

Effective Treatment of a Dog with Insulinoma

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Case Report

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Abstract: Insulinoma is a rare neoplasm with a poor prognosis and few cases of healing in the world literature. A seven-years-old Dachshund presented with a history of spasms of the legs, the laboratory tests it was found hypoglycemia and hyperinsulinemia, and the ultrasonography identified a pancreatic nodule. The clinical treatment had no effect and partial pancreatectomy was performed with resolution of the case. Therefore, veterinarians should be alert for this uncommon condition, in order to identify and treat early.

Keywords: Canine, pancreatic neoplasm, hyperinsulinemia.

INTRODUCTION

Insulinoma is a beta islet cell pancreatic tumor with low incidence, accounting for 0.2 to 0.4% of tumors in dogs and it rarely occurs in cats [1, 2]. Clinical signs of the disease are nonspecific and often found in other diseases, which complicates the diagnoses. In the majority of cases, when a dog is presented, insulinoma is already severe and metastatic [3].

Hematological and imaging exams are necessary for diagnosis; ultrasonography and exploratory laparotomy are sensitive methods that allow primary and possible metastatic tumor visualization. A definitive diagnosis is based on documentation of both hypoglycemia and hyperinsulinemia [4, 3].

There are two treatment options: medical treatment consists of dietary management and/or use of drugs that increase glucose absorption in the gastrointestinal tract, which enhance gluconeogenesis and hepatic glycogenolysis or reduce insulin synthesis, secretion or peripheral action, which are: glucocorticoids, diazoxide and somatostatin analogues [2, 5, 6].

Partial pancreatectomy with tumor removal is the treatment of choice. However, it must be carefully evaluated due to possible postoperative complications. Primary tumor location and metastasis may be complicating factors [7]. Long term prognosis for dogs with insulinoma is guarded to poor due to high incidence of metastatic disease, dogs medically treated have an overall survival of 12 months and for the ones submitted to surgery, survival may be up to 16 months [4], and the average life expectancy after surgery is 12.3 months [1]. But inexplicably was reported an animal with insulinoma and liver metastasis that showed hypoglycemia controlled with the use of corticosteroids only 23 months after partial pancreatectomy surgery [8].

The case reported here is the second national report of a dog successfully treated by surgery, with no recurrence and the animal still alive, with good quality of life after 16 months of treatment.

CASE REPORT

A seven-years-old male Dachshund was presented, weighting 10,7 kg. The owner reported the animal had had two episodes of leg spasms followed by falling and maintenance of spasms on the same morning. Blood glucose level during examination (day 0) was 37 mg/dL.

Physical examination was within normal limits, and a blood sample was collected for a complete blood count (CBC) and biochemistry panel. Intravenous infusion of lactated Ringer's solution and 5 mL glucose boluses were administered.

Hematological examination did not show alterations on CBC, blood glucose level was low (28 mg/dL), blood insulin level was high (73.6 mcU/mL) (Fig. 1), cholesterol was low (64 mg/dL), hepatic enzymes were high: aspartate aminotransferase (AST)

132 UI/L and alanine aminotransferase (ALT) 203 UI/L and blood urea nitrogen (BUN)/creatinine ratio was low (13.73). An abdominal ultrasound revealed a 0.4 cm diameter hypoechoic nodule on right pancreatic lobe, corroborating with insulinoma.

The animal was given Karo® honey every two hours, to temporarily elevate blood glucose level, a protein and complex carbohydrate (bread, rice, potatoes, pasta) diet every three hours on the third day of hospitalization, and 1 mg/kg prednisolone every 24 hours (day 10). Therefore, stabilization through medical treatment (frequent feeding and glucocorticoids) was not successful and surgical treatment was recommended.

Octreotide (Sandostatin) was given (10 mcg/kg, IV, every 24 hours), 3 days before surgery to stabilize the patient. Preanesthetic medication were

atropine (0.04 mg/kg, SC) and meperidine (3 mg/kg, IV), induction with etomidate (1 mg/kg) and anesthetic maintenance with isoflurane.

