Case Report

Use of PCSO-524® for Supplementary Treatment of Protein Losing Nephropathy in Animals

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Antinol (PCSO-524®)
Case Study Contest 2020

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Abstract

An intact male Shih Tzu dog weighed 5.8 kilograms was referred to Suvarnachad Animal Hospital with signs of polydipsia, polyuria, edema and ascites due to accumulation of fluid in the abdominal cavity.

Biochemical tests found hypoalbuminemia, hyperglobulinemia, hypercholesterolemia, increased urine protein creatinine ratio (UPC) to 5.88 and no signs of inflammation or infection of the urinary tract.

Protein losing nephropathy from glomerular disease was diagnosed based on the biochemical indicators. Medication was given to the dog in order to control kidney damage and minimize the clinical symptoms.

Anti-proteinuric drug, for example ACE inhibitor to reduce blood pressure, was particularly selected for the treatment in conjunction with prednisolone and PCSO-524® as supplementary treatment.

During the 10 months follow up, the dog showed improvement of clinical symptoms, no edema, lack of accumulation of fluid in abdomen cavity, and serum albumin that was increased to normal level.

Keywords: Anti-proteinuric drug, hypoalbuminemia, PCSO-524, protein losing, nephropathy, UPC

Introduction

Protein losing nephropathy is caused by damage of glomerulus and, as a result, excess amount of serum protein leaks from the filtration, especially albumin, and the reabsorption by proximal convoluted tubules is insufficient. The glomerulus and tubule cells are damaged leading to chronic renal failure eventually.

The main etiology of protein losing nephropathy is immune-complex glomerulonephritis, of which influential factors include infection, such as bacterial infection, blood parasite and heart worm infestation, which are common in young to middle age animals and cancer, particularly in senile animals. The second most common etiology of the disease is amyloidosis that is caused by accumulation of **amyloid A protein from chronic inflammation** and usually congenital in Shar-pei dogs. The most accurate diagnostic method is renal biopsy (Vaden, 2016).

Clinical signs of the disease depend on the level of proteinuria and sometimes not specific, for example, loss of body weight and lethargy. If the loss of protein continues to be more than 3.5 grams per day, the symptoms are more specific and called nephrotic syndrome, which include 4 clinical symptoms; proteinuria, hypoalbuminemia, ascites or edema when serum albumin is less than 1.5 mg/dl, and hypercholesterolemia. The proteinuria is indicated by the ratio of urine protein and creatinine higher than 0.5 and classified as glomerular origin when reached 2.0.

More than 80% of dogs with protein losing nephropathy, with or without azotemia, usually show sign of **hypertension**.

Treatment of protein losing nephropathy is consisting of finding and treating underlying causes, restriction from high protein diet, and administration of antiproteinuric drugs, such as ACE inhibitors, angiotensin receptor blockers, and aldosterone receptor blocker. A success in reducing proteinuria, will also retard the deterioration of renal function.

Supplementation with fatty acids in omega-3 group is proved to be effective in humans and animals for prevention of damage to glomerular tubules and delay the progression of **end stage renal disease**. It also works with omega-6 fatty acids to increase glomerular filtration (GFR), decrease cholesterol level with anti-oxidative and anti-inflammatory effects, control hypertension, and reduce protein loss in urine (Broen et al., 2013, Grant and Forrester, 2001 and Grauer, 2005).

Vetz Petz® Antinol® was selected for supplemental therapy in this study since its active ingredient, PCSO-524®, extracted from greenshell mussel (GSM) or green lipped mussel (GLM), Perna canaliculus, from New Zealand, is consisting of more than 90 natural fatty acids. **The essential elements that are effective against inflammation are omega-3 fatty acids, EPA and DHA to be specific**, unsaturated fatty acids from olive oil that are mediator for transportation of PCSO-524® to duodenum and inhibition of the action of gastric enzymes, and vitamin E (tocopherol) that has anti-inflammatory effect (Eason et al., 2018 and Brown et al., 1998).

