

**2016  
Antinol.**

# **Case Study Contest**



**Effects of PCSO-524®  
on Inflammation Control  
in Cats with Chronic Renal  
Disease after Keratectomy  
and Conjunctival Pedicle  
Graft for Treatment of  
Corneal Sequestrum from  
Indolent Ulcer**

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## Abstract

A female spayed cat aged 13 years with chronic renal disease later affected with indolent ulcer, and consequently followed by corneal sequestrum. After azotemia was controlled, the cat was surgically treated with keratectomy that used conjunctival pedicle graft for suture closure. The cat received 4mg/kg Tolfenamic acid (Tolfedine®, Vétquinol, Best Agro; Thailand) for 3 days, 2.5 mg/kg Doxycycline monohydrate (Vibravet®, Zoetis, Thailand) for 2 weeks and 1 tablet per day of New Zealand Green-lipped mussel extract, PCSO-524®(Vetz Petz Antinol®, DKSH, Thailand)for long-term control of inflammation. The latter was used as an antioxidant and alternative to Non-steroid, which is a contradiction for chronic renal failure. The cat showed decreased severity of inflammation, normal clinical symptoms, and fine control of azotemia. It is concluded that PCSO-524®(Vetz Petz Antinol®) can be used to support long-term anti-inflammation treatment and reduce the damage in cats with medical contraindication due to chronic renal disease

### Key word :

Cat, chronic renal disease, indolent ulcer, PCSO-524®, Antinol®

## Case history

A female spayed domestic short hair cat aged 13 years and weight 4.6 kg was diagnosed with chronic renal disease and on continuous treatment for approximately 1 year. In January 2016, the cat started to show signs of blinking, red conjunctiva, watery eyes, and opaque cornea. The examination found indolent ulcer at the cornea that was not respond to corneal debridement,prophylaxis antibiotic and artificial tears. Surgical treatment was considered for replacement of medication and debridement, however, the cat was not ready for the operation due to uncontrolled azotemia from chronic renal failure. Preliminary steps were to perform corneal debridement with a sterilized cotton swab, applying antimicrobial eye drops and artificial tears, control inflammation and infection of the cornea. Later, it was found that the symptoms had developed into corneal sequestrum, mortification of the cornea. Two months later, the azotemia was under control and the corneal sequestrum was surgically removed.

## Diagnosis Plan and Results

### Diagnosis and treatment prior to the operation

The etiology of indolent ulcer was corneal ulcer which was continued for over 2 weeks without any response. Since the chronic renal disease was present prior to the corneal ulcer, treatment plan was consisting of medication, scrubbing of corneal epithelium with sterilized colon swab (debridement), antimicrobial eye drop, atropine sulphate eye drop to reduce ciliary muscle spasm, and artificial tears. Systemic treatment to control infection consisted of 2.5 mg/kg Doxycycline monohydrate (Vibravet® , Zoetis)for 2 weeks and 1 capsule per day of PCSO-524® (VetzPetz® Antinol®, DKSH Thailand).

Since the first visit at the ophthalmology clinic, the cat was put on a routine schedule for blood analysis, blood pressure measurement, and ultrasound examination of abdominal cavity to evaluate the condition of chronic renal disease during the azotemia therapy. The eye examination was scheduled weekly during the first month to assess cornea condition since indolent ulcer in cats can induce other dysfunctions of the cornea such as corneal sequestrum. Once the azotemia was controlled, operation would be performed.

The severity of inflammation was reduced after the medication treatment and debridement as observed from ameliorated red conjunctiva and less blinking. However, indolent ulcer, which was the cause of inflammation, still persisted and developed into corneal sequestrum that did not respond to medication so damaged part of the cornea must be surgically removed. Two months after the first visit, the corneal sequestrum was surgically treated after azotemia was controlled.

