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Management of clindamycin induced Acute Kidney Injury by Intermittent Hemodialysis - An unusual case report in a pup

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Abstract

A 4 month old Labrador Retriever breed pup with history of clindamycin feeding from past 15 days was presented to our hospital. History taking revealed anorexia, vomiting (5-6 episodes/day), lethargy and dark yellow urine from last seven days. On clinical examination, the pup was disinclined to move and was having rectal temperature – 102.2^{0}F, heart rate- 85bpm, respiration rate-25 breaths/minute, blood pressure (doppler)- 145 mmHg, mucous membrane- pale, and normal lymph nodes. The hemato-biochemical profile of pup revealed severe uremia and electrolyte imbalance with blood urea nitrogen (BUN)- 115 mg/dl, Creatinine- 8.3 mg/dl, Phosphorus-14.2 mg/dl, sodium-148 mEq/L, potassium- 4.0 mEq/L, chloride- 121 mEq/L and calcium- 13.5 mg/dl. Initially, the pup was prescribed standard medicinal treatment of AKI for one week with no significant improvement. Thus, after one week, intermittent hemodialysis (IHD) was selected as treatment of choice. After single IHD session the pup showed significant improvement with reduction in uremic toxins and correction of electrolyte imbalance.

Keywords: Clindamycin, Acute kidney injury, Pup, Intermittent hemodialysis, Uremia

In small animal Veterinary Medicine, medications are one of the most frequent trigger for onset of acute kidney injury (AKI) in canine patients. This AKI in dogs is manifested as a consequence of acute damage to the hemodynamic, filtration or excretory function of the kidney leading to reduced glomerular filtration rate and ultimately accumulation of uremic and metabolic toxins in the body (Vaden *et al.,* 1997 and Eubig *et al.,* 2005). Initial management of AKI in dogs include removal of inciting cause of renal injury, correction of hypovolemia, intravenous fluid therapy, correction of electrolyte and acid-base imbalance along with supportive care for management of clinical signs of uremia. Majority of AKI cases are potentially reversible if proper diagnosis is achieved at initial stage and adequate treatment strategy is rigorously followed. Clindamycin is a commonly used antibiotic both in human and veterinary medicine with broad antimicrobial activity, but the frequency of reported side effects has recently increased (Xie *et al.,* 2013), with majority of the reports from human patients (Wu, 2010).

Intermittent hemodialysis (IHD) is considered for management of AKI if medical management fails to yield desired results (rising azotemia, electrolyte and acid-base imbalance unresponsive to medical management). The primary goal of IHD in dogs with AKI is to clear accumulated uremic toxins, correct acid-base, fluid, and electrolyte imbalances over a short period of time in order to minimize further insult to renal parenchyma (Cowgill and Francey, 2012; Cowgill 2011; Bloom and Labato, 2011). The prescription and prognosis of IHD in veterinary practice vary for each patient depending on the severity of underlying etiology, degree of renal impairment, and presence of comorbidities (Fischer *et al.,* 2004).

Here, we present a rare case of clindamycin induced AKI in a pup which required intermittent hemodialysis for its recovery.

Case History and Clinical Observations

A 4 month old male Labrador Retriever breed pup weighing 10 Kg was presented at Medicine OPD of Multispecialty Veterinary Hospital, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, Punjab, India with history of anorexia, vomiting (5-6 episodes/day), lethargy and dark yellow urine from past seven days. Previously, before presentation, the pup was operated for abscess in left inguinal region and was prescribed clindamycin 150 mg orally once a day for five days. Detailed history from owner revealed that contrary to the prescribed dosage, the pup was fed clindamycin 150 mg orally twice daily from past 15 days. On clinical examination, the pup was disinclined to

