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Case Report: Chronic Kidney Failure in Local Dog

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Abstract. Chronic kidney failure is defined as a progressive kidney disease that has been going on for several months to years, whereas kidney tissues have lost their function irreversibly. The disease affects dogs of all ages but is more common in older dogs. A Female local dog-weighed 9 kg was examined with complaints of seizures, lethargy, drinking much water, and lost appetite for the past 2 weeks. Clinical examination showed abnormalities in circulation, respiration, and pale mucosal membrane. Complete blood check and biochemistry check then carried out with result showing anemia and significant elevation on BUN (>112 mg/dL) and creatinine (11.2 mg/dL). An ultrasonography examination was about to be carried out but the animal seized again and decided to be carried out when the dog was more stable. With a history of urine incontinence and polydipsia, along with the clinical signs, CBC, and biochemistry blood test, the animal was diagnosed with chronic kidney failure. Diazepam (IV: 0,5 mg/kg BW) and intravenous fluid therapy with RL of 2280 mL/day. After 38 hours of treatment, the dog experienced another seizure and died.

Keywords: dog, chronic kidney failure, chronic kidney disease

I. INTRODUCTION

The primary function of the urinary system is to excrete metabolism products, maintain an extracellular environment with water and electrolyte conservation and excretion, production of erythropoietin hormone for hematopoiesis, production of renin hormone that regulates blood pressure and sodium reabsorption, and metabolize vitamin D to its active form, 1,25-dihydroxycholecalciferol [13].

Many abnormalities of the urinary system can be diagnosed from signalment, history, physical examination, hematology and biochemistry serum check, urinalysis, and urinary bacterial culture. A complete history of water consumption habits, urinating frequency and volume, and the animal's behavior. Information regarding the history of medication, the animal's appetite and feeding, also any weight changes are important to be taken into consideration in

diagnosing urinary system disease Physical examination should cover palpation of vesica urinary and genitalia external. Diagnostic examinations such as a complete blood check, blood pressure check, abdomen radiography and/or ultrasonography, and contrast of the lower and upper urinary tract could reveal important information [13].

Chronic kidney failure is defined as a progressive kidney disease that has been going on for several months (>3 mo) to years, whereas kidney tissue losses its function [4, 11]. The damage could occur in every part of the nephron, including the glomerulus, renal tubules, interstitial tissue, or blood vessels, which could cause irreversible damage and the nephron's loss of function leading to a decrease in glomerulus filtration rate (GFR) causing decrease of creatinine serum clearance, increase of phosphate serum, and decrease of calcium serum (O'Neill *et al.*, 2013). These unused products are toxic and accumulate in the bloodstream resulting in azotemia which then becomes uremia. The accumulation of these toxic substances will manifest in clinical symptoms that will appear after 75% of the kidney nephrons are not functioning [12]. *Chronic Renal Disease* (CRD), *Chronic Kidney Disease* (CKD), dan *Chronic Renal Insufficiency* (CRI) refer to the same condition [16].

Clinical and pathological signs in dogs with chronic renal failure depend on the severity (stage), duration, and progressive degree of kidney disease and the presence or absence of co-morbidities. Clinical symptoms that can be observed are anorexia, depression, lethargy, weight loss, halitosis, nausea, vomiting, polyuria, and polydipsia accompanied by pale mucous membranes, dehydration, stomatitis, oral ulceration, dull and dry hair, poor body condition score (BCS). These things can be observed in clinical examination [3].

Meanwhile, a common cause of kidney failure in dogs is an acute kidney disease that progresses to pyelonephritis, glomerulonephritis, nephrolithiasis, and ureterolithiasis. The underlying cause can be from specific diseases, such as Fanconi syndrome, Lyme disease in dogs, renal amyloidosis, renal dysplasia, renal lymphoma, or blood parasites such as canine babesiosis and canine monocytic ehrlichiosis (CME) (Hall et al., 2014; Sharma et al. al., 2016; Tufani, 2019). Predisposing factors for kidney failure in dogs include age, breed, diet, and periodontal disease (O'Neill, 2013).

Diagnosis in dogs requires consideration of evidence from a variety of sources, including renal function tests such as blood urea nitrogen (BUN), serum creatinine,

serum electrolyte concentration and acid-base status, blood pressure, urinalysis, and renal radiography. Dogs with kidney failure can be categorized according to guidelines issued by the International Renal Interest Society (IRIS) and these guidelines have been accepted by the American and European Societies of Veterinary Nephrology and Urology. The category is divided into four stages based on kidney function, proteinuria, and blood pressure [14].

