters	Result	Normal range
Sodium (mmol/L)	108.3	140-155
Chloride (mmol/L)	92.4	96-122
Alanine aminotransferase (U/L)	159.6	5-90
Alkaline phosphatase (U/L)	105	40-100
Urea (mmol/L)	16.8	3.0-7.5

All radiographs were unremarkable. During the follow-up visit a week later, the fasting glucose level measured using a glucometer (ACCU-CHEK<sup>®</sup>) was 1.4 mmol/L while the insulin level measured via direct chemiluminescent technology by Pathlab (Malaysia) was 31.8 IU/L (220.85 pmol/L). Both the results strongly pointed to a diagnosis of insulinoma. Upon abdominal ultrasonography no masses or abnormal structures were detectable on the pancreas. Prednisolone 5mg (0.30 mg/kg, 1/4 tab, twice daily) was started along with S-Adenosyl-L-Methionine 75mg, (Samylin Small Breed, Vetplus), 10 mg/kg, 1 tab, once daily as a hepatoprotectant. The owner was instructed to provide small amounts of food and glucose syrup frequently to the dog to maintain normal blood glucose levels. For 6 months since the diagnosis till present, the dog has not seized. The liver enzymes such as ALT and ALP were also monitored closely to keep track of the extent of steroid hepatopathy in which the latest readings were 286.0 U/L and 371 U/L, respectively.

### DISCUSSION

Insulinoma or pancreatic islet cell tumour is a neoplasm that results in insulin overproduction, which is rarely diagnosed in dogs. Most insulinomas in dogs are adenocarcinomas. There are three stages of severity of insulinoma growth. In stage I, the tumour cells are confined to the pancreas whereas in stage II, the tumour cells are found both in the pancreas and the regional lymph nodes. In stage III, the tumour cells are found in distant metastatic sites such as intra-abdominal lymph nodes, liver, mesentery, and the omentum (McDermott, *et al.*, 1999; Garrett, 2003).

Insulinomas are more often seen in medium and large dogs but there is no particular breed or sex predisposition (Kruth *et al.*, 1982; Mehlhaff *et al.*, 1985). Middle aged dogs around 8years old are most frequently affected (Rijnberk, 1996).

The patient in this report was presented with weakness and seizures. These are the most common presenting signs of dogs with insulinoma cases as reported by Garrett (2003) where 60% of the cases showed

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seizures, 45% weakness, 25% collapse or ataxia, 15-20% muscle twitching and/or lethargy and/or bizarre behaviour, 10% polydipsia, polyuria, and/or polyphagia, and 5% syncope.

Most often, the diagnosis of an insulinoma is accomplished via the demonstration of a low blood glucose level at the same time a blood insulin level is found to be inappropriately elevated (Garrett, 2003). From An insulin value of above 144 pmol/L with typical symptoms and concurrent hypoglycaemia (glucose below 3.3 mmol/L) confirms the diagnosis of insulinoma (Feldman and Nelson, 1996). However, others have proposed a lower limit with insulin of  $\geq 70$  pmol/L and glucose level of below 3.5 mmol/L to be sufficiently diagnostic for insulinoma (Rijnberk, 1996). In this case, the patient had a fasting glucose level of 1.4 mmol/L and a fasting insulin level of 31.8 IU/L (220.85 pmol/L), which was within the above diagnostic thresholds.

Insulinomas are typically small therefore, abdominal radiographs are usually unremarkable. Although abdominal ultrasound may reveal a mass in the pancreas, the detection rate by ultrasound is generally low, that is 36% (Tobin *et al.*, 1999) and 56% (Trifonidou *et al.*, 1998) in 2 respective studies. Nevertheless, most patients have microscopic or gross metastases to the intra-abdominal lymph nodes, liver, mesentery, and omentum at the time of diagnosis (Garrett, 2003). However, we were unable to detect either the pancreatic mass nor any evidence of metastasis radiographically and/or ultrasonographically.

Siliart (2004) reported an overall mean survival time of 11.9 (SD  $\pm$  0.8) months; 16.8 (SD  $\pm$  5.3) months with surgery, 12.5 (SD  $\pm$  1.1) months with medical treatment, 17.8 (SD  $\pm$  4.8) months with surgery and concurrent medical treatment, and 2.5 (SD  $\pm$  0.9) months without treatment.

Medical treatment includes the administration of glucocorticoids, diazoxide, and streptozotocin (Garrett, 2003). Glucocorticoids antagonize insulin at the cellular level, leading to decreased cell uptake and increased blood glucose, stimulate hepatic gluconeogenesis, and indirectly provide substrates for glycogenolysis. Diazoxide, a benzothiadiazide diuretic, works by inhibiting insulin secretion and cellular glucose intake, and stimulating gluconeogenesis and epinephrine release. Streptozotocin is a nitrosourea chemotherapeutic that is specifically toxic to beta cells, however, its effectiveness has yet to be proven (Garrett, 2003). Prednisone alone or with diazoxide significantly improved the survival time compared to diazoxide alone or no medical treatment. There was no significant difference between prednisone and a combination of prednisone and diazoxide (Jaillardon, *et al.*, 2011). While surgery allows for a definitive diagnosis and prolongs the survival time, the old age (14-year-old) and the risk of post-operative complications (such as pancreatitis and diabetes mellitus) outweighed the benefits, and hence glucocorticoids (prednisolone) was the treatment of choice for our patient. The prognosis for the disease is guarded to poor, depending on the degree of malignancy and stage of the tumour (Feldman and Nelson 1996), regardless of whether it is managed medically or surgically.

## CONCLUSION

Insulinoma is a pancreatic islet cell tumour which occurs in middle and old aged dogs, resulting in over-production of insulin and subsequent hypoglycaemia. Therefore, seizures in dogs of this age group should raise suspicion of this neoplasm when intracranial causes, metabolic diseases and infectious diseases are ruled out.

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