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move and was having rectal temperature – 102.2^{0}F, heart rate- 85bpm, respiration rate-25 breaths/minute, blood pressure (doppler)- 145 mmHg, mucous membrane- pale, and normal lymph nodes. Blood, urine and serum samples were taken from dog for evaluation of complete blood count (CBC), urine specific gravity and biochemical profile including alanine aminotransferase (ALT), Alkaline phosphatase (ALKP), total protein, albumin, glucose, Blood urea nitrogen (BUN), creatinine, sodium (Na), potassium (K), Phosphorus (P), chloride (Cl) and calcium (Ca). X-ray of chest (lateral and VD views) along with ultrasound of abdomen was also carried out. Results revealed Hb- 10.2 g/dl, TLC- 8,220 (N-86%, L-14%), TEC- 6.41 X 10^6, PCV- 34.4 % and Platelet count- 306 X 10^3 (table 1). Urine specific gravity was 1.015 with mild proteinuria (1+). Biochemical profile revealed ALT- 74 u/L, ALKP- 175u/L, Total Protein- 6.2 g/dl, Albumin- 2.8 g/dl, Glucose 88 mg/dl, BUN- 115 mg/dl, Creatinine- 8.3 mg/dl, Phosphorus-14.2 mg/dl, Na- 148 mEq/L, K- 4.0 mEq/L, Cl- 121 mEq/L and Ca- 13.5 mg/dl (table 1). X-ray of chest (lateral and VD) revealed no abnormality of heart and no appreciable free fluid in chest. Moderate bronchial pattern on right caudal aspect of lung was appreciable (Fig. 1). The abdominal ultrasound revealed hyperechoic renal cortex with satisfactory cortico-medullary differentiation. Based on history and laboratory findings, the case was diagnosed and treated as clindamycin induced acute kidney injury (AKI). As on the day of presentation, the dog was already on oral clindamycin from past 15 days, the owner was advised to stop medication with clindamycin and prescribed standard AKI treatment which included intra venous fluid administration (Ringer lactate and dextrose normal saline @ 20 ml/kg), loop diuretic (furosemide @ 2mg/kg IM BID), proton pump inhibitor (Pantoprazole @ 1 mg/kg IV once), anti-emetic (Metoclopramide @ 0.2mg/kg IM BID) and antibiotic (Ampicillin @ 22.5mg/kg IM BID) for one week. After one week of treatment, the pup was again presented to hospital with no signs of improvement. The pup was again assessed by submitting blood samples for hemato-biochemistry the results of which revealed persistent uremia and derailed electrolyte balance (Table 1). As the health of dog was progressively deteriorating even after one week of medicinal treatment, IHD was considered as a promising modality as the age of pup was only four months. Before initiating IHD session, electrocardiography (ECG) was performed to rule out any major cardiac insufficiency/ involvement. The result of ECG were within normal range with normal sinus rhythm, atrial fibrillation, widening of P wave, mild ST slurring with P (A)- 0.2mv, P (W)- 0.02 sec, R (A)- 1.6mv, R (W)- 0.04 sec, T (A)- 0.1mv and T (D)- 0.02 sec (Fig. 2). Single IHD session was performed with Fresenius 4008S machine, using jugular catheterization with 8.5 Fr. double lumen catheter (Fig. 3) and Fresenius Fx_5 dialyzer having surface area 1.0 m^2. The dialysate K concentration was adjusted to 3.5 mEq/L whereas, base and prescribed Na levels were kept at 142 mEq/L. The hemato-biochemical profile was carried out immediately after end of IHD session and the results showed significant reduction in BUN, creatinine, Phosphorus along with correction of electrolyte imbalance (Table 1).

Discussion

The most common causes of AKI in dogs include toxin ingestion, hypovolemia, general anesthesia and sepsis. Among toxins, ingestion of grapes, raisins, aminoglycoside antibiotics, chemotherapy agents and non-steroidal anti-inflammatory medications (NSAIDS) are commonly reported (Stanley and Langston, 2008). In veterinary medicine, Clindamycin is mostly used to treat diseases of the skin, mouth, bone, and respiratory tract with oral dose ranging from 5 to 11 mg/kg and is rarely associated with AKI. Although, the common adverse effects of Clindamycin after oral administration include gastroenteritis, esophagitis, esophageal strictures and hyper salivation but cautious administration is recommended in very severe renal and/or hepatic disease cases and prescription is completely avoided in neonatal small animals (Plumb, 2018). In present case, the pup was prescribed Clindamycin 150 mg orally once a day only for five days but due to owner's ignorance it was fed double the prescribed dose (150 mg orally twice a day for 15 days) for extended period of time which might have led to acute renal insult. The exact mechanism of drug-induced AKI in dogs varies depending on causative agent and includes acute tubular necrosis in case of aminoglycosides, acute interstitial nephritis for ampicillin, hemodynamic perturbations for NSAIDS and angiotensin-converting enzyme inhibitors (Dennen *et al.,* 2010). Although, extensively metabolized in the liver, by the cytochrome P450 isoenzyme 3A4, 10 per cent of the Clindamycin is excreted by the kidney which may precipitate in the renal tubular lumen leading to tubular damage and renal function impairment (Giovanni and Giuseppe, 2003). Initially, the pup was treated for