In this case, the case dog experienced clinical and historical symptoms and the results of blood tests matched those of chronic kidney failure. Clinical signs that point to the possibility of chronic renal failure are the findings of typical uremic halitosis on clinical examination. The purpose of writing this article is to diagnose chronic kidney failure in dogs and the necessary treatment for this condition.

II. CASE DESCRIPTION

Signalment and Anamnesa. The case animal was a female local dog, +- 6 years old, sterile, weighing 9 kg, black-haired with a white pattern on the chest and feet. The case dog reported losing appetite since December 2020. Owners thought it was because the case dog was left out of town for several months and experienced weight loss on February 2021. On May 2021, the case dog experienced a seizure and loss consciousness for several minutes after.

It is noted that the case dog had a behavior of drinking lots of water and experienced urine incontinence in early 2020. Complete vaccination (DHPPi-LR: Distemper, Hepatitis, Parvovirus, Parainfluenza< Leptospira, dan Rabies) was given annually along with anthelmintic. The case dog lived inside the house and was given kibble with chicken back or chicken liver. After the seizure case, the dog was then rushed to Udayana University Veterinary Teaching Hospital and a physical examination along with a complete blood check then carried out with the result listed in Tables 1, 2, and 3.

Physical Examination. It was noticed that the dog seemed lethargic, apathetic, and tamed. Results showed abnormality in the respiration system for respiration frequency increased (tachypnoea), pale mucosal membrane on conjunctiva and gum, and skin turgor increased. Pulsus and heart rate normal, temperature slightly decreased but still within normal range.

Clinical Examination. The case dog was rushed to Udayana University Veterinary Teaching Hospital on 03 May 2021. Data

obtained from the examination showed abnormality in musculoskeletal, circulation,

Table 1. Physical Examination Result

No.	Examination	Result	Range *)	Description
1	Heart Rate (x/min)	88	60 – 140	Normal
2	Pulse (x/min)	92	60 – 140	Normal
3	CRT (seconds)	>2 sec	< 2 sec	Decreased
4	Respiration (x/min)	40	10 – 30	Increased
5	Temperature (°C)	37,8	38,0 – 39,1	Normal
6	Turgor	>2 sec		Decreased
7	Mucosal Membrane	Pale	Pink Pale	Abnormal

respiration, urogenital, and gastrointestinal, along with mucosal and lymph nodes. Crust and dandruff are found in the integumentary system but no tick or other external parasite. Tachypnoea found but breath sounds normal. Other clinical signs from the oral cavity were noticed such as halitosis with typical uremic odor, nausea, and vomitus that occurred after wet food hand-feeding, but the dog react well to drinking. The mucosal membrane was pale, especially on the eye's conjunctiva and gum. Capillary refill time (CRT) was over two seconds whereas heart rate and pulse were normal. Dog's caudal extremities were weak and stiff, but given pulling force reflected well, proving the nerve was good. Eye discharge and changes in lymph node consistency were also observed during a clinical examination. According to the owner, the case dog also had a history of urinary incontinence. The results of the clinical examination are listed in Table 2.

Table 2. Clinical Examination Result

No	Examination	Description
1	Integumentary	Abnormal
2	Musculoskeletal	Abnormal
3	Nerve	Normal
4	Circulation	Abnormal
5	Respiration	Abnormal
6	Urogenital	Abnormal
7	Digestive	Abnormal
8	Mucosal	Abnormal
9	Lymph Nodes	Abnormal
10	Eyes	Abnormal

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Laboratory Exanimation. Blood samples drew from the vena cephalic and collected in an EDTA tube then tested for a complete blood check using Haematology Analyzer and biochemistry serum using Idexx Laboratories with results listed in Tables 3 and 4.

A complete blood check showed Anaemia and lymphocytosis. Meanwhile, biochemistry serum showed a significant elevation of blood urea nitrogen (BUN), creatinine serum, globulin, and alkaline phosphate according to the International Renal Interest Society (IRIS) (Table 5), the case dog is considered to be in Stage 4 (end-stage). Total protein, albumin, and ALT were within the normal range. Supporting diagnostic approach, such as ultrasonography, was about to be carried out, but then the case dog experienced another seizure and it was decided to be carried out later when the dog had a more stable condition. After 38 hours of treatment, the case dog experienced another seizure and died, making USG fail to be carried out.

