



## Case report

# A case report of peritoneal dialysis for management of acute kidney injury caused by Russell's viper envenomation in a dog

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## Abstract

This report describes a five-year-old dog who had been bitten by a Russell's viper. The patient presented clinical signs of anorexia, vomiting, lethargy, and anuria. Collectively with the laboratory test results of azotemia and hyperkalemia, acute kidney injury was diagnosed. Peritoneal dialysis (PD) was instigated when the azotemia became worse and anuria persisted, despite aggressive medical and fluid therapy. After 14 days of PD, the anuria was resolved, and the patient was discharged 7 days later. At the end of the last dialysis cycle, there was a significant reduction in the severity of the azotemia, and the serum hyperkalemia had returned to normal. One month after PD, the patient no longer had any abnormal clinical signs. Both the patient's serum blood urea nitrogen level and creatinine levels returned to within the normal limits. PD proved to be an effective management of acute kidney injury in Russell's viper envenomation in the reported dog. This report also describes a detailed procedure of PD which can be instigated in any veterinary practice.

**Keywords:** Acute kidney injury, Anuria, Dog, Peritoneal dialysis, Russell's viper

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## INTRODUCTION

Acute kidney injury (AKI) is a sudden decline in renal function, which is characterized by elevated serum creatinine and urea nitrogen levels, decreased urine output, and electrolyte imbalance, especially metabolic acidosis and hyperkalemia (Legatti et al., 2018). Legatti et al. also stated that many causes of AKI include infections, exposure of nephrotoxic agents, hemodynamic decline, and urinary tract obstruction. AKI may be contributed to one or more causes and may vary in severity (Brown et al., 2015; Lee et al., 2012). The overall mortality rate for AKI in dogs and cats ranges from 45% to 55% (Guimaraes-Okamoto et al., 2016).

Russell's viper (*Daboia siamensis*) venom is a nephrotoxic agent, which triggers AKI via mechanisms of renal hemodynamic impairment, hypotension, disseminated intravascular coagulation, and direct tubular necrosis (Chaiyabutr et al., 2014; Patil et al., 2012; Tungthanathanich et al., 1986). Approximately 29% of dogs developed AKI after envenomation (Adhikari et al., 2019).

Although supportive treatment is still the mainstay for AKI management, renal replacement therapy (RRT); namely, peritoneal dialysis (PD) should be considered when medical management has failed (Bersenas, 2011). There are many reports on successful PD treatment in leptospirosis and drug-induced AKI cases (Beckel et al., 2005; Guimaraes-Okamoto et al., 2016). However, the use of PD in the management of AKI in companion animals caused by Russell's viper venom has never been reported. Therefore, this case report describes both the medical treatment and PD procedure in managing Russell's viper envenomation induced AKI in a dog.

## HISTORY CLINICAL DIAGNOSIS AND FINDING

A five-year-old intact male mixed-breed dog was presented at Kasetsart University Veterinary Teaching Hospital (KUVTH), Hua Hin, Thailand. According to the owner, the patient was bitten by a Russell's viper 4 days before the hospital visit. Two days later, the patient began to display signs of vomiting, anorexia, and lethargy. The patient was an outdoor dog with no prior laboratory assessment.

Clinical signs at presentation included depression, lethargy, vomiting, anorexia, and diarrhea. From physical examination, the patient had pale pink mucous membrane, 5% dehydration status, normal heart and lung auscultation sound and normal abdominal palpation. Heart rate, respiratory rate, systolic blood pressure, temperature, body weight and body condition score were 80 bpm, 20 bpm, 130 mmHg, 100.58 °F, 34 kg and 3/9 respectively. Blood samples were taken for hematological, biochemical, blood gas analyses and coagulation assays revealing anemia, severe azotemia, hyperkalemia, and some other minor abnormalities. According to IDEXX VetTest Chemistry Analyzer's reference ranges, the abnormal serum biochemical parameters included blood urea nitrogen (BUN, 236.5 mg/dL), creatinine (21.16 mg/dL), and phosphorus (16.1mg/dL) as shown in Table 1. A complete blood count was frequently