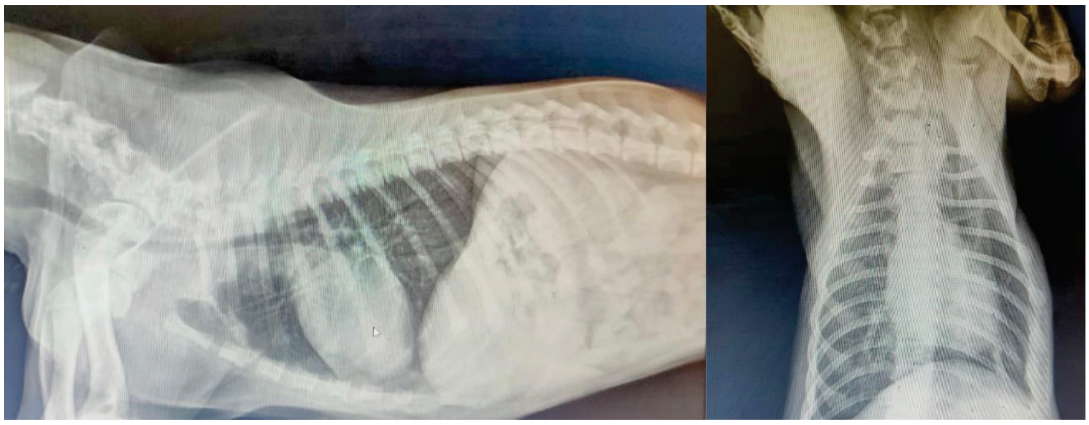

Fig. 1. Thoracic radiograph of pup in lateral and ventro-dorsal view showing moderate bronchial pattern

