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## Diabetic ketoacidosis and associated hepatopathy in a Pomeranian dog: A case report

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### Abstract

Diabetic ketoacidosis can be considered as a complex disorder as a sequelae of untreated diabetes mellitus. A six year old male dog was presented in a state of coma and recumbency, at Teaching Veterinary Clinical Complex, Mannuthy. Haematological findings were suggestive of severe anaemia and blood transfusion was performed. Laboratory findings included hyperglycemia, glucosuria, ketonemia, ketonuria, hyponatremia, hypochloremia, hypokalemia and increased liver specific enzymes (alkaline phosphatase and alanine aminotransferase). Urinalysis revealed glucosuria and ketonuria. Based on the physical, clinical and laboratory findings, the case was diagnosed as diabetic ketoacidosis. Even though regular crystalline insulin therapy was initiated intravenously following the protocol, the animal died during the course of treatment. Diabetic ketoacidosis is often presented with non specific clinical signs making the diagnosis difficult and the condition requires emergency veterinary assistance.

**Keywords:** Coma, diabetic ketoacidosis, hyperglycemia, regular insulin

### Introduction

Diabetic ketoacidosis is a life threatening condition characterised by hyperglycemia, ketonemia or ketonuria and metabolic acidosis. Diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar syndrome (HHS) are the main complications of diabetes mellitus (O'Brien, 2010) [5]. Decreased insulin concentration or increased insulin resistance along with increased counter regulatory hormones concentration may contribute to increased peripheral lipolysis leading to production of ketone bodies such as acetoacetate, beta-hydroxybutyrate and acetone (Bresciani *et al.*, 2014) [1]. Signs of uncomplicated diabetes mellitus (polydipsia, polyuria, polyphagia and weight loss) may be exhibited initially which progress to lethargy, inappetance and vomiting in unattended cases. The treatment is aimed at providing rehydration, insulin administration and correcting electrolyte abnormalities (Durocher, 2008) [2].

### Case History

A six year old male Pomeranian dog weighing four Kg was referred to Teaching Veterinary Clinical Complex, Mannuthy for blood transfusion. The animal was earlier presented to a nearby hospital with a complaint of anorexia, polydipsia and polyuria and was treated with Tab. Doxycycline for the same for five days. On physical examination, animal was found to be in comatose state and recumbent with pale, icteric conjunctival mucous membrane. The rectal temperature was recorded as 101.5°F. Hepatomegaly and thickened intestinal loops were evident on abdomen palpation. Both blood smear and buffy coat smear examination were negative for haemoparasites. Faecal sample examination did not reveal the presence of any parasitic ova. On complete blood count examination, severe anaemia (Table1) was detected. Based on the clinical signs and the haematology results, it was decided to perform emergency blood transfusion. A unit (350ml) blood was collected from a healthy donor weighing 35 Kg. Plasma was separated from the whole blood by centrifuging at 3000 rpm for a period of seven minutes at 4°C in order to obtain packed red blood cells (pRBC). From the standard formula, 60 ml of pRBC was required to increase PCV by ten per cent and was transfused over a period of four hours (Figure 1). Animal showed a mild improvement on the next day by starting to take food and standing by its own. The condition again deteriorated on the third day. Vomiting, anorexia and dullness were reported and it was decided to perform a detailed examination. Serum biochemical analysis showed elevated alkaline phosphatase (ALP),

alanine aminotransferase (ALT), total and direct bilirubin. Serum creatinine and blood urea nitrogen (BUN) values were within the normal range (Table 2). Mild hepatitis was detected on abdomen ultrasonography. Blood glucose examination indicated hyperglycemia (727.9 mg/dL). Urinalysis revealed glycosuria and ketonuria (Table 3). Urine glucose concentration was estimated to be 655 mg/dL. Blood β-hydroxy butyric acid (BHBA) concentration was recorded high as 4.9 mmol/L. Hyponatremia (110 meq/L), hypokalemia (3.34 meq/L) and hypochloremia (8.86 meq/L) observed were suggestive of electrolyte imbalance in the dog. Urine rothera test was performed and presence of ketone bodies was confirmed by the formation of a purple ring at the junction (Figure 3). The condition was diagnosed as diabetic ketoacidosis based on the symptoms and clinicopathological findings.