Case History

A 9 years old, intact male Shih Tzu dog weighed 5.8 kilograms with 7/9 body condition score was admitted to Suwanachad Animal Hospital with history of anorexia, lethargy, polydipsia, polyuria, and abdominal enlargement for 10-14 days. The dog showed no signs of vomiting, diarrhea, and coughing.

Physical examination

Upon examination, the dog was alert with 101 °F body temperature, pink mucous membrane, less than 2 seconds of capillary refilling time.

Normal heart and lung sound, 140 beats per minute heart rate, 30 per minute respiratory rate.

No sign of dehydration, abdominal enlargement, and peripheral edema of both hind limbs, ventral abdomen and scrotal sac (Figure 1A and 1B)

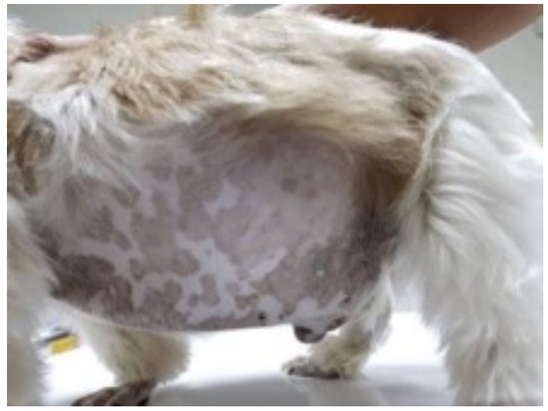

Figure 1A and 1B. The dog with abdominal enlargement and edema

Diagnosis and Results

Laboratory results from complete blood count and serum biochemistry profiles and urinalysis (Table 1A and 1B) revealed hypoalbuminemia, hypercholesterolemia, and above normal level of urine protein creatinine ratio.

Table 1A. Blood chemical and hematological test results

CBC	Normal Value	Results
RBC (106/µl)	5.5-8.5	7.92
Hb (g/dl)	10-20	17.6
PCV (%)	35-57	50
MCV (Fl)	66-77	63.3
MCH (g/dl)	19.9-24.5	22.2
MCHC (g/dl)	31-34	35
TP (g/dl)	6-8	6
WBC (µl)	5,500-17,000	15,470
Neutrophil (µl)	3,000-11,500	13,150
Eosinophil (µl)	100-1,250	154
Lymphocyte (µl)	1,000-4,800	2,165
Monocyte (µl)	150-1,250	-
Platelet (105/µl)	2-5	8.13
Blood parasite	NF	NF
SNAP 4DX	Negative	Negative
Blood chemical Profiles	**Normal Value**	**Results**
SGPT (U/l)	17-78	36
ALP (U/l)	47-254	211
Creatinine (mg/dl)	0.4-1.4	0.6
BUN (mg/dl)	9.2-29.3	20
Albumin (g/dl)	2.6-4.0	1.5
Globulin (g/dl)	1.7-3.8	4.5
Cholesterol (mg/dl)	111-312	>450
Sodium (mEq/l)	141-152	144
Potassium (mEq/l)	3.8-5	4.9
Chloride (mEq/l)	102-117	109
Glucose (mg/dl)	80-180	102

Table 1B. Urinalysis results

Parameters	Results
Transparency	Clear
Specific gravity	1.032
pH	6.5
WBC	Negative
RBC	Negative
Nitrite	Negative
Protein	+3
Glucose	Negative
Urobilinogen	Negative
Bilirubin	Negative
Urine C/S	No Growth
UPC	5.87 (void 24 h)

Abdominal Radiographic findings

Radiographic images in right lateral recumbency (Figure 2A) and dorsal recumbency view (Figure 2B) showed normal sized heart and **the vertebral heart score (VHS) was 10.**

Abdominal Ultrasonographic findings

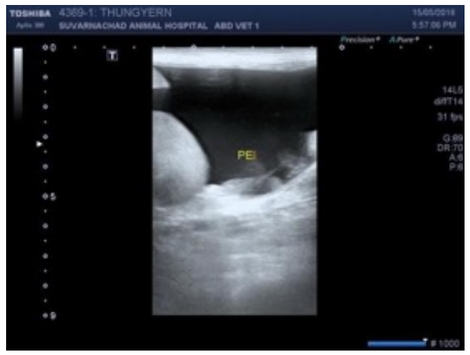

Figure 3. Abdominal Ultrasonography revealed large volume of anechoic peritoneal fluid