monitored and showed a declining trend of the hematocrit (HCT) level (Table 2). According to the IDEXX Coag Dx Analyzer (IDEXX Laboratories, USA), the patient had prolonged activated partial thromboplastin time (aPTT; 114 sec; reference range 72-102 sec) and normal prothrombin time (PT; 13 sec; reference range 11-17 sec). Thus, a fresh whole blood transfusion was given on the first day of PD therapy and again on Day 10 when the HCT level became critically low. Urine collected via catheterization revealed specific gravity of 1.010, pH 8.0, protein 2+, bacteria 1+/hpf and red blood cells of over 300 cells/hpf (Table 3).

**Table 1** Serum biochemistry analyses in a dog with anuric acute kidney injury before peritoneal dialysis (PD; Day 0), during PD treatment (Day 1-17), and after PD ended (Day 18-81).

Day	BUN	Creatinine	Phosphorus	Albumin	Potassium
Reference range*	7-27 mg/dL	0.5-1.8 mg/dL	2.5-6.8 mg/dL	2.3-4 gm%	3.5-5.8 mEq/L
0	236.5	21.16	16.1	2.3	7.8
1	210	18.11	15.7	2	6.29
2	149.7	14.5	N/A	2.1	5.04
4	86.7	11.4	N/A	N/A	3.76
6	76.3	10.85	N/A	N/A	3.97
8	68.2	8.37	N/A	1.6	3.32
10	57.9	8.16	N/A	N/A	3.21
11	51.6	8.35	N/A	1.7	3.98
13	55.9	7.49	N/A	1.8	4.25
15	47.7	5.33	N/A	1.6	4.1
16	48.6	4.54	N/A	2.1	3.58
17	38.2	4.35	4.5	2	4.09
18	41.9	5.47	N/A	N/A	3.47
20	34	4.66	N/A	3.2	3.75
29	15	1.5	N/A	N/A	N/A
51	13.9	2	N/A	2.8	N/A
81	16	1.6	N/A	N/A	N/A

Reference ranges of serum parameters analyzed by IDEXX VetTest Chemistry Analyzer, BUN: Blood urea nitrogen, N/A: not applicable.

**Table 2** Complete blood count in a dog with anuric acute kidney injury before peritoneal dialysis (PD; Day 0), during PD therapy (Day 1-17), and after the PD ended (Day 18-81).