Table 2. Complete Blood Check Result

Hematology	Unit	Result	Range	Description
WBC	$x10^9/L$	9.1	6.0 – 17,0	Normal
Lymph#	$x10^9/L$	6.1	1.0 – 4.8	Increased
Grand#	$x10^9/L$	1.6	4.0 – 12.6	Decreased
Lymph%	%	66.8	12,0 – 30,0	Increased
Grand%	%	17.3	60,0 – 83,0	Decreased
RBC	$X10^{12}/L$	2.93	5.5 – 8.5	Decreased
HB	g/dL	7.1	12,0 – 18,0	Decreased
MCV	fL	55.2	60,0 – 77,0	Decreased
MCH	pg	24.3	14,0 – 25,0	Normal
MCHC	g/dL	43.9	32.0 – 36. 0	Increased
HCT	%	16.2	37.0 – 55.0	Decreased
PLT	$x10^9/L$	43	170 – 400	Decreased

Table 3. Biochemistry Serum Result

Test	Unit	Result	Range	Description
Glucose	mg/dL	133	74 – 143	
Creatinine	mg/dL	11.2	0.5 – 1.8	H
BUN	mg/dL	>120	7 – 27	H
TP	g/dL	7.9	5.2 – 8.2	
Albumin	g/dL	2.5	2.3 – 4.0	
GLOB	g/dL	5.4	2.5 – 4.5	H
ALB/GLOB		0,5		
ALT	U/L	35	10 – 125	
ALKP	U/L	551	23 – 212	H

Table 4. CRF Stages in Dogs and Cats According to Renal Interest Society (IRIS)

Stage	Creatinine Serum (mg/dL or µmol/L)	
	Dogs	Cats
Stadium 1	<1,4/<125	<1,6/<140
Stadium 2	1,4-2,0/125-179	1,6-2,8/140-249
Stadium 3	2,1-5,0/180-439	2,9-5,0/250-439
Stadium 4 (*end-stage*)	>5,0/>440	>5.0/>440

Diagnosis and Prognosis. Case dog diagnosed with chronic kidney failure stage 4 with prognosis infausta based on clinical signs, anamneses, CBC, and biochemistry serum.

Therapy. Diazepam at a dose of 0,5 mg/kg BB via IV was given to treat a seizure. Intra-vena fluid therapy with ringer lactated was also given to rehydrate and flush. With an estimation of dehydration degree of 12%, 2280 mL/day of RL was given. After being given treatment, the case dog showed a good response and started eating again, but after the owner left the hospital, the case dog lose appetite again and showed aggressive behavior. After 38 hours of treatment, the case dog died after experiencing another seizure.

III. DISCUSSION

Chronic renal failure (CRF) is defined as progressive kidney disease that has been going on for months (> 3mo) to years, whereas kidney tissue losses its function. [4, 13]. *Chronic Renal Disease* (CRD), *chronic kidney disease*, dan *Chronic Renal Insufficiency* refer to the same condition [16].

Cause of this condition is not one single disease but is caused by several causes, including congenital malformations of the kidneys (birth defects), chronic bacterial infections with or without kidney stones (pyelonephritis), high blood pressure (hypertension), and diseases related to the immune system, such as lupus and glomerulonephritis, or acute kidney injury such as poisoning (plants or heavy metal) that causes kidney damage [16]. In young animals, it is usually caused by congenital or genetic factors, meanwhile, in older animals, it is usually acquired. As a result, the kidney is unable to perform its function such as excretion of metabolic waste, fluid, acid-base, electrolyte hemostasis, and endocrine system [10]. In mentioned condition, the kidney will do compensation for the remaining healthy nephrons, leading to more nephron damage progressively, which is the character of CRF.

With a 7% prevalence in a dog, CRF is common in small animals. It can occur at any age but is most common in older dogs. Dogs with CRF showed symptoms of anemia, low Body Condition Score (BCS), proteinuria, hypertension, hypoalbuminemia, and the International Renal Interest Society (IRIS) stage [4]. There are 4 stages of IRIS used for animals diagnosed with CRF, where stage 1 is a condition where the kidneys are damaged but clinical symptoms and azotemia have not been seen, in general, kidney disease is very rarely detected at this stage. At stage 2, the disease has progressed, Glomerulus Filtration Rate (GFR) is <25% of normal, and azotemia is detected, but clinical symptoms have not been seen. However, at this stage, it may be associated with increased urine volume and impaired urine concentration. Stage 3 is characterized by the occurrence of azotemia, decreased GFR, and clinical signs that have been seen. Stage 4 shows more progress in azotemia and clinical symptoms [13]. Clinical observations in the early stages of CRF are generally not visible, but renal damage is already present. Kidney function in dogs with CRF usually remains stable or declines slowly over months or years, unless kidney injury or damage persists or progresses due to other disease-specific factors [14].

