



A Suspected Case of Digitalis Toxicity Secondary to Therapeutic Management of Congestive Heart Failure in A Boerboel Dog

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ABSTRACT

A 15 months old male Boerboel, weighing 25kg presented to Veterinary Teaching Hospital, Abeokuta, Nigeria, with complaint of abdominal distention, emaciation and anorexia was diagnosed of congestive heart failure (CHF) of unknown etiology. At presentation, prominent S- wave voltages in lead II, III electrocardiogram, a positive R-wave in lead AVR and a mean electrical axis of -90° suggestive of right ventricular enlargement were evident. A right atrial enlargement was also suspected due to the presence of a tented P-wave on the electrocardiogram. Digoxin was administered at 0.01 mg/kg orally, once daily to increase cardiac contractility and reduce heart rate; Enalapril given at 0.5 mg/kg orally once daily was to blunt the renin angiotensin aldosterone response, Furosemide at 2mg/kg orally, once daily was administered to increase natriuresis and diuresis. After 2 weeks of medication the dogs exhibited signs of digitalis toxicity such as ventricular premature contraction, ventricular tachycardia. This case is a rare occurrence and has not been reported in our veterinary clinics. The management of CHF with standard dose regime of digitalis requires therapeutic drug monitoring as it could result in breed specific toxicity.

KEYWORDS: Congestive Heart Failure, Digoxin, Electrocardiogram, Ventricular Arrhythmia

CASE HISTORY

A 15 months old male Boerboel dog was presented to the Veterinary Teaching Hospital of Federal University of Agriculture, Abeokuta, with a chief complaint of weight loss, emaciation, anorexia and abdominal distention. It was also revealed that the dog had received routine vaccination against canine distemper, canine parvovirus, hepatitis and leptospirosis. On physical examination, it was observed that body condition score was 4/9 and distended abdomen was due to effusion. The temperature was 38.7°C. On auscultation, there were gallop rhythms, murmurs and tachycardia (heart rate was 150/minute). Abdominocentesis was done to relieve the distended abdomen. Blood sample was also collected via cephalic vein for blood

chemistry, hematology and haemo-parasite screening. A six-lead ECG examination was done immediately. The ECG showed pronounced S-waves in leads II and III, a positive R waves in lead AVR and a mean electrical axis of -90 degrees. The p-wave was also tented (figure 1). The dog was scheduled for another ECG at two weeks after commencement of medication. The medication was comprised of the following; Digoxin (0.01mg/kg) PO daily \times 2/52; Enalapril (0.5mg/kg) PO daily \times 2/52; Furosemide (2mg/kg) orally daily \times 2/52; Vitamin B12 (2ml) IM \times 2/52; Praziquantel (10mg/kg) PO. The dog was discharged after a week when appetite was restored, ascites subsided and the body condition score appeared to have improved. The client was advised to continue medication

for 2 weeks. Two weeks after medical management commenced; lethal ECG signs such as ventricular premature contraction, ventricular tachycardia and atrial fibrillation were observed (figure 2). Although the ascites, body condition score and heart sound has improved tremendously, the ECG has worsened compared to the previous one.

Table 1: Serum haemato-biochemical parameters of dog at presentation

PARAMETERS	VALUES AT PRESENTATION	RANGE OF NORMAL VALUES
Packed cell volume (PCV%)	22	35-55
Total WBC ($10^6/\mu\text{L}$)	14.3	6-17
Neutrophil ($10^3/\mu\text{L}$)	12.87	3-11
Lymphocyte($10^3/\mu\text{L}$)	1.14	1-4.8
Eosinophils ($10^3/\mu\text{L}$)	0.29	0.2-1.4
Alanine aminotransferase (IU/L)	12.5	10-120
Aspartate Aminotransferase (IU/L)	8.5	16-40
Alkaline phosphatase (IU/L)	92.3	35-280
Total bilirubin(mg/dL)	0.5	0-0.4
Conjugated bilirubin(mg/dL)	0.3	0-0.5
Unconjugated bilirubin(mg/dL)	0.2	0.06
Total protein(g/L)	70.5	63-76
Albumin(g/L)	45.2	25-43
Globulin(g/L)	25.3	26-50

DISCUSSION

A diagnosis of congestive right sided heart failure was made because of electrocardiographic evidences of right axis deviation such as the presence of pronounced S waves in leads II and III, a positive R waves in lead AVR and a mean electrical axis of -90 degrees (Cote and Ettinger, 2005; Kim et al., 2017; Oyama et al., 2005). The

low voltage QRS complex in lead I could be caused by ascites (De-Morais and Schwartz., 2005) and the tented p waves suggestive of right atrial enlargement (Mcdonald and Johnson, 2005).