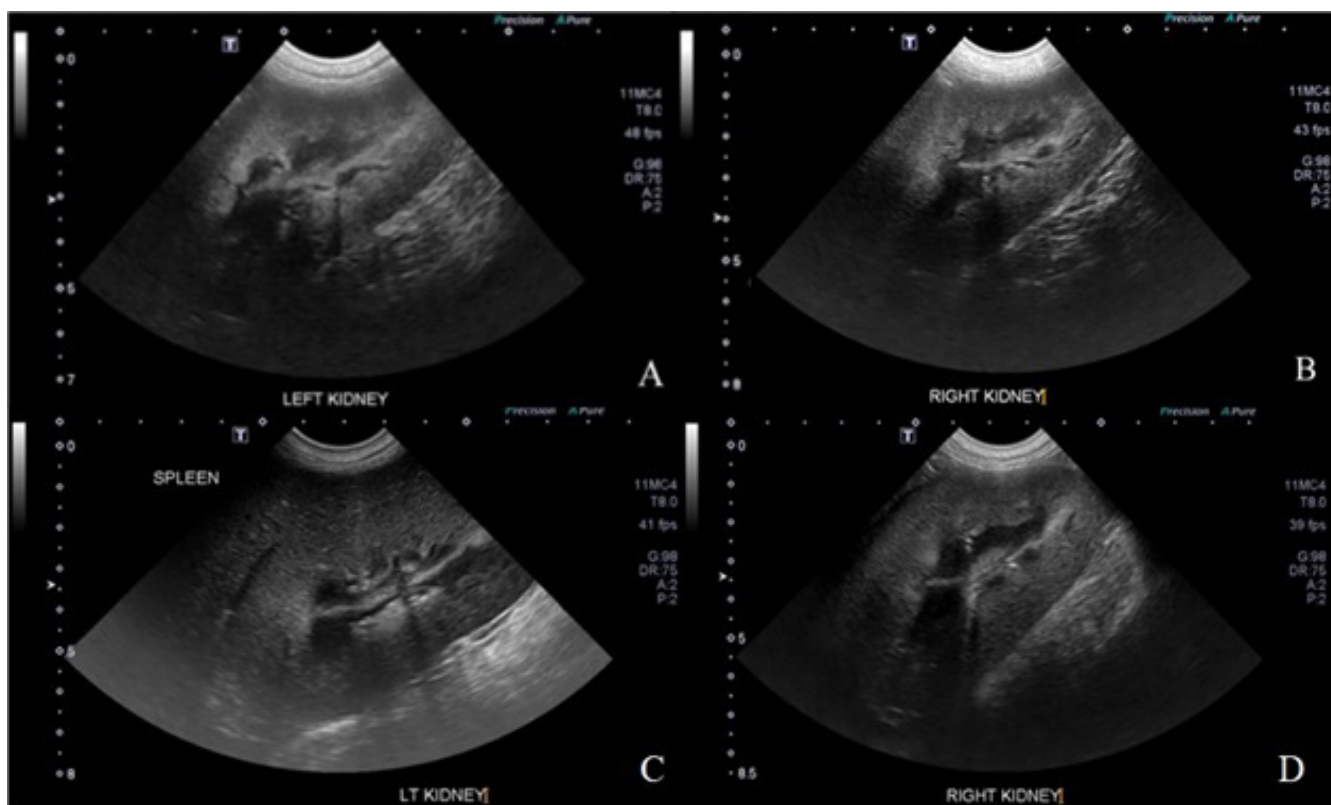
Day	Hematocrit	White blood cells	Platelets	Plasma protein
Reference range*	30-45%	5.5-19 x 10 <sup>3</sup> /μL	200-500 x 10 <sup>3</sup> /μL	5.8-7.8 gm%
0	23	29.88	165	8.0
1	20	27.16	112	6.0
2	16	21.13	118	6.2
4	15	19.22	164	6.0
6	17	23.41	265	6.0
8	19	26.17	450	6.4
10	16	29.16	597	6.0
12	20	30.47	582	6.2
14	21	28.65	476	6.0
18	24	16.10	267	6.2
29	33	12.00	653	N/A
51	37	17.00	350	8.0
81	38	7.00	324	N/A

**Table 3** Urinalysis of a dog with anuric acute kidney injury before peritoneal dialysis (Day 0 and Day 1) and during peritoneal dialysis treatment (Day 11).

Day of collection	Appearance	Sp. Gr.*	pH	Urine strip findings	Microscopic finding
Day 0	Yellow, cloudy	1.010	8.0	Rbc* 2+ Protein 2+	Rbc >300 cells/hpf* Bacteria 1+ CaOx* monohydrate 2+ CaOx dihydrate 1+
Day 1	Red, cloudy	1.018	9.0	Rbc 1+ Protein 1+	Rbc >500 cells/hpf
Day 14	Colorless	1.012	6.0	Rbc 1+ Protein 1+ Glucose 1+	Rbc 10 cells/hpf CaOx monohydrate 2+ CaOx dihydrate 1+

\*Sp. Gr.: Specific gravity, Rbc: Red blood cell, hpf: high power field, CaOX: Calcium Oxalate.  
Reference ranges of parameters analyzed by ZOETIS VETSCAN UA Urine Analyzer,

Abdominal ultrasound (Xario 100MX, Canon Medical System Japan), was performed in the dorsal recumbency position via the ventrolateral approach to further assess the degree of the damage to the kidneys. The size of both kidneys were still within normal limits. However, hyperechogenicity of the renal cortex and medulla were observed, as well as poor corticomedullary junction (CMJ) distinction (Figure 1). The findings could be interpreted as interstitial and glomerulonephritis, acute tubular nephrosis or necrosis, or end-stage renal disease (Adams et al., 1991; Barr et al., 1989; Eubig et al., 2005; and Forrest et al., 1998).