**Treatment**

Therapy was initiated by intravenous administration of 0.9% Normal saline @ 10ml/Kg for fluid resuscitation. Ondansetron (Inj. Emeset) was given @ 0.5 mg/Kg intravenously. The most common insulin used for treatment of DKA in dogs is regular insulin (Walsh *et al.*, 2016) [9]. Fluid therapy was followed by intravenous administration of regular insulin (Inj. Human Actrapid 40 IU/ml) @ 2.2 IU/Kg in 0.9% Normal saline as constant rate infusion. A gradual decline in blood glucose value was recorded (Table 4) and the mentation of the animal improved (Figure 4). After a period of five hours, haematochezia and bilirubinuria was noticed (Figure 5). Eventhough clinical improvement was noticed, the animal succumbed to death eventually.

**Table 4:** Blood glucose values during regular insulin CRI

Time	Blood Glucose (mg/dL)
After 1 hour	534
After 3 hours	453
After 4 hours	392
After 5 hours	387



**Fig 1:** Blood transfusion

**Table 1:** Haematological analysis

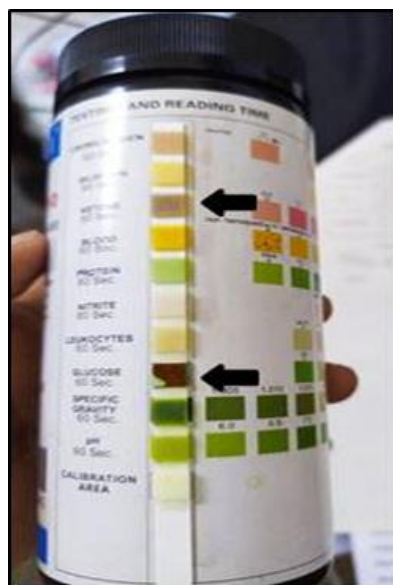
Parameters	Day of Presentation	After Transfusion (Post 3 days)
WBC (10 <sup>3</sup> /μL)	16.9	13
RBC (10 <sup>6</sup> /μL)	1.59	3.9
Haemoglobin (g/dl)	3	8.6
Packed cell volume (%)	11	24
Platelet (×10 <sup>3</sup> /μL)	782	750

**Table 2:** Serum biochemical analysis

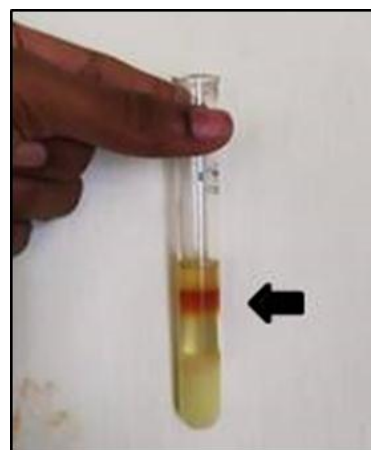
Parameters	Values
Alanine aminotransferase (IU/dL)	113.2
Alkaline phosphatase (IU/dL)	1205.4
Total bilirubin (mg/dL)	2.17
Direct bilirubin (mg/dL)	1.75
Creatinine (mg/dL)	0.71
Blood urea nitrogen (mg/dL)	14.77

**Table 3:** Urinalysis

Parameter	Values
pH	6.5
Specific gravity	1.005
Glucose	++++
Leukocytes	+
Protein	+
Bilirubin	+++
Ketone	+++
Blood	-
Nitrite	-



