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Review

URINARY CAPILLARIOSIS IN DOGS

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Abstract

Background. Urinary capillariosis in dogs is caused by *Capillaria plica* (syn. *Pearsonema plica*), a ubiquitous parasitic nematode resembling a string which belongs to the family *Capillariidae*. It parasitizes the feline, canine and musteline urinary bladder, and has been found in ureters and renal pelvises as well. *C. plica* has an indirect life cycle, with earthworms (*Lumbricina*) as intermediate hosts and domestic and wild animals (dog, cat, fox and wolf) as primary hosts. Infection of primary hosts occurs *via* ingestion of earthworms that contain infective first stadium (L1) larvae. An alternative path of infection for primary hosts is assumed to be ingestion of soil contaminated by infectious larvae derived from decomposed earthworms. Infection is mostly asymptomatic, but the clinical picture presents with pollakiuria, dysuria, haematuria, polydipsia, incontinence and/or fever.

Scope and Approach. The