**Figure 1** Longitudinal ultrasound images of the left kidney (A) and the right kidney (B) in a dog with anuric acute kidney injury (AKI) caused by Russell’s viper envenomation before peritoneal dialysis therapy. Ultrasound images of the left kidney (C) and the right kidney (D) in a dog with anuric acute kidney injury caused by Russell’s viper envenomation 3 weeks after peritoneal dialysis therapy

After the initial assessment of the patient, the dog was hospitalized. The urine output (UOP) was initially monitored hourly revealing anuria (Table 4). UOP monitoring was then reduced to every 4 hrs until the patient was discharged. When combining the patient’s history, clinical signs, laboratory test results, ultrasound findings and UOP monitoring, AKI was diagnosed.

**Table 4** Average daily urine output (UOP) of a dog with anuric acute kidney injury before peritoneal dialysis (PD; Day 0), during PD therapy (Day 1-17), and after the PD ended (Day 18-20).

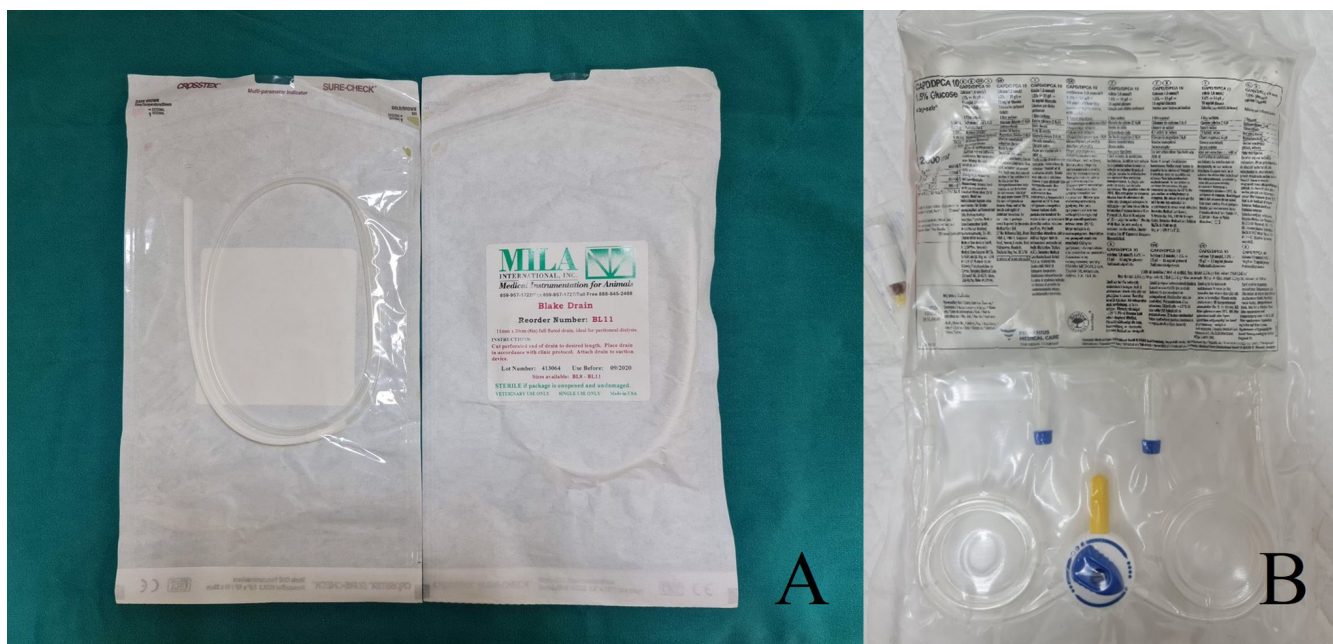
Day	0	1	2	3	4	6	7	8	10	12	14	16	18	20
UOP (ml/kg/hr)	0.00	0.03	0.10	0.18	0.10	0.10	0.18	0.30	0.58	0.77	1.50	2.70	3.54	4.4