Figure 4. Serous fluid from abdominal cavity

Large amount of fluid accumulated in abdominal cavity was found from ultrasonography examination without other signs of abnormalities. (Figure 3)

Examination of ascitic fluid found transudate with protein level less than 0.2 g/dl and 50 cells/µl of red and white blood cells (Figure 4).

The dog was diagnosed with protein losing nephropathy caused by glomerular disease without azotemia.

Treatment

Since the true cause of the disease is unidentified, **supportive therapy** is designed for the treatment. The regular diet was replaced with diet formulated for dogs with kidney disease.

PCSO-524® (Vetz Petz® Antinol®) 1 capsule every 24 hours, and benazepril 0.5 mg/kg were prescribed to reduce urinary loss of protein. Additional medications, clopidogrel to prevent thromboembolism and amino acid to increase serum albumin, were given. Therapeutic paracentesis is employed to reduce ascitic fluid and 2 mg/kg every 24 hours of spironolactone, a diuretic drug, was given.

During the first month of treatment, the dog did not show any improvement since serum albumin was still under 1.5 mg/dl, as a result, signs of edema, ascites, and hypovolemia still persisted. Colloid used for intravenous fluid resuscitation was 17 grams of human serum albumin to maintain cardiovascular volume and blood pressure.

PCSO-524® (Vetz Petz® Antinol®) was increased to 2 capsules every 24 hours and amlodipine was given at 0.5 mg/kg every 24 hours to control hypertension.

To reduce inflammation of glomerulus, prednisolone 0.5 mg/kg every 24 hours was prescribed for 2 weeks, and then tapered off to 0.25 mg/kg every 24 hours and 0.25 mg/kg every 48 hours, respectively.

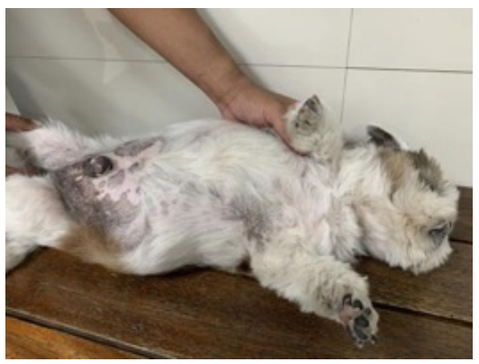

Figure 5. The dog showed no sign of clinical abnormality after 10 months of treatment

Treatment Follow up

Physical examination to evaluate response to the treatment found that clinical signs had improved and the abdominal distension and ascites were disappeared after 3 months of the treatment (Figure 5).

Blood chemistry test showed that serum albumin was more than 2.5 mg/dl after 4 months and urine protein creatinine ratio (UPC) was less than 50% of the starting value after 10 months. There was no increase of creatinine and potassium above the normal level during 10 months follow up (Table 3).

		Month of follow up					
Parameter	**1st visit**	**1**	**2**	**3**	**4**	**6**	**10**
Albumin (g/dl)	1.5	1.4	1.7	2.3	2.7	2.3	2.4
Creatinine (mg/dl)	0.6	0.3	0.3	0.4	0.6	0.4	0.5
K (mEq/l)	4.9	-	4.5	-	-	4	4.8
UPC	5.87	8.7	13	11.9	6	4	2.8

Table 3. Blood chemistry test results prior to and after the treatment

Discussion

Diagnosis of protein losing nephropathy (PLN) is based on evaluation of urine protein creatinine ratio (UPC), which obtained from at least 2-3 sample collections within 24 hours. Continuing loss of protein and UPC greater than 2 indicates the damage of glomerulus.