## Complete Blood Count Analysis Results

parameter	Ref.range	unit	Mth 4 <sup>th</sup> (6/5/2016)	Mth 6 <sup>th</sup> (25/7/2016)	Mth 7 <sup>th</sup> (24/8/2016)	Mth 8 <sup>th</sup> (24/9/2016)	Mth 9 <sup>th</sup> (21/10/2016)
RBC	4.60-10.20	10 <sup>6</sup> /μL	7.05	7.38	6.98	7.84	8.09
Hb	8.5-15.3	g/dl	11.05	12.5	11.8	12.6	13.0
Hct	26-47	%	37.3	37.3	39.2	41.3	45.6
MCV	38-54	fL	52.9	50.6	56.1	52.7	56.4
MCH	11.8-18.0	Pg	16.4	17.0	16.9	16.1	16.1
MCHC	29.0-36.0	g/dl	30.9	33.5	30.1	30.5	28.5
Platelet	100-518	10 <sup>3</sup> /μL	15.8	115	144	160	156
WBC	5.5-19.5	10 <sup>3</sup> /μL	5.7	6.47	8.12	7.64	5.55
Seg	3.12-12.58	10 <sup>3</sup> /μL	3.86	4.3	6.11	5.05	3.97
Lymph	0.73-7.86	10 <sup>3</sup> /μL	1.06	1.55	1.4	1.65	0.97
Mono	0.07-1.36	10 <sup>3</sup> /μL	0.03	0.16	0.03	0.19	0.13
Eos	0.06-1.93	10 <sup>3</sup> /μL	0.75	0.46	0.58	0.76	0.48
Baso	0.00-0.12	10 <sup>3</sup> /μL	0	0	0	0	0
SGPT	10-60		65	NA	NA	NA	NA
Crea	0.8-2.1	Mg/dl	3.3	3.1	3.3	3.0	2.8
BUN	5-30		29	30	24.4	25.6	23
Blood pressure	mmHg	mmHg	140	N NA	150	140	140

Remark: CBC-complete blood count, RBC-red blood cell, WBC-white blood cell, g-gram, dL-deciliter, mm3-cubic millimeter, SGPT- serum glutamic pyruvic transaminase, ALT-alanine aminotransferase, MCV-meancorpuscular volume, MCH-mean corpuscular hemoglobin, MCHC-mean corpuscular hemoglobin concentration, fL- femtoliter, pg-picogram, NA-not applicable

## Ocular Examination Results

parameter	Month 0		Month 4 <sup>th</sup>		Month 6 <sup>th</sup>		Month 8 <sup>th</sup>		Month 11 <sup>th</sup>	
	OD	OS	OD	OS	OD	OS	OD	OS	OD	OS
STT	17	22	18	19	19	20	17	15	16	15
IOP	16	14	20	17	21	18	22	18	19	18
Fluorescein Menace	-	+	-	-	-	-	-	-	-	-
PLR	+	+	+	+	+	+	+	+	+	+
conjunctiva	N	PLH	N	-(dilate) Mild PLH	N	N	N	N	N	N
Cornea	N	ulcer	N	graft	N	graft	N	graft	N	graft
Aqueous	clear	clear	clear	clear	clear	clear	clear	clear	clear	clear
Lens	clear	clear	clear	clear	clear	clear	clear	clear	clear	clear
fundus	normal	normal	normal	normal	normal	normal	normal	normal	normal	normal
Ocular pain score	0	3	0	0	0	0	0	0	0	0

Remark : STT-Schirmer tear test, IOP-intraocular pressure, PLR-pupillary light reflex, PLH-perilimbal hyperemia, OD-Ocular dexter, OS-Ocular sinister, N-normal

## Ocular pain score assessment The score was determined according to the following;

### Assessment by external appearance and blepharospasm(Clark et al., 2011):

0-normal eye opening; 1-75% eye opening; 2-50% eye opening and slightly watery eyes; 3-75% eye closed and moderately watery eyes; 4-100% eye closed and highly watery eyes

### Assessment by size and depth of corneal ulcer, response to inflammation in the anterior chamber, white blood cell in cornea, and keratomalacia(Ledbetter et al., 2009):

Size of corneal ulcer is measured by the proportion of corneal area dyed with fluorescein stain: 0-less than 25%; 1-26-50%; 2-51-75%; 3-more than 76%

Corneal ulcer depth is measured at the deepest point of the ulceration relative to total corneal depth: 0-less than 25%; 1-26-50%; 2-51-75%; 3-more than 76%

Anterior chamber reaction:0-no clinical symptoms; 1-slight aqueous flare; 2-moderate aqueous flare; 3-hypopyon

Corneal edema:The proportion of edema area of the cornea is measured: 0- not more than 25%; 1-25-50%; 2-51-75%; 3-more than 75%

Corneal leukocyte infiltration: 0-none; 1-slight infiltration; 2-moderate infiltration; 3-high infiltration

Keratomalacia: 0-none; 1-benign; 2-moderate, 3-severe

## Ultrasonic diagnosis: Chronic kidney disease

Decreased cortex-medulla differentiation and hyper-echoic parenchyma contour were diagnosed. The shape and size of the kidney were normal and no remarkable renal calculi, cyst abscess or tumor was found.