## CASE MANAGEMENT

The patient was treated with intravenous administration of 0.9% normal saline solution (General Hospital Products Public Co., Ltd., Thailand) at a rate of 250 mL/hr to correct hydration within 6 hrs. After rehydration, anuria was observed. As a consequence, a bolus of 2 mg/kg of furosemide (L.B.S. Laboratory Ltd., Thailand) was introduced intravenously to induce diuresis. An hour later, the UOP remained unchanged, so a combined constant rate infusion (CRI) of furosemide at a rate of 0.5 mg/kg/hr in 0.9% normal saline solution (10 mL/hr) and dopamine (Siam Bheasach Co., Ltd., Thailand) at 3 µg/kg/min in 5% dextrose and 0.45% sodium chloride solution (20 mL/hr) were introduced through 2 separate intravenous (IV) lines. Despite several attempts, anuria and hyperkalemia persisted. Subsequently, regular insulin (Biocon Limited, India) was given at 0.25 unit/kg IV as a bolus followed by 2 g of 25% glucose per unit of insulin (A.N.B. Laboratories Co., Ltd., Thailand) IV. Thereafter, PD was instigated to reverse the anuria and hyperkalemia condition.

As a part of the PD procedure, 11 Fr Blake drain (MILA International, Inc., Florence, KY, USA) (Figure 2) was placed in the abdominal cavity while the patient was under general anesthesia and positioned in dorsal recumbency. A catheter was inserted by utilizing the aseptic technique to prevent catheter-related infections. Partial omentectomy was also performed to prevent complications of omental wrapping. In addition, an esophagostomy tube placement was also performed on the patient to ensure that daily energy requirement is met under anorexia condition. The patient was strictly kept on a prescriptive diet throughout the treatment.



**Figure 2** 11 Fr Blake drain (A) and dialysate solution containing 1.5% of glucose (B) used during the peritoneal dialysis.

During the first 24 hrs, only one-half of 30 mL/kg of commercial dialysate solution containing 1.5% of glucose (Fresenius Medical Care, Bangkok, Thailand) was instilled during each cycle by gravity into the peritoneum and was allowed to dwell for 40 mins (Figure 2B). In the meantime, the patient was monitored for dialysate leakage, abdominal distension, respiratory rate and abnormalities. As none of the mentioned complications were observed the dialysate volume was increased to 30 mL/kg per cycle on day 2 and the volume was continuously given until the end of the PD procedure. At the beginning of the initial cycle, 500 U/L of heparin (GLAND PHARMA Ltd., India) was added to the solution to prevent fibrin occlusion of the catheter. Over the initial 48 hrs, the dialysis was performed hourly (Figure 3), after which it was then reduced to every 1-2 hrs (Table 5). As the patient's degree of azotemia, urine output, and electrolyte disturbances gradually improved, the frequency of exchanges was further reduced to every 3-6 hrs which extended the length of dialysate's dwell time. Effluent volume, color, and turbidity of the drainage fluid from each cycle was recorded. The patient's body weight, temperature, hydration status, and blood pressure were also monitored daily. The patient remained normotensive throughout its hospitalization.

**Table 5** Sensitivity to different antibiotics of *E.coli* isolated from abdominal fluid sample sent on Day 5 after peritoneal catheter placement in a dog with anuric acute kidney injury.