Glomerular disease is categorized by the severity into 3 stages;
Tier I) Proteinuria is found without hypoalbuminemia or azotemia,
Tier II) Proteinuria is concurrently found with hypoalbuminemia but not azotemia, and **Tier III)** Proteinuria, hypoalbuminemia and azotemia are found.

This study case was in Tier II since the dog showed proteinuria, hypoalbuminemia and without azotemia. The treatment and prognosis is similar to that of chronic kidney disease.

The study case was additionally diagnosed with chronic inflammation from increased number of platelets and the presence of hyperglobulinemia. Standard treatment was employed to reduce protein loss and the damage of glomerular and tubular tissue, prevention of complications associated with glomerulopathy, and delay the progression of end-stage renal failure.

Renal diet is considered a high quality, reduced protein content diet formulation is used to maintain adequate calorie and reduce proteinuria with **low sodium and phosphorus** in order to control systemic hypertension and reduce renal damage progression, and also contains omega-3 fatty acids, which is proved to be effective for proteinuria reduction (Grauer, 2005).

The antihypertensive drugs effective for reduction of protein loss are **ACE inhibitors**, such as enalapril, benazepril and ramipril, of which adverse effects that should be concerned include dehydration that could lead to hypotension, hyperkalemia, and high creatinine (Vaden, 2016).

There are demonstrations of **omega-3 fatty acid** supplementation in dogs, for example, EPA and DHA that are elements of GSM. GSM inhibits thromboxane that induces agglutination of platelets at the glomerular capillary arterioles and causes glomerulonephritis (Grauer, 2005). The amount of protein leak at glomerulus exceeding the limit that convoluted tubules can absorb causes oxidation of lipoprotein transferrin and other proteins, which then causes free radicals and damage to glomerular cells and surrounding tissues.

Omega-3 fatty acids have anti-oxidative and anti-inflammatory effects since they inhibit **cyclooxygenase (COX) and lypo-oxygenase (LOX)** function, therefore damage and inflammation of cells are controlled (Grauer, 2002).

The other effects include decreasing level of cholesterol and triglyceride, which is caused by increasing lipoprotein from the liver to compensate the loss of albumin when PLN occurs (Vaden, 2016).

The previous studies had proved that omega-3 fatty acids are effective against inflammation and proteinuria caused by glomerulonephritis.

The recommended dosage is 250-500 mg of Omega-3 fatty acid/kg every 24 hours according to Brown et al. (2013).

A study by Lascells et al. (2010) found that GLM contained only little amount of omega-3, therefore further study on active ingredients of GLM extracted is necessary.

After 1 month of the treatment, the dog showed deterioration of clinical signs due to hypovolemia from the leak of intravascular fluid, then dosage of PCSO-524® (Vetz Petz® Antinol®) was doubled in order to increase the amount of omega-3 fatty acids and other anti-inflammatory agents. Prednisolone 0.5 mg/kg every 24 hours was added to the prescription to reduce the inflammation in case of severe clinical signs and no response to the standard treatment scheme (Brown et al., 2013).

The treatment follow-up in this case found the clinical signs were improved as ascites and edema disappeared, serum albumin was increased to normal level (higher than 2.5 mg/dl), and there was more than 50% reduction of UPC.

No adverse effects of ACE inhibitors were observed during the 10-month follow up since potassium level was lower than 6 mEq/L and creatinine did not exceed 30% of the initial value. Since there was no cure for the disease, the dog needs a follow up on clinical signs and supportive treatment to delay the progress of the damage and to prevent complications. The disease prognosis is similar to that of chronic kidney failure.

Conclusion

The success of the treatment of **protein losing nephropathy** depends on rapid and accurate diagnosis and identification of underlying causes. For the presented case, hypertension is highly suspected to be the underlying cause considering no other die was found. Although the animal may not show sign of azotemia in the first visit, the development of kidney failure must be concerned.

Supportive therapy concurrently used with prevention of complications is necessary for the treatment and selection of wrong choices of medication may accelerate the kidney damage.

PCSO-524® was used for supplementary treatment due to various properties to prevent kidney damage without causing adverse effects. The inflammatory effect was reported in treatment of inflammation of the other systems such as musculoskeletal diseases, gastroenteritis, pancreatitis, hepatic diseases, and cancer.