A ventral midline laparotomy was performed, careful and gentle pancreatic manipulation, the neoplasm was removed with oncological safety margins and properly kept for histopathological examination.

Lymph node, hepatic, splenic e duodenal metastases were searched. Metastasis was not found and suture was performed as usual.

In the immediate postoperative period the animal received metoclopramide (0.5 mg/kg, TID, IV), ranitidine (2 mg/kg, BID, SC), tramadol (2 mg/kg, QID, IV), enrofloxacin 2.5% (5 mg/kg, BID, IV), dypirone (25 mg/kg, TID, IV) and prednisone (1 mg/kg, BID, VO).

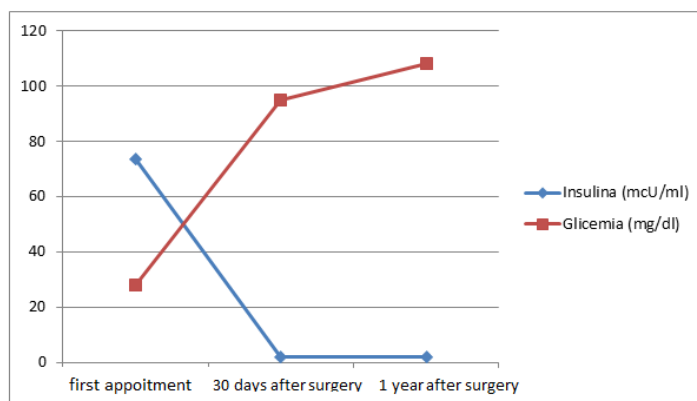


Fig-1: Blood insulin and glucose level before and after surgery

Fasting was maintained for 48 hours and parenteral nutrition was administered: 20 % lipid emulsion (2 Kcal/mL), 10% amino acids solution (0.4 Kcal/mL) and 50% dextrose (1.71 Kcal/mL).

From the third day on the animal voluntarily consumed water and Royal Canin Digestive Low Fat® mixed with mineral water in small amounts several

times a day and blood glucose level was measured every 3 hours (Table 2).

Animal had an excellent postoperative period, without vomiting, normoglycemia between 80 and 120 mg/dL (Tab. 1), and water and food uptake reestablished gradually.

Table-1: Blood glucose level mean values measured during pre and postoperative period, hospitalization is considered day 0

Glycemia (mg/dl)			
Reference interval (65 - 118mg/dl)			
Preoperative	Number of of	Postoperative	Number of measures
37,00 (0d)	01	100,00(16d)	01
40,00 (1d)	06	89,00(17d)	05
74,00(2d)	05	105,00(18d)	06
53,00(3d)	03	90,00(19d)	05
57,00(4d)	02	80,00(20d)	04
48,00(5d)	07	-	-
58,00(6-9d)	38	-	-
68,00(10d)	09	-	-
45,00(11d)	06	-	-
75,00(12d)	07	-	-
80,00(13-15d)	18	-	-

Preoperative: 0d – first appointment, 50% dextrose supplementation; 3d – special diet introduction every 3 hours; 5d – animal discharge; 6d – 9d – blood glucose level measured by owners, return to the veterinary office; 10d – glucocorticoid administration introduction (prednisone 1 mg/kg BID); 12d – octreotide administration introduction (10 mcg/kg SID); 15d – partial pancreatectomy. Postoperative: 16d – end of surgical procedure measure; 17d – parenteral nutrition introduction; 18d – feeding introduction; 19d – patient discharge.

Histopathological exam detected an encapsulated neoplasm and the diagnosis was a histologically low malignant neoplasm classified as pancreatic adenoma.