Sensitivity*	Antibiotic
Sensitive	Gentamicin, Imipenem, Meropenem
Intermediate	Azithromycin
Resistance	Amoxicillin, Amoxicillin-clavulanic acid, Cefixime, Ceftiofur, Ceftriaxone, Cephalexin, Cephazolin, Ciprofloxacin, Clindamycin, Doxycycline, Enrofloxacin, Erythromycin, Metronidazole, Marbofloxacin, Norfloxacin, Sulfa-trimethoprim

\*According to disc diffusion clear zone diameter interpretative standards for *E. coli* ATCC 825922

On Day 2, a sample of the drained dialysate was sent for bacterial culture revealing no bacterial growth after incubation. Five days after initiating PD, the drainage fluid turned turbid and the patient developed a fever, so a sample was sent for another bacterial culture and cells count. The test came back positive, and the fluid's white blood cells count was greater than 100/ $\mu$ L, thus suggesting peritonitis. Bacterial culture revealed *E. coli* with sensitivity to meropenem, trimethoprim/sulfamethoxazole and gentamicin. Consequently, reduced dosage of 24 mg/kg meropenem was given q24h IV for 14 days (M&H Manufacturing Co., Ltd., Thailand) and reduced dosage of 30 mg/kg trimethoprim/sulfamethoxazole (Siam Bheasach Co., Ltd., Thailand) was administered q12h PO for 14 days. Due to AKI, the dosages of the antimicrobial were adjusted according to the following formula:

$$\text{Reduced dosage} = \text{normal dosage} \times \left( \frac{\text{normal serum creatinine}}{\text{patient serum creatinine}} \right)$$

Reduced dosage of the antimicrobial drugs used on the patient varied daily, depending on creatinine level from blood collected each day. Moreover, an intermittent dosage of 0.6 mg/kg of gentamicin (T.P. Drug Laboratories Co., Ltd., Thailand) was given by intraperitoneal route (IP) once daily, during each day's last dialysis cycle. Three days after the combined antimicrobial therapy, a sample was again collected revealing no bacterial growth. Therefore, intraperitoneal gentamycin was discontinued.

While undergoing PD therapy, the patient developed hypokalemia on day 8 and 10 and developed hypoalbuminemia on day 8, 11, and 15 (Table 1). The conditions were corrected before resuming the next cycle of dialysis.

After a week of the PD treatment, a gradual increase in the UOP volume was observed. Fourteen days after the PD was instigated, the anuria condition was finally resolved. At the end of the last cycle, the serum BUN level decreased to 38.2 mg/dL, creatinine to 4.35 mg/dL, and phosphorus to 4.5 mg/dL. The serum potassium level returned to normal from 7.8 mEq/L to 4.09 mEq/L. Three days later, the PD catheter was removed, and abdominal ultrasound was repeated. Both kidneys appeared less hyperechoic compared to the last examination, but the poor CMJ distinction still remained suggesting that the lesion had become chronic (Figure 1C and 1D). After being discharged on Day 21, the patient was kept on a prescriptive diet, and subcutaneous fluid was continuously administered to the patient at a veterinary clinic. Day 29 after initiating the PD although both the patient's serum blood urea nitrogen level and creatinine levels returned to within normal limits, but chronic kidney disease (CKD) was diagnosed in this patient.

## DISCUSSION

This is the first report on PD in the management of Russell's viper envenomation induced AKI in a dog. In the study, PD was imperative in stabilizing the snake bitten dog patient with AKI because medical therapy alone did not reduce the severity of azotemia. On the contrary, the azotemia became worse despite aggressive fluid therapy and raised the necessity of a more invasive therapy to induce diuresis. The PD utilized the peritoneum as a semipermeable membrane to move the solutes and water between the blood within the peritoneal capillary and the dialysate infused into the peritoneal cavity. This procedure helped maintain the electrolytes and acid-base homeostasis, while allowing time for the recovery of the renal tubular function and the restoration of the normal UOP volume.