The right axis deviation could be caused by either right ventricular hypertrophy or right bundle branch block. The morphology of the QRS waves in all leads is not suggestive of a right bundle branch block but rather a right ventricular enlargement. The right ventricular enlargement is commonly caused in dogs by heart worm disease, pulmonary hypertension, tricuspid valve insufficiency and congenital pulmonic stenosis. Although not commonly seen in dogs, a diagnosis of right sided congestive heart failure was made in this case because of the clinical sign of ascites and electrocardiographic evidences shown by the dog at presentation. The right ventricular enlargement could be caused by volume

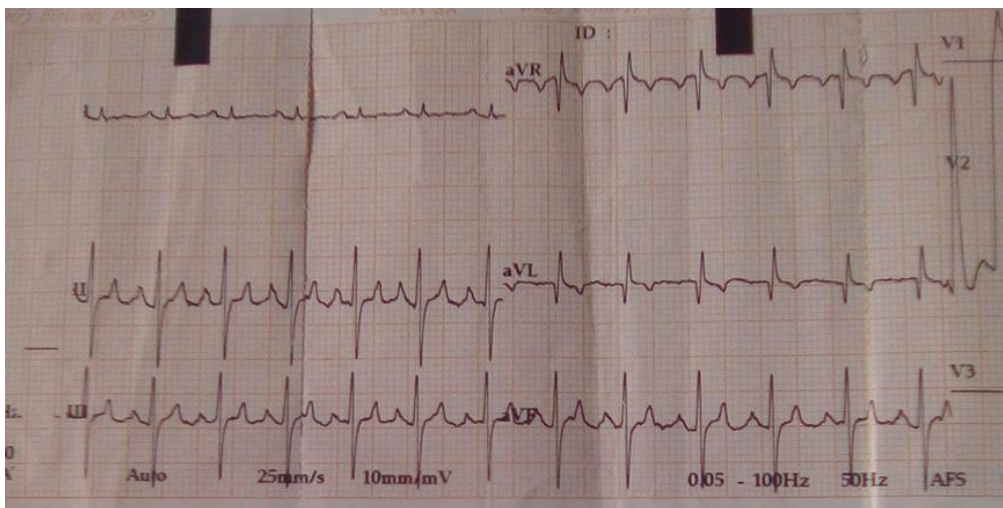


Figure 1: The ECG on presentation. Note the pronounced S and positive R in leads II and AVR respectively

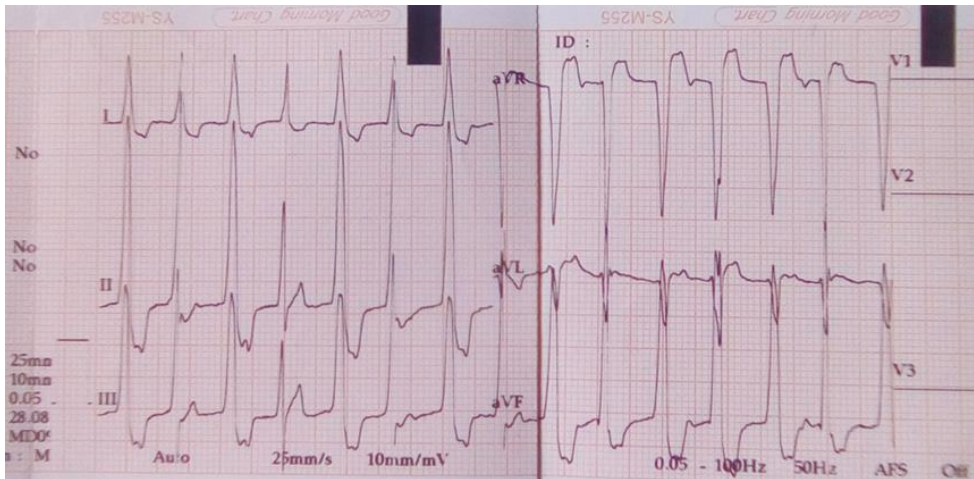


Figure II: The ECG after 2weeks of medication with Digoxin, note the Ventricular Tachycardia in all leads

or pressure overloading of the ventricle. This normally results in poor venous return and fluid retention leading to ascites.