One month after surgery, the owner brought the animal for exam and case follow up. CBC did not show alterations, biochemical profile showed mild alterations in ALT, alkaline phosphatase, BUN, cholesterol and blood insulin level (2,0 mcU/mL; 5-25 mcU/mL).

Twelve and twenty months after surgery the owner brought the animal for case follow up and abdominal ultrasound and CBC were performed and did not show alterations, blood insulin level were normal.

DISCUSSION

Insulinoma are usually malignant beta cell pancreatic neoplasms that cause excessive insulin secretion. According literature review [9, 2, 7, 6, 5, 10] only 20% of cases had overall survival longer than 8 months [8-10]. The animal reported here is healthy and disease free for 20 months evaluated clinical, laboratorial and ultrasonography ally.

Clinical signs showed by the patient reported here were leg spasms followed by falling, lethargy and weakness and are in accordance with the literature [7, 3].

Laboratory findings, especially hypoglycemia and hyperinsulinemia (Fig. 1 and Tab. 1), corroborate clinical suspicion of insulinoma as was reported [5, 10]. In this report the serum insulin concentration test was processed a few days after collection, this adversity reduces exam accuracy and reliability and impairs early diagnosis. Insulin concentration measurements may easily provide incorrect data due to laboratory mistakes, since figurate blood elements still consume glucose and insulin *in vitro* [3].

Liver enzymes and BUN/creatinine alterations can be explained because the liver and kidneys are the main organs of insulin catabolism, they have proteases that reduce disulfide bonds in various peptides and amino acids, besides, the liver is also responsible for glycogenolysis and gluconeogenesis, so insulin excess

secreted by the tumor overloaded these two organs [3, 1].

The major imaging methods for pancreatic evaluation are magnetic resonance, computed tomography (CT) and abdominal ultrasound, and the first two are less available [11]. Ultrasound evaluation was very important for diagnosis in this case, because a small hypoechoic nodule in right pancreatic lobe was seen. Fenton [6] and Cox [10] diagnosed insulinomas through ultrasound observation of a pancreatic mass also on the right lobe.

It is known that among the imaging exams that can be used, the ultrasound is largely accessible in veterinary medicine, but it is more operator dependent, if compared with CT, which is more specific (75% versus 60%) for pancreatic tumors [11].

As for the treatment [9, 6, 1], frequent feeding (from day 3), three times a day, and glucocorticoid administration (from day 10) (table 2) were attempted, but did not show any improvement. Glucocorticoids elevate blood glucose level through insulin peripheral resistance, stimulating glycogenolysis and providing substrate for gluconeogenesis, both hepatic [3, 2].

According to the literature [9, 6] frequent feeding should be complex carbohydrates and protein based, divided in small portions and offered to the animal 3 to 6 times a day with the intent to offer a constant source of calories as a substrate for the excess of insulin secreted by the tumor and to slow down gastric emptying, and so reduce peak postprandial glycemic and insulin secretion stimuli by the tumor.

As reported by Fenton [6], 10 mcg/kg of octreotide (day 12) was administered to the animal, which was successful for pre-operative stabilization (table 2). This medication is a somatostatin analogue that increases blood glucose concentration due to inhibition of insulin secretion by normal and tumoral cells. In patients with resectable tumors, it may aid in restoration and maintenance of normoglycemia in pre-operative period.

In the post-operative period, with the objective of avoiding complications, especially pancreatitis, the animal was fasted for 48 hours. However, only in this report parenteral nutrition was utilized, to avoid further clinical deterioration of the animal and inhibiting the production of pancreatic juices, due to the possibility of developing pancreatitis after surgical procedure [8, 3]. Feeding restart was gradual and controlled as recommended by Cox [10] and Vallee [5].

After the surgical procedure, there were three follow up appointments, the first after 30 days, the second and the third after 13 and 20 months, respectively. Routine evaluations were performed, as

the exams showed in table 1. Therefore it is the first Latin America case of clinical resolution of this neoplasia that usually results in death in a short period of time.

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