**Fig 2:** Urine dipstick analysis (glucosuria & ketonuria)



**Fig 3:** Urine rothera test-Presence of purple ring



Fig 4: Improved mentation during insulin therapy



Fig 5: Bilirubinuria

## Discussion

Diabetic ketoacidosis (DKA) is a complication of unregulated diabetes mellitus and requires emergency care. Hyperglycemia, metabolic acidosis, hyperketonemia and electrolyte imbalance noticed in severely affected patients can be life threatening. The accumulation of ketones in serum is associated with metabolic acidosis that is manifested as diabetic ketoacidosis (Durocher, 2008) [2]. In agreement with the present findings of urinalysis, Rucinsky *et al.* (2010) [6] also reported the presence of glucose, protein and ketones in the urine of dogs diagnosed with DKA. It is always advised to perform urine culture in glycosuric animals, due to the increased susceptibility to infections (Rucinsky *et al.*, 2010) [6]. In the present case, anaemia might have occurred due to heinz body formation or red blood cell oxidative injury. Non-regenerative anaemia, left shift neutrophilia and thrombocytosis were detected in a previous study (O'Brien, 2010) [5]. Gkamprela *et al.* (2017) [3] reported the occurrence of anaemia in about 75 per cent of patients with advanced liver disease. Alteration of iron homeostasis leading to iron deficiency and haemolysis are the common causes of anaemia in patients with liver diseases. Hyperglycemia, hyperlipidemia, insulin resistance, insulin deficiency, oxidative stress, inflammation, endothelial dysfunction are the main factors contributing to increased platelet reactivity in diabetes (Schneider, 2009) [7]. In a retrospective study of thrombocytosis in 715 dogs by Woolcock *et al.* (2017) [10], endocrine diseases contribute to thrombocytosis in 12 per cent of the total dogs studied. DKA should be suspected in dogs with capillary BHBA >3.8 mmol/L (Bresciani *et al.*, 2014) [1]. The BHBA value was of 4.9 mmol/L can be correlated with the severity of condition of the dog in this case. Decreased hepatic perfusion and hepatocellular damage as a sequelae to hypovolemia can lead to increased serum liver enzyme activity (O'Brien, 2010) [5]. Bilirubinuria might have occurred in the terminal stage due to high bilirubin level in blood. Elevation in direct bilirubin in this case also confirms

the presence of liver pathology. As reported by Durocher *et al.* (2008) [2], serum sodium and chloride levels was found lower in the present case, whereas serum potassium was also found lower contradicting their findings of higher serum potassium concentration in diabetic dogs. According to Hume *et al.* (2006) [4], hypokalemia and hypophosphatemia are common in dogs with DKA due to their shift from intracellular space to extracellular space as a result of hyperglycemia and hypoinsulinemia. Shilo *et al.* (1985) [8] have documented hypophosphatemia in poorly controlled diabetes cases. Hypophosphatemia may lead to decreased synthesis of 2,3-diphosphoglycerate (2,3-DPG) and adenosine triphosphate (ATP) which are essential for oxygen delivery to tissues and red blood cell energy metabolism. The deficiency of 2,3-DPG and ATP result in impaired membrane function and haemolysis. Eventhough a possibility of haemolytic anaemia resulting from hypophosphatemia exist in the present case, lack of evidence regarding hypophosphatemia makes it difficult to confirm it as the cause of anaemia. The most common insulin used for treatment of DKA in dogs is regular insulin. Administration of regular insulin as constant rate infusion or as hourly intramuscular injections is the common protocol followed in cases of diabetic ketoacidosis. As carried out in the present case, it is recommended to initiate IV CRI of insulin following fluid resuscitation as blood glucose concentration decreases significantly with fluid resuscitation alone (Walsh *et al.*, 2016) [9]. Timely diagnosis and intervention is required for favourable prognosis in case of DKA. Chronic untreated diabetes mellitus might have triggered the occurrence of diabetic ketoacidosis and severe anaemia that resulted in fatal outcome in the present case.

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