Although the cause of the present condition was not known and a definitive diagnosis cannot be made, it was tentatively considered congenital pulmonic stenosis because of the young age of our patient. Although canine heart worm infestation could also cause right sided congestive heart failure in dogs, this was not considered because the buffy coat examination was negative for the microfilaria and dog has been prophylactically treated against heart worm infestation. The possibility of a viral endocarditis was also considered in this case even when the vaccination record of the dog was up to date and most dogs presented for parvo-enteritis in our clinic were always presented with enteric form of the disease. Depending on its severity, an involvement of the tricuspid valve could impair myocardial function causing a right sided congestive heart failure. There is a likelihood that some dogs presented to the clinic may suffer from cardiac form of the disease because quality of vaccine, maternal immunity and pathotype of

etiologic agent are not exclusively under the control of veterinarian.

The result of hematology revealed a stress hemogram.

The neutrophilia, lymphopenia in the absence of monocytosis may be due to stress associated with the condition. Except for marginal decrease in AST which may be overlooked, other liver function enzymes and serum proteins indices were normal in the dog at

presentation. This is an indication that ascites may not be related to any hepatic abnormality.

Although none of the common haemo-parasites was detected on blood screening, the packed cell volume was below physiological range. Several authors have also reported the occurrence of anemia in congestive heart failure (Sandhu *et al.*, 2010; Siverberg *et al.*, 2004). The extensive elaboration of bone marrow depressing cytokines associated with this condition could be the reason for the observed anemia.

Our approach to management of this condition was to relieve the abdominal distension through abdomino-centesis and by the administration of furosemide, a diuretic. It was also our intention to reduce heart rate while improving contractility by using Digoxin.

Two weeks after medical management commenced; lethal ECG signs of ventricular tachyarrhythmia such as ventricular premature contraction and ventricular tachycardia were observed. Although the ascites, body condition and the heart sound has improved tremendously, the ECG has worsened compared to the previous one.

Ventricular extra systoles or ventricular premature contraction are known to occur when a

certain region of the ventricles become over excited and depolarizes ahead of other regions. This phenomenon has been reported in cardiac or extracardiac conditions. Systemic and metabolic disorders such as hypoxia, hypokalemia and anemia are all known to be potent stimulus for the formation of extra systoles (Gaztanagu *et al.*, 2012). We ascribed these ECG features to digoxin toxicity because digoxin is known to have a narrow therapeutic index and toxicity has been known to occur at the normal therapeutic dose (Chadha *et al.*, 2011; Vyas *et al.*, 2016). Digoxin is capable of causing diverse forms of arrhythmia and some of the arrhythmias that have been reported in digoxin toxicity in dogs include bradyarrhythmias, tachyarrhythmias and atrioventricular blocks (Gordon and Kittleson, 2008; Kelly and Smith, 1992; Tobias *et al.*, 1989).

The incidence of digoxin toxicity in the study area is not well documented and this case may be the first to be reported. The narrow safety margin of digoxin makes it imperative to evaluate and monitor drug concentration in patient during treatment (Maddison *et al.*, 2008). The toxicity of digitalis to the myocardium is caused by poisoning of the Na/K ATPase pump. This may result in delayed after- depolarization which could cause ventricular premature contraction (Roberts *et al.*, 2015). In the present case, ventricular tachy-arrhythmias consisting of ventricular premature contraction and ventricular tachycardia were observed. The interaction of digitalis with other drugs is also a major factor determining its toxicity. Digoxin toxicity is potentiated by agents that use up potassium, cause hypokalemia and thereby exposing the potassium binding sites of Na/K ATPase (Shapiro, 1992). One of the drugs used on this dog, Furosemide, could cause potassium depletion and potentiate the toxicity of digoxin. The 0.01mg/kg/day dose of digoxin administered to the dogs was within the 0.005 to 0.01mg/kg q12hours range recommended (Godson and Kittleson, 2008). Similarly, Tobias *et al.*, (1989)

observed signs of toxicity in beagles administered with 0.01mg/kg/day digoxin. The authors are of the opinion that administering digoxin at the same dose on the basis of body surface area could improve safety profile of the drug. It has also been observed that a lower dose of 0.003mg/kg/q12hours that targets lower serum concentration could be more beneficial (Bulmer and Sisson, 2005). The dose of digoxin used was within the accepted dosage range for dogs and the toxicity experienced in this dog may be as a result of individual variation in drug exposure indices. It is against this background that therapeutic drug monitoring has been advocated during digitalis therapy (Maddison *et al.*, 2008). Digitalis toxicity is commonly associated with dysfunctions of gastrointestinal tract, central nervous system and myocardium. Gastrointestinal signs of digitalis toxicity such as vomiting, diarrhea, anorexia is often apparent and noticeable by clients (Bulmer and Sisson, 2005). In the present case, no clinical sign of central nervous system and gastrointestinal tract involvement was reported by the clients after digoxin treatment. This could therefore suggest that system susceptibility to the toxicity of digitalis may vary with dog breeds.

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