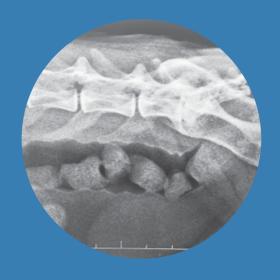
PRIVATE ANIMAL HOSPITAL



2018
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Cat Case
Study Contest

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USE OF PCSO-524® ALONG
WITH PHYSICAL THERAPY FOR
CONTROLLING PAIN AND
INFLAMMATION IN A CAT SUFFERING
FROM OSTEOARTHRITIS, CHRONIC
KIDNEY DISEASE AND TRIADITIS

Mananya Danpitakkul, DVM Pitcha Pornmingmas, DVM Supattra Yongsiri, DVM

Abstract

A spayed female domestic shorthaired cat aged 21 years and weighed 4.2 kilograms with history of chronic kidney diseaseand triaditis was referred to Suvarnachad Animal Hospital. The cat showed signs of both hind limb weakness, limp tail and pain around posterior body part. Other signs included polydipsia, polyuria, and diarrhea. Radiographic examination revealed osteoarthritis at lumbosacral joint, elbow and both stifle joints. Hematological and blood chemistry tests showed mild anemia, neutrophilic leukocytosis, increased serum amyloid A and Increased Feline pancreatic lipase. Administration of PCSO-524® and physical therapy were provided to reduce systematic and local pain and inflammation. The supportive treatment was continued for 15 months, during the first 2 months of which, the lumbosacral joint painwas reduced and then disappeared after 5 months. The control of elbow and knee joint pain was satisfied for the whole treatment period. The cat was able to move the tail and resume normal walking after the 1st and 5th month of the treatment, respectively. Ability to jump and climb returned in the 5th and 8th month. However, the cat had improved defecation within 3 months. Testing of feline pancreatic lipase and serum amyloid A showed normal levels after 7 months of the treatment.

Keywords

chronic kidney disease,osteoarthritis, PCSO-524®, triaditis

1 Suvarnachad Animal Hospital, Saphan Sung, Bangkok *Corresponding author E-mail: mananya_vet@yahoo.com

Introduction

PCSO-524® is extracted from greenshell mussel (GSM) or Green Lipped Mussel (GLM) known as Perna canaliculus. It is consisted of several fatty acids, including EPA (eicosapentaenoic acid), DHA (docosahexaenoic acid), furan fatty acid (F-acid), sphingolipids, phytosterols, diacylglycerols, diterpenes, sesquiterpenes and saponin. Other components are anti-oxidants such as carotenoids, xanthophylls and anthocyanins. The active ingredients that have anti-inflammatory effects are EPA and DHA, which are omega-3 fatty acids.

Use of PCSO-524® has been known since 1970. There are more than 150 research publications about PCSO-524®, especially its effect on improving clinical signs of osteoarthritis in humans, dogs, and cats (Eason et.al., 2018; Kwananocha et.al., 2016 and Soontornvipart et.al., 2015), and reduction of inflammation caused by acute myositis and muscle pain in humans after 30 km. running (Eason et.al., 2018). There are studies using omega-3 fatty acids and PCSO-524® for treatment of inflammation, particularly that caused by diseases related to immunological function such as asthma and inflammatory bowel disease (Eason et.al., 2018 and Mickleboroughet.al., 2013). PCSO-524® also has anti-cancer effect but its mechanism is still unknown (Eason et.al., 2018).

Physical therapy in animals has increased its popularity during the past years, but not very common in cats due to limitation of cooperation of cats. Veterinarians who provide physical therapy need to have professional skill and understanding of feline behavior and must be able to plan the physical treatment that is least invasive, taking time the least and appropriate for each individual cat (Drum et.al., 2015 and Sharp B, 2012).

Osteoarthritis is abnormality of cartilage, subchondral bone, synovium, ligament and capsule. Abnormality of one or more components can cause osteoarthritis. Osteoarthritis can occur only at synovial joints and cartilaginous joints, but never occurs at fibrous joints. Synovial joints can be found in appendicular skeletal such as stifle joint, elbow joint, tarsal joint, and hip joint. Clinical signs of osteoarthritis include synovial thickening, articular cartilage degeneration, subchondral bone sclerosis, osteophyte formation, and joint capsule thickening. Cartilaginous joint is the junction between vertebrae which is axial skeletal. When degeneration of intervertebral disk occurs, there is stenosis of intervertebral space and thickening of sclerosis of body end plate and osteophyte called spondylitis deformans. Prevalence of feline osteoarthritis has increased 13.6% each year (Epstein et.al., 2015). The disease is common in elderlycats as 90% of cats in this age group are affected (Clarke et.al., 2006).