The first indication for PD in dogs and cats is anuric AKI refractory to fluid therapy. PD may also be indicated in non-anuric patients with severe acute uremia, in which the BUN level exceeds 100 mg/dL, or the creatinine level exceeds 10 mg/dL, or when the electrolyte and acid-base disturbances cannot be managed with medical therapy (Cowgill, 1995). The International Renal Interest Society (IRIS) created the AKI grading scale (I-V) as well as subgrade for dogs and cats based on the level of fasting blood creatinine, UOP and the need for RRT (Segev et al., 2016). In presenting severe azotemia (creatinine >10 mg/dL), anuria, and requiring RRT since medication was rendered ineffective, this patient's condition was classified as AKI grade V.

The concentration of dextrose in the dialysate defined the osmotic gradient intensity and rate of movement of fluid in the peritoneal cavity (Garcia-Lacaze et al., 2002). The concentration of dextrose in the dialysate solutions ranged from 1.5% to 4.5%. In patients with a normal hydration status (as in this case), a 1.5% dialysate solution was recommended. However, in patients with fluid overload or high serum osmolality, 2.5% or 4.5% of dialysate solution should be considered instead. The dialysate bag and line should be



warmed to 38°C to 39°C by heating pads or PD fluid warmers to enhance the permeability of the peritoneum and to increase the patient's comfort during the procedure (Cowgill, 1995). In this case, none was used because of the limitation of equipment.

When the peritoneal dialysis catheter is placed, it should be connected to a closed collection system and carefully bandaged with dry sterile dressings. At the end of each respective cycle, a disinfection cap (Fresenius Medical Care, Bangkok, Thailand) was placed for disinfection.

In addition, there was no consensus in the literature that designated the most appropriate RRT in cases of AKI. In humans, PD is still the main therapy used in patients with AKI and CKD in many countries (Gabriel et al., 2008). Compared to other forms of RRT; for instance, hemodialysis (HD) which requires a dialysis machine, PD seems relatively less complicated. HD also requires high user expertise and may increase a risk of electrolyte imbalances. However, the eradication of toxins occur more slowly in PD when compared to HD (Gallatin et al., 2005).

The pathogenesis of Russell's viper envenomation induced AKI is not yet well understood. AKI may occur from direct nephrotoxicity of the venom which induces acute tubular necrosis. It may also occur secondary to hypotension, intravascular hemolytic anemia, or disseminated intravascular coagulation (DIC) caused by the venom. This patient shown hemolytic anemia, hematuria and thrombocytopenia with prolonged aPTT, indicating DIC. Therefore, DIC may have contributed to AKI following Russell's viper snakebite.

The patient received a fresh whole blood transfusion on Day 1 of the PD procedure. However, its HCT level dropped from 20% to 16% the next day. Possible explanations from most likely to least likely includes failure of the kidneys to produce sufficient quantities of erythropoietin; Russell's snake envenomation induced intravascular hemolytic anemia; inflammation of the kidneys from AKI; a complication of the patient receiving PD; and shortened survival of red blood cells from uremic toxins.

In previous studies, low dose dopamine therapy has been suggested as a treatment of oliguric and anuric conditions in dogs. However, recent studies have shown that the use of dopamine does not decrease morbidity and mortality in humans with these conditions. Consequently, it is no longer recommended for treatment of anuria in humans. Similar to humans, when administered low dose dopamine of 1 µg/kg/min IV by CRI in dog, increase in diuresis and GFR could not be achieved (Srirattanaprteep et al., 2018). Nevertheless, the effect of higher doses of dopamine in improving oliguric and anuric conditions still need further investigation.

The complications of PD include catheter obstruction by fibrous adhesions, fibrin or blood clots; omental wrapping, dialysate leakage; hypoalbuminemia from protein loss via dialysate; electrolyte imbalance such as hypokalemia; catheter exit-site infections; and peritonitis (Gabriel et al., 2008). Complications observed during the PD in this case included hypoalbuminemia, hypokalemia, and peritonitis.