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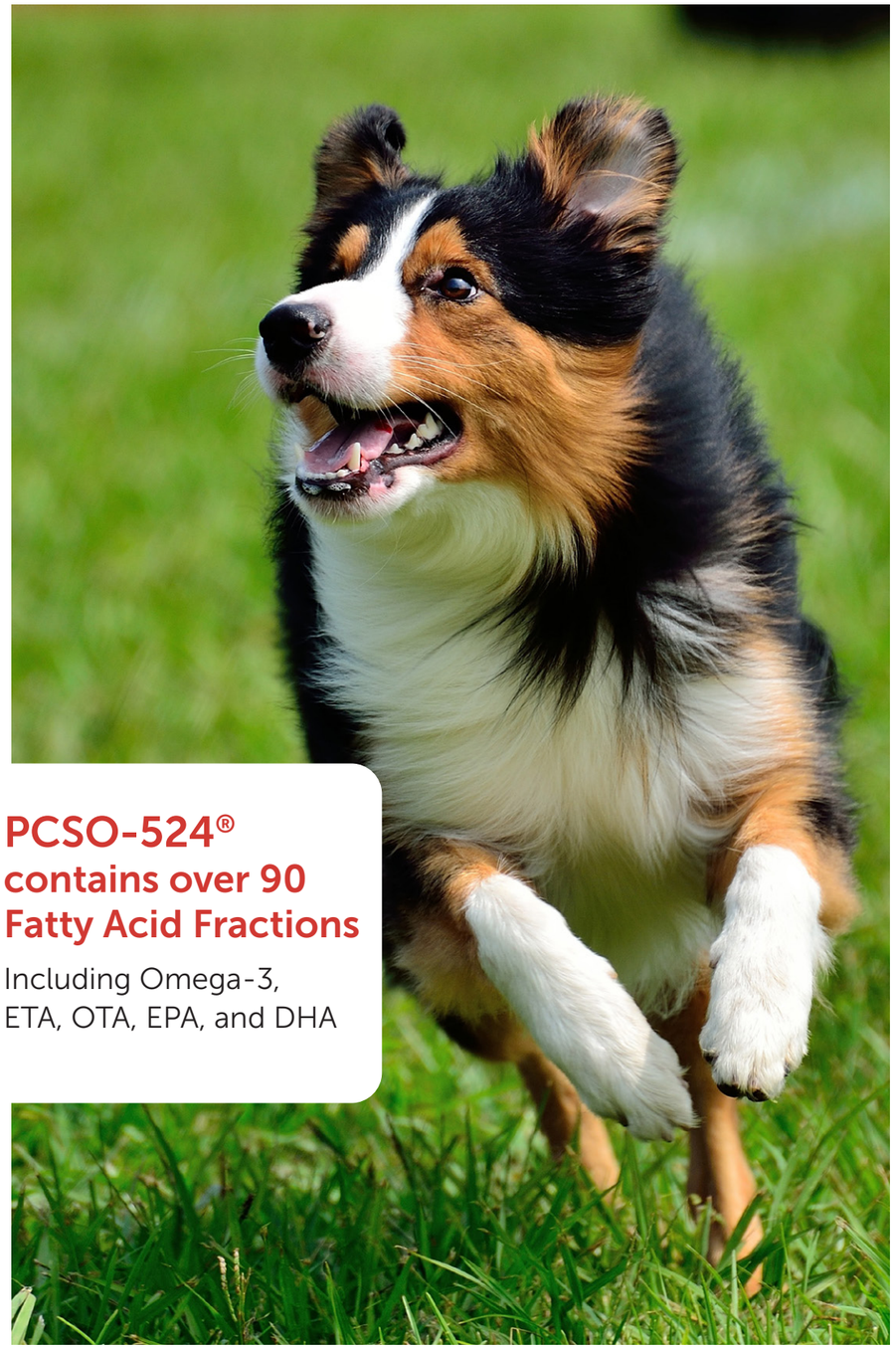

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