Triaditis is inflammation of gall bladder, pancreas, and intestine. Chronic kidney disease is a common disease in old cats and caused by deterioration of internal organs. Since the cat in this case study is senior and affected with many systemic diseases, use of NSAIDs to reduce pain and inflammation caused by osteoarthritis is not appropriate due to severe adverse effect found in long term use. Therefore, PCSO-524® was selected as alternative to NSAIDs and used concurrently with physical therapy to reduce inflammation and pain.

Case history

A spayed female domestic shorthair (DSH), 21 years old, and weighed 4.2-kilogram cat was referred to Suvarnachad Animal Hospital. The cat had history of chronic kidney disease andtriaditis and the body condition score was 3/5. The cat showed signs of both hindlimb weakness, limp tail, and pain around posterior body part. Other signs included polydipsia, polyuria, and diarrhea. Prior to this visit, the cat was treated with oral prednisolone, tramadol and gabapentin for over 1 month.

Physical examination

Physical examination found that the cat was alert and responsive. Her body temperature was 101°F. She had pink mucous membrane, normal heart and lung sound. Her capillary refilling time (CRT) was 1-2 seconds. Her heart rate and respiratory rate were 196 beat/min and 34 per min, respectively. Abdominal palpation did not find cramping pain and peripheral lymph nodes were within normal size. Fresh fecal smear did not find significantly increased number of pathogens. Hematology and blood chemistry tests showed mild anemia, neutrophilic leukocytosis, increased serum amyloid A and increased feline pancreatic lipase.

Orthopedics and neurological examination

The cat showed signs of plantigrade stance (Figure 1) and pain around posterior body part. She was unable to move the tail. When elbows and knees were palpated, sound of crepitation was detected. Proprioceptive reflex and flexor reflex test were normal. Spinal reflex test showed decreased degree of response indicating that the cat had lower motor neuron disorder of both hind limbs.



Figure 1. Plantigrade stance walking posture

Radiographic examination

Radiographic image of lumbar spinal vertebrae in lateral view (Figure 2) showed osteophyte and stenosis of lumbosacral space.

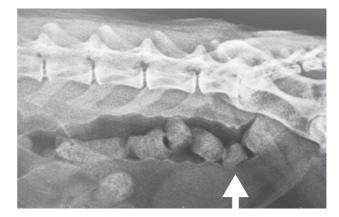


Figure 2. Radiographic image of lumbar vertebrae, lateral view, showed osteophyte and stenosis of lumbosacral space (white arrow)

Radiographic images of all limb in lateral and ventrodorsal view showed osteophyte and subchondral bone sclerosis at both side of elbows and knees (Figure 3).







Figure 3. Radiographic image of both hindlimb, lateral view (A) andventrodorsal view (B) and elbow joints, lateral view (C) showedosteophyte and subchondral bone sclerosis

Abdominal ultrasonography

Abdominal ultrasonography found enlarged liver with homogenous hyperechogenicity. Sludge was found inside gall bladder and gall bladder wall thickness was 2 mm. Kidneys size was normal but heterogenoushyperechogenicity was found with unclear corticomedullary junction. There was mixed-echogenicity of parenchyma at the right lobe of pancreas and mild hyperechoic of peripancreatic tissue. Muscularis layer of duodenum was thickenening and the peristalsis of duodenum was decreased.

According to the history, physical examination and further investigations of the cat, the diagnosis included osteoarthritis, chronic kidney disease and triaditis.

Treatment

The cat was treated with PCSO-524® (VetPetz,Antinol®) 1 capsule PO every 24 hours for 15 months starting month 2 to month 15 of the treatment. Prednisolone 1 mg/kg/day PO was prescribed for 5 months, during which the dosage was tapering down to 0.5 and then 0.25 mg/kg/day. Gabapentin 10 mg/kg was administered every 12 hours during the first month of the treatment then every 24 hours for the next 3 months. The cat received tramadol at the dosage of 2 mg/kg PO every 12 hours in the first month. Hematic drug and vitamin B12 were given during the early treatment for anemia. Other supportive treatment included subcutaneous fluid therapy 1-2 times per week, medication for liver enhancement, and specific diet formulated for treatment of digestive tract. Physical therapy was applied 1-2 times per week, then reduced to 1-2 times per month until the end of treatment, in order to control pain and restore limb function (Table 1).