## Diagnosis and surgical treatment

Keratectomy was selected for surgical treatment in combination with conjunctival pedicle graft for enclosure suture of keratectomy. The corneal problem of the cat was chronic and causing large corneal sequestrum that approximately damaged 90% of the cornea. Consequently, keratectomized area was wide and deep and conjunctival pedicle graft was necessary for enclosure suture. Post-operative care included anti-inflammation, systemic antibiotic, and eye drops. The eye drops consisted of 0.5% Moxifloxacin (Vigamox®, Alcon) every 2 hours, 1% Aropine sulphate (1% Isopto atropine, Alcon)bid for pain relief and anti-spasm of ciliary muscle. Doxycycline (Vibravet®) was given at 2.5 mg/kg sid for 2 weeks and NSAIDs (Tolfenamic acid ; Tolfidine® Vétoquinol, Best Agro) at 4 mg/kg sid was given for 3 days. One capsule of PCSO-524®(Antinol®) sid had been given orally since prior to the operation. Subcutaneous fluid therapy was provided daily. Blood chemistry analysis was performed to evaluate azotemia condition. Eye examination was scheduled on day3, day7, day14, day28, and then every 2 months after the operation.

## Results after the surgical treatment

The severity of inflammation was reduced. The grafted conjunctival issue was still intact. The visual was normal and no additional disorders were observed. Physical examination showed normal health condition, appetite, defecation and urination. The cat gained some weight. Azotemia was less severe. Supportive fluid therapy every other day and 1 capsule sid of PCSO-524® was still continued.

## Discussion

Indolent ulcer (epithelial erosion) orrefractory ulcer is epithelial ulcer of cornea. The etiology of indolent ulcer is not clearly identified. Keratoconjunctivitis sicca, feline Herpesvirus-1 viral infection, continuous irritation from diseases of eyelid or eyelash, and deterioration from old age are suspected to cause detachment of epithelium basement membrane from cornea stroma. Consequently wide but shallow ulcers may exist for longer than 10-14 days. The treatment essentially includes removal of affected tissue, such as debridement using sterile cotton swab, Alger brush diamond burr, grid keratotomy, or superficial keratectomy with various grafts for corneal enclosure.

Corneal sequestrum is the necrosis of cornea of which the corneal tissue becomes dark brown to black. The disease is particularly found in cats with unknown cause. Other names include corneal necrosis, corneal sequestration, corneal mummification, corneal nigrum, focal degeneration, feline keratitis nigrum, primary necrotizing keratitis, isolated black lesion and chronic ulcerative keratitis. It commonly occurs following other corneal disorders such as chronic corneal ulcer in this case. Corneal disorders result in chronic inflammation and consequently cause pain, red and watery eyes, blinking, and constricted iris. Cats may be depressed, spend more time sleeping, or trying to wipe the eyes (Barnett and Crispin, 1998). The pain caused by disorders such as corneal ulcer, uveitis, or glaucoma was classified as severe pain out of 4 levels of pain; excruciating, severe, moderate, and mild (Wright, 2002).The detail of each classification can be added from specific symptoms or alteration of behavior post operation (Williams, 2016). The therapy necessarily includes continuous pain and inflammation treatment with anti-inflammation medication and cycloplegia for relief of pupillary constrictor muscle and ciliary muscle.

Renal failure occurs when kidney fails to maintain normal hemodialysis, filtration or excretory function, resulting in accumulation of uremic toxins, loss of electrolyte and acid-base balance. Consequently, azotemia occurs when blood urea nitrogen (BUN), or blood creatinine increases and maintenance of urine specific gravity is impaired (<1.040) (Lappin, 2001). The use of NSAID and steroid in renal failure cats is limited due to prohibition of cyclooxygenase (COX) which produces prostanoids, substance important for maintenance of electrolyte and acid-base balance and glomerular filtration rate. Therefore alternative anti-inflammation that has no adverse effects on kidney is necessary (Suemanotham, 2014).

PCSO-524® or Antinol® (VetzPetz® Antinol®, DKSH, Thailand) is oil extracted from New Zealand Green-lipped mussel (*Perna canaliculus*) using liquefied carbon dioxide. It can prevent or reduce severity of inflammation (McPhee et al, 2007; Coulson et al, 2013; Coulson et al., 2015). Other properties included gastroprotective, antihistaminic effect, antioxidant, anticytokines, and antiarthritis. Most of the extracted peptide from New Zealand Green-lipped mussel (*Perna canaliculus*) is anti-microbial, anti-oxidant, cohesive, and anti-hypertension substance (Coulson et al., 2015). Additionally, PCSO-524® assists in balance of intestinal flora (microbiota), sequence of internal and external inflammation of intestine, for example, rheumatoid arthritis, and osteoarthritis. Metabolism of intestinal bacteria will change or alter the nutrient structure resulting in contact of host and the changed component. This will increase or decrease the effect of nutrients on health. The understanding of association between extract from New Zealand Green-lipped mussel and the change of probiotics and pathogenic bacteria can help controlling internal and external inflammation of the intestine (Coulson et al., 2013; Coulson et al., 2015).