There are many causes involved in the pathogenesis of acquired CRF, including glomerular disease, infectious diseases (Leptospirosis, Lyme nephritis, Candidiasis, Blastomycosis, Leishmaniasis), metabolic disorders, recurrent ischemic events, nephrotoxicity, neoplasia, history of acute kidney injury (AKI) or urinary obstruction, but often, the exact etiology is unknown at

presentation and remains unidentified throughout the disease [4,10]. Due to the limited diagnostic limits, CRF is often only diagnosed in the later stages, when the impaired renal function has exceeded the compensatory mechanism and is irreversible, where severe renal parenchymal damage has occurred [4].

Based on medical records and anamnesis, the case dog had a history of polydipsia, low appetite, and weight loss, along with urinary incontinence. Physical examination showed slowed skin turgor, pale mucosal membrane, lethargy, uremic halitosis with vomitus, and nausea. Urogenital palpation showed kidney shrinking but this should be confirmed with a diagnostic image. The key finding, in this case, was the presence of uremic halitosis along with the owner's anamnesis that case dog had a history of urinary incontinence. Therefore, the examination then continued with routine hematological and biochemical serum examinations. According to Saini (2017), anorexia, vomitus, and polyuria are found in 70% of cases of kidney diseases.

The kidney's main function is to excrete metabolic waste, maintain an extracellular environment with water and electrolyte excretion and conservation, production of erythropoietin hormone for hematopoiesis, production of renin enzymes that regulates blood pressure and sodium absorption, as well as converting vitamin D to its active form, 1,25-dihydroxycholecalciferol [13]. Kidneys with damaged nephrons cannot perform these functions resulting in nonregenerative anemia, and increased levels of metabolic waste products in the blood such as urea and creatinine, resulting in clinical symptoms such as polyuria and polydipsia, and hypertension. Lefebvre and Watson (2002) explained that the clinical symptoms of anorexia and nausea that occurred in CRF animals were caused by increased levels of gastrin in the blood due to reduced gastrin catabolism by the kidneys, a condition known as uremic gastropathy. Gastrointestinal complications of CRF are the typical uremic syndrome in end-stage CRF [9]. These include decreased appetite and reduced feed intake, nausea, vomiting, ulcerative stomatitis/necrosis along halitosis which are the most common clinical signs in dogs with stage 4 (end-stage) CRF due to renal azotemia or very high serum BUN and creatinine levels high [14].

In the case of CRF, the inability of the distal tubules and/or collectives ducts to respond to vasopressin causes the decrease of permeability of the distal tubules and collectives ducts to water, resulting

reabsorption process of water decreases. Under these conditions, the hypotonic fluid that passes through the proximal loop of Henle into the distal tubule and collecting duct of the kidney remains hypotonic, therefore, a large volume of diluted urine causes polyuria (Elliot et al., 2017). This is then compensated by polydipsia.

A complete blood check showed low RBC (2.93 $x10^{12}$/L), Hb (7.1 g/dL), HCT (16.2 %), and PLT (43 $x10^{9}$/L) that portrays anemia. Pathogenesis of anemia in a dog with CRF stages 3 and 4 is complex and multifactorial, however, the main cause is the decreased levels of the erythropoietin hormone which stimulates the formation of erythrocytes in the bone marrow. Erythropoietin is produced mainly in the peritubular interstitial cells of the inner renal cortex and outer renal medulla (Maiese et al., 2008). Case dog had a PCV rate of 16.2% which according to McGrotty (2014), is non-regenerative anemia or severe anemia which can be seen from PCV levels below 20%, where the bone marrow cannot perform hematopoiesis due to reduced or even absent of erythropoietin.