Table 1. Fifteen-month Treatment plan

Month Treatment	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
PCSO-524°		Х	х	Х	X	Х	Х	х	Х	Х	Х	Х	Х	Х	x
Physical therapy	Х	х	Х	×	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	×
Subcutaneous Fluid	Х	×	X	×	Х	X	Х	x	x	x	Х	Х	Х	Х	×
Prednisolone	Х	×	Х	×	Х										
Gabapentin	Х	х	Х	X											
Tramadol	Х														

Treatment follow-up

Treatment of osteoarthritis was evaluated from 1) Pain score, 2) Tail movement, 3) plantigrade stance, 4) Jumping, and 5) Climbing ability. Pain score was classified using simple destructive scale (SDS) as 0: no pain, *: mild pain, **: moderate pain and ***: severe pain (Mathews K.et.al., 2014). Pain score at the cat's spinal cord was decreased continuously and reached 0 score in the 5th month. Moderate pain in the elbows and knees was reduced to slightly pain and remained throughout the treatment. Tail movement was described as *: Movement detected and -: No movement. The cat was able to move its tail within 1 month of the treatment. Plantigrade stance, * if detected and – if not, disappeared within 5 months of the treatment. Jumping ability, * if able to jump and – if not, recovered also within 5 months of the treatment. Climbing ability, * if able to climb and – if not, was observed again within 8 months of the treatment (Table 2). The cat had improved defecation in the third month, in which fecal score was 3 (Table 2).

Pancreatitis was evaluated using feline pancreatic lipase test kit (snap fPL[®]: IDEXX laboratories, U.S.A.) and the normal result was detected in the 7th month. The test for serum amyloid A (V-check: Bionote Inc., Korea) which is an indicator for inflammation, was within normal range in the 7th month (Table 3). Ultrasonography examination in month 10 of the treatment found that severity of lesion at the liver, pancreas and gall bladder was decreased. However, duodenum wall thickening and heterogenous hyperechogenicity and unclear corticomedullary junction of the kidney still remained. Hematology and blood chemistry test in month 7 and 15 found only neutrophilic leukocytosis (Table 3).

Table 2. Evaluation of treatment outcome during 15-month treatment

month evaluation	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Pain score: Lumbosacrum*	+++	+++	++	+	-	_	-	_	_	-	-	-	-	-	-
Pain score: elbow and stifle*	+	+	++	+	+	+	+	+	+	++	+	+	+	+	÷
Tail movement	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Plantigrade stance	+	+	+	+	-	-	-	-	-	-	-	-	-	-	-
Jumping	-	-	-	-	+	+	+	+	+	+	+	+	+	+	+
Climbing	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+
Fecal score**	6	4	3	3	3	3	3	3	3	3	3	3	3	3	3

^{*} Mathews K. (2014) **Deborah SG.(2011)

Table 3. Hematology and blood chemistry test results before, at month 7 and month 15 of the treatment

Parameter	Normal range	Before	Month 7	Month 15
RBC (x10 ⁶ /μI)	5.92-9.93	6.02	7.10	7.16
Hct (%)	29-48	27.9	37.9	36.5
Hb (g%)	9.3-15.9	9.5	12.3	11.6
WBC (μl)	3,500-16,000	20,140	25,890	22,150
Neutrophils (μl)	2,500-8,500	15,105	20,712	19,270
Eosinophils (μl)	0-1,000	604	258	443
Lymphocytes (µI)	1,200-8,000	4,430	4,919	5,094
Monocytes (μΙ)	0-600	0	0	0
Platelets(x10³/ μl)	200-500	219	286	233
SGPT(IU/L)	10-100	58	69	52
Creatinine(mg/dl)	0.6-2.4	1.7	1.4	1.4
BUN (mg/dl)	14-36	31.3	32.1	30.8
fSAA** (μg/ml)	< 0.5	38.7	< 0.5	< 0.5
Snap fPL	Normal	Abnormal	Normal	-

Ref.NorsworthyGD. (2016) *BionoteInc., Korea ** IDEXX laboratories, U.S.A.

®

Discussion

Spondylitis deformans in cats was commonly found at 7th-10th thoracic vertebrae. However, the severe form usually found at lumbar and lumbosacrum. Incidence of osteoarthritis is associated with old age, therefore, monitoring for the disease in elderly cats is crucial. Cross breed, domestic shorthaired cats and overweight cats are at risk, but some published articles reported that age, body weight are not associated with the disease (Lascelles, 2010; Baltatanu and Tudor, 2016).

Osteoarthritis can occur at appendicular skeletal, especially hip, elbow, knee and tarsal joint (Lascelles, 2010). Clarke et al. (2006) reported that feline osteoarthritis was common at the elbows. The diagnosis in this case agreed with what was previously reported as the cat showed severe neurological signs and the lesions were found at lumbosacrum of axial skeletal and elbows and knees, which are appendicular skeletal.

Treatment outcome was evaluated using subjective assessment consisting of pain score, which was measured by degree of lameness, gait disturbances, and behavior changes, such as hiding, loss of or reduced ability to jump, less grooming, and increased aggression. Subjective assessment is more appropriate than objective assessment, which is more common and a standard measure in dogs and humans (Lascelles, 2010). The disadvantage of subjective assessment is due to limitation of the use of some equipment such as kinetic force plate and accelerometer.