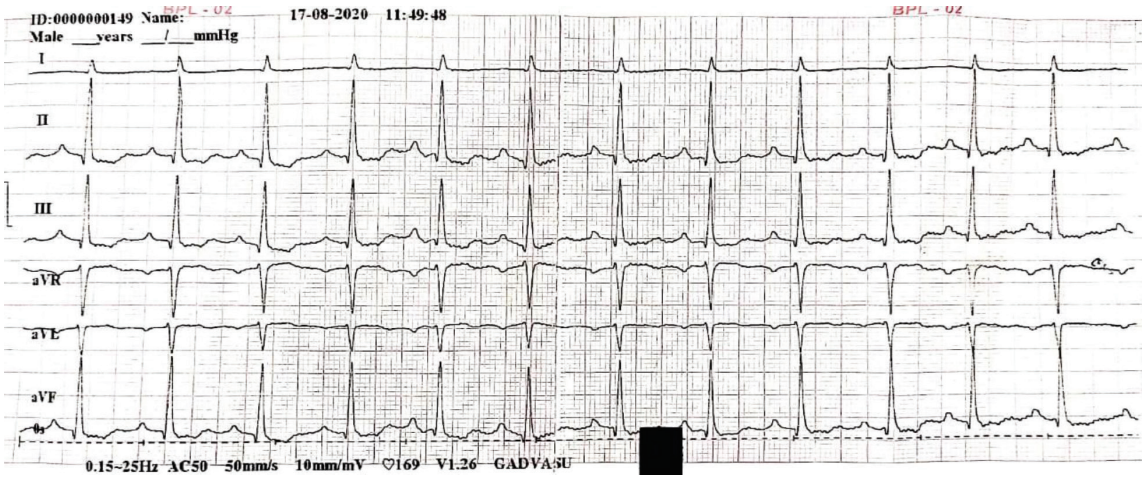

Fig. 2. Electrocardiograph of pup before initiation of dialysis session

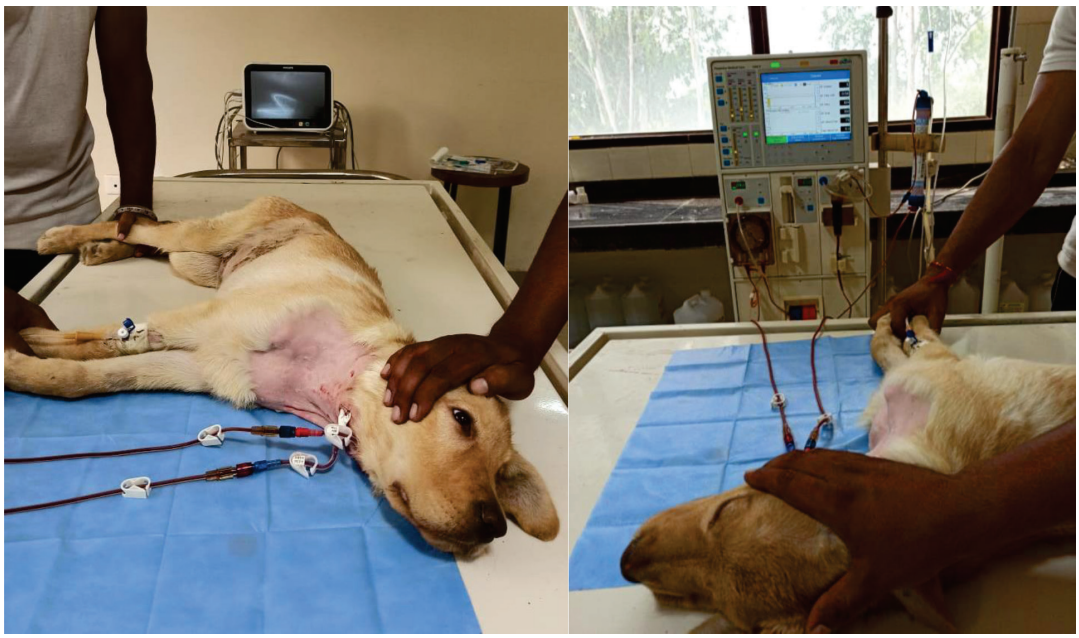

Fig. 3. Jugular Catheterization of pup with 8.5 Fr. double lumen catheter

Table 1. Hemato-biochemical profile of pup suffering from Clindamycin induced AKI and undergoing IHD

Parameter	On the day of 1st presentation	One week after standard medicinal treatment and pre-dialysis	Post dialysis session
Hb(g/dL)	10.20	10.80	9.60
TLC	8,220	15,720	16,630
TEC ($x10^6$)	6.41	6.33	6.44
PCV (%)	34.40	37.30	35.10
Platelets ($x10^3$)	306	511	232
ALT (U/L)	74	45	50
ALKP (U/L)	175	304	357
T. Protein (g/dL)	6.20	6.50	6.80
Albumin (g/dL)	2.80	2.90	3.20
BUN (mg/dL)	115	88	22
Creatinine (mg/dL)	8.30	6.20	2.0
Phosphorus (mg/dL)	14.20	10.80	3.7
Sodium (mEq/L)	148	151	138
Potassium (mEq/L)	4.0	4.3	3.40
Chloride (mEq/dL)	121	123	116
Calcium (mg/dL)	13.50	13.60	12.30
Glucose (mg/dL)	88	91	86

Ultrafiltration Goal (UF Goal):- 100ml

AKI without any significant improvement by early identification and removal of causative agent along with intravenous fluid therapy, diuretics, correction of electrolyte and acid-base imbalance for one week. Thus, IHD was considered as a final modality to save the pup from pansystemic ramifications of severe uremia (Fischer *et al.,* 2004). The dialyzer (Fresenius Fx5) was selected on the basis of pups' body weight (Cowgill, 2011) keeping a balance between effective surface area and priming volume. At the start of IHD session the blood flow rate was kept 45 ml/min which was slowly increased to 80 ml/min over a period of 10 minutes to achieve desired outcomes. At the end of session, there was improvement in dog with significant reduction in levels of BUN, Creatinine, Phosphorus along with correction of electrolyte imbalances. The pup was kept on oral medications like L- carnitine, furosemide, pantoprazole and B-complex supplementation for next five days. The condition of dog was reassessed after one week revealing complete recovery with normal physical activity, appetite and complete cessation of emesis.

Conclusions

In this study, we present a rare case of Clindamycin induced AKI in a pup, successfully managed by IHD. Despite the presence of severe uremia refractory to standard medicinal treatment, the outcome was quite good. Clindamycin-induced AKI should not be overlooked in case of young pups since it may potentially cause serious complications.

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