The results of the blood chemistry of the case dog showed BUN and creatinine were severely above the normal range, with these results it could be concluded that the dog had impaired kidney function which matched the clinical signs of halitosis that occurred in the oral cavity during a clinical examination. Dunaevich et al. (2020) reported that dogs with CRF have anemia (hematocrit <37.1%), low RBC, and significant increases in urea, creatinine, and phosphate values. Based on the levels of BUN and creatinine in the dog's blood, it was categorized into CRF stage 4 according to IRIS (Table 5). According to McGrotty (2014), plasma creatinine and urea levels are usually used as biochemical markers of kidney disease. Creatinine is eliminated from the body by glomerular filtration, a decrease in the glomerular filtration rate (GFR) will cause the accumulation of creatinine in the blood. The relationship between plasma creatinine concentration and GFR is exponential, which means that GFR is likely to have decreased significantly before plasma creatinine exceeds the upper limit of normal [5].

Hamed et al. (2020) describe that recurrent seizures, including generalized myoclonic and tonic-clonic, are a common uremic complication of the central nervous system and can occur as a manifestation of acute metabolic disorders such as hypocalcemia, hypomagnesemia, hyperphosphatemia, hyperkalemia, acidosis, and renal hyperparathyroidism. In end-stage

CRF, uremic encephalopathy, a condition in which the animal experiences neurological disorders including seizures, is very common. Kidney failure leads to the accumulation of urea toxin which is known to be the cause of neurological complications. Electrolyte disturbances condition in CRF has an important role in the pathophysiology of seizures caused by uremia. Creatinine is thought to have the ability to block GABA receptors and stimulate stimulation of NMDA receptors in the brain which causes calcium inflow to neuron cells. As a result, an imbalance of stimulation and inhibition in the brain occurs [15].

Low levels of calcitriol in the blood cause excessive activation of the renin-angiotensin-aldosterone system due to an increase in vasopressin and sympathetic tone leading to systemic atrial hypertension (systolic >160 mmHg). Generally, this atrial hypertension occurs at stages 2-4 CRF and can cause left ventricular hypertrophy followed by left heart failure. As a result, neurological disorders such as ischemic encephalopathy, seizures, and eye vascular disorders such as hemorrhage and blindness, which end with death occur [1].

The therapy given was diazepam to treat seizures. Benzodiazepines, widely used to treat certain types of seizures, bind to GABAa receptors, increasing its opening frequency, thereby GABA flow increases, and neurons are inhibited. It is metabolized by the liver and excreted by the kidneys, but the metabolic waste products of this drug are so small that in cases of kidney disease, the dose does not need to be changed [15].

Crystalloid fluids such as RL are ionic liquids composed of various ions to mimic the physiology of extracellular fluid [8]. In kidney failure, urea toxin accumulates in the body so the administration of fluids that are two to three times more than the maintenance dose can assist the excretion of urea toxins by increasing urine output. The volume of fluid needed is different in each case, but in general, the volume range that must be given every day is 2.5-6% of the animal's body weight plus the volume of maintenance fluid (Langston, 2009). In the case dog with a calculated dehydration rate of 12%, fluid therapy was given as much as 2280 mL/day to flush and rehydrate.

The case dog died after 38 hours of therapy. According to Nicholls et al. (2021), therapy failure may occur in late-stage cases. The case dog had a seizure, indicating that urea had disrupted the nervous system, which usually occurs in late-stage CRF. Unfortunately, a necropsy was not performed on the case dog because the owner did not

agree. Necropsy results performed on patients with CRF generally show small, pale kidneys with indistinct margins, hardening, and possible calcification [10].

IV. CONCLUSION

The case dog was diagnosed with chronic kidney failure. This is supported by anamnesis, clinical examination, routine hematological examination, and blood chemistry which showed anemia and BUN along with creatinine levels that greatly exceed normal limits. However, it is unfortunate that an ultrasound examination, which can provide a more detailed picture of this condition, cannot be performed. Chronic kidney failure does not show clinical symptoms (asymptomatic) in its early stages so the prognosis of Fausta is difficult to obtain if treatment is carried out at a later stage. Examination in this case should be done carefully and as early as possible after the first symptoms appear.

A complete and thorough veterinary examination is required considering that chronic renal failure generally occurs asymptomatically. Blood pressure checks and ultrasounds will help confirm the diagnosis. For this reason, early diagnosis of CRF in small animals, especially dogs or cats, is required with a new diagnostic approach such as the biomarker symmetry dimethylarginine assay (SDMA) which can detect kidney damage as early as possible.

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