Study of osteoarthritis in cats is limited and etiology of the disease is still unknown. Accepted treatment is to use NSAIDs to reduce pain and inflammation. Surgical treatment of osteoarthritis is not common in cats. There are reports of joint arthrodesis performed in cats that severely suffer from pain and endoscopic surgery used to remove bone fragment in case of osteoarthritis with bone fracture, but no reports on total joint replacement. There are a few medical reports that use decompression surgery in case of spinal cord compression and entrapment neuropathy at the lumbosacrum. There are no other medical evidences of effective treatment for osteoarthritis (Lascelles, 2010 and Epstein et. al., 2015). GLM is proved that it has positive effect on mobility of the body and can be used in case of rheumatoid arthritis and osteoarthritis in humans, dogs and horses (Bui, 2001 and Eason et. al., 2018). The only study of GLM in osteoarthritic cats belongs to Lascelles et al (2010), in which supplement consisting of EPA, DHA, glucosamine and chondroitin sulfate was effectively used to improve mobility. Objective assessment using accelerometer to evaluate the effects of supplement consisting of EPA ad DHA on pain caused by osteoarthritis indicates that omega-3 fatty acid is effective for reduction of topical pain and pain of central nervous system. However, Lascelles et al (2010) reported that GLM had very little of omega-3 and mechanism of GLM is still unknown perhaps due to unidentified etiology of osteoarthritis in cats. Further study on active ingredient of GLM extract, its concentration and mechanism is necessary. Additional studies on comparison of the effect of GLM, NSAIDs and other medications for osteoarthritis treatment are also important (Eason et. al., 2018 and Lascelles, 2010).

Physical therapy is not very common in cats because osteoarthritis in cats is less prevalent than in dogs, lack of understanding of the disease, and cat behavior that tends to resist physical restraint. The success of physical therapy in cats therefore highly requires cooperation of the cat (Drum et.al., 2015). The cat in this case cooperated most with low level laser therapy, which is supportive therapy and acts more like pain reducer that anti-inflammatory treatment or joint strengthener, therefore other type of treatments are also necessary (Pryor et.al., 2015).

Conclusion

PCSO-524® has been proved to be effective for systemic treatment in concurrent with physical therapy for local treatment of pain and inflammation caused by osteoarthritis in senile cats, cats with limitation of surgical treatment and long-term use of NSAIDs. The cat has improved clinical signs and quality of life without any adverse effects. Although using of PCSO-524® and physical therapy does not result in fully recover from the disease, it is supportive therapy and prevents the progression of the disease. PCSO-524® may reduces the degree of inflammation in some other diseases, such as enteritis, chronic pancreatitis, hepatitis and cholecystitis and may inhibit development of chronic renal failure in cats. A further study on this issue needs to be explored.

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Pharmalink and Vetz Petz® would like to thank everyone involved with the Antinol® research competition

At Pharmalink and Vetz Petz® we have a passion for Scientific Research and know that only this type of scientific proof is good enough to prove the benefits of ANTINOL® to the Veterinary community and owners alike. We also share the Vets passion for providing the best care for companion animals. This level of care and the credibility that goes with a Veterinarians recommendation cannot be achieved in good conscience if we do not have the participation and co-operation of the scientific community and Veterinarians alike. So we will continue to provide funding for projects that help companion animal owners and their Veterinarians to provide the best care for our beloved companion friends.

We would also like to offer a special thanks to ALL the committee members, Dr. Achinee and DKSH for their hard work organizing and hosting this very and unique event. You have graciously PROVIDED your time and vast experience and for that we thank you VERY much.

This project is the first of its kind for Pharmalink and Vetz Petz® and we are very excited about the research opportunities that have been shown as result of this competition. The future of Antinol® research is very bright and we are very thankful to everyone in loved.

John Dennis Waitzer Director

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Vetz Petz® group

Antinol® Contest has been organized successfully for 3 years since 2016 in Thailand. The key objective of this scientific contest is to encourage knowledges sharing amongst the Vet practitioners on how to treat the companion animals inflammatory cases safely & effectively by using Antinol® in conjunctive with others medicines especially the NSAIDs (Non Steroidal anti-inflammation drugs) which is the drug of choices of anti-inflammatory problems. However as we know apart from the high efficacy of NSAIDs it also can cause serious side effects such as renal or liver damage if it's used too long or no close monitoring when applied in animals.

Recently we have seen the increasing trend of cats populations adopted as the companions; Cat is the specie that has quite limited type of anti-inflammatory drug with safely applied. Therefore 2018 Antinol contest would like to promote the Vet practitioners to share their knowledges and experiences of using Antinol® as the drug of choices of anti-inflammatory cases in cats to demonstrate the option of safe and effective treatment which has been very successful applied as the combined therapy from different cases study in this contest resulted Antinol® is become commonly used as the safe choice of anti-inflammation in cats.

Dr. Achinee Runcharoen

DVM

CEO ASIA