Peritonitis was reported as a complication of the PD at a rate of 22% (Crisp et al., 1989). The common source of peritonitis was contamination of the bag spike or tubing. In this case, the authors hypothesized that peritonitis occurred from urine contamination. To confirm this, a sample of peritoneal

lavage and urine were collected for bacterial culture. Both were positive with *E. coli* with the same antibiotics' sensitivity proving that it was urine contamination as predicted.

After initiating PD, when the drainage fluid turned turbid and the patient developed a fever, a sample was collected for another bacterial culture and drug sensitivity test and meropenem was instantly administered while waiting for the drug sensitivity test result. Even so, WBC count increased, and as the bacteria cultured from the sample was sensitive to trimethoprim/sulfamethoxazole, the antimicrobial was later introduced. WBC level was re-evaluated 2 days later revealing that WBC level was still rising, thus, the authors chose to combine gentamicin with the other 2 drugs but through IP administrative route.

Unlike in humans, estimation of the dose fraction (Kf) based on the serum creatinine value in order to define the glomerular filtration rate (GFR) under a renal-impaired condition for dosage regimen adjustment in dogs was contraindicated (Lefebvre, 2002). This was due to the fact that there was no single linear relationship between the serum creatinine concentration and GFR. Hence, only the serum creatinine level was used in the dosage adjustment in this case.

As an alternative, antibiotics could be administered via the IP route as either a continuous or intermittent dosing depending on the type of the chosen antibiotic (Low et al., 1996). In intermittent dosing, the antibiotic containing dialysate must be allowed to dwell within the peritoneal cavity for at least 6 hrs to allow adequate absorption. IP antibiotics should be added after the medical port has been disinfected with povidone iodine 5 minutes prior to insertion of the needle (Tosukhowong et al., 2001).

When gentamicin is administered through the IP route, it can be directly absorbed into the systemic circulation especially in case of peritonitis in PD patients where the permeability of the peritoneal membrane is altered allowing increased drug absorption through the peritoneum. Although gentamicin is one of the leading causes of drug induced nephrotoxicity, when given in patients undergoing PD therapy, it will not only be eliminated from the blood prominently by glomerular filtration but also through the PD channel, subsequently minimizing systemic absorption and potential toxicity to the nephrons. Furthermore, Varghese et al. reported that reducing IP gentamicin dwelling time to 3 hrs yields the same amount of drug absorption and minimum inhibitory concentration into the systemic circulation as the recommended 6 hrs duration and it also minimizes the known drug's side effects.

Since its first presentation, the patient had decreased body condition score, pale pink mucous membrane, inappropriate urine concentration despite its dehydrated condition and poor distinction of corticomedullary region from ultrasound. Hence, there is a possibility that the patient might have CKD from the start. Without the patient's prior background blood profile, it is hard to determine whether the patient had AKI on top of CKD or AKI which later progressed into CKD.

In conclusion, this case provides information for veterinarians and specialists on PD procedure for management of AKI. Nowadays, despite its benefits, PD is still rarely opted in case of AKI refractory to conventional therapy. Unlike HD, PD does not require a dialysis machine and is a less

expensive option. Therefore, with sufficient knowledge on PD procedure, it can actually be performed in any veterinary practice. In this report, PD was shown to be effective in managing AKI secondary to Russell's viper envenomation. However, PD protocol used in this case can also be implemented in the management of intoxication, metabolic abnormalities, or severe temperature extremes.

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## AUTHOR CONTRIBUTIONS

The dog patient in this case was first presented to P.T. After realizing that the patient was not responding to medical treatment, P.T. offered the option of peritoneal dialysis (PD) to the dog owner, who later gave consent on performing the procedure. Consequently, P.T. conceived the idea of reporting the procedure protocol and findings in this case.

S.C. assisted P.T. in the diagnosis of this patient via abdominal ultrasound. Both the authors then decided to collaborate together. From that point on, both P.T. and S.C. equally contributed on this case report–research; protocol drafting; patient care and monitoring; and writing the manuscript until it reached completion.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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