## Conclusion

Corneal sequestrum as a consequence of indolent ulcer in cats is common. It causes chronic keratitis or uveitis, resulting in pain or chronic discomfort that leads to the loss of eyeballs due to severe uveitis or staphyloma of cornea from detachment of sequestrum that expands throughout the cornea. Medication usually does not work well. Specific treatment includes operation that removes the affected corneal tissue in combination with various grafted enclosure and systemic and topical medication. In this case, the operation could not be performed in the beginning due to chronic renal disease of the cat. Anti-inflammation drugs are prohibited in this category; therefore PCSO-524® (Antinol®) and antibiotics were used for long term control of inflammation and control and prevention of inflammation, respectively.

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## Illustrations

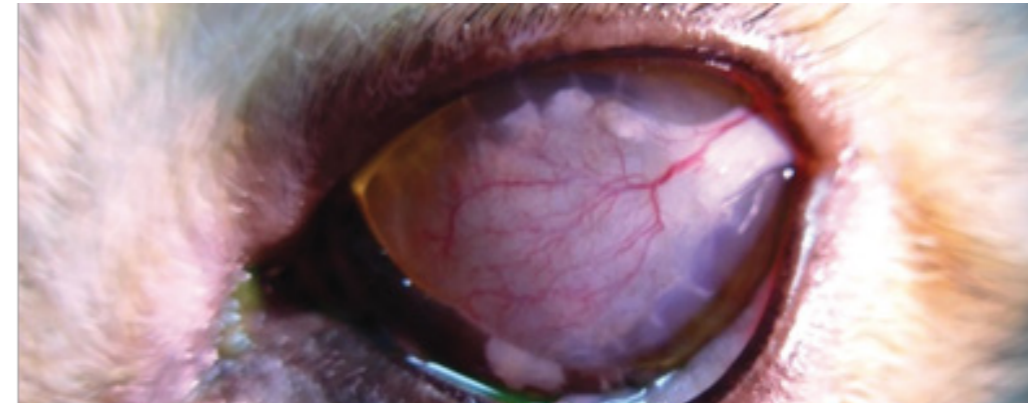


Figure 1.

One month post-operation. The keratectomy area was covered with grafted conjunctiva. The operated area was wide and deep therefore the chance of staphyloma was high. Conjunctival tissue was used to replace the damaged and removed corneal stroma collagen. The inflammation is nearly disappeared as observed from lacks of swollen and redness of conjunctiva, no tears, no blinking, inability to dye the cornea, and clear fluorescein aqueous. The pupil is dilated due to mydriatic administration.

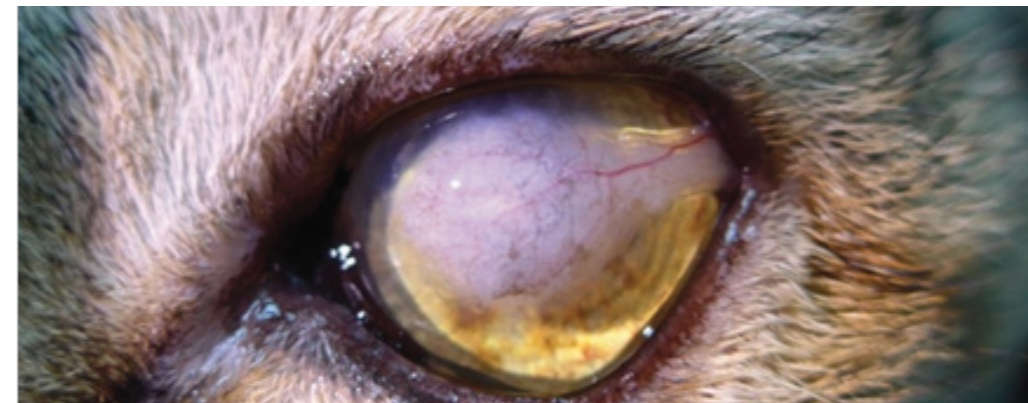


Figure 2.

Six months post-operation. Conjunctival pedicle graft that covers the cornea is thinner than before. The size of vessels at the grafted area is reduced. The grafted is left without removal. Overall appearance shows no inflammation of the cornea and other tissues. The cat is able to see through the area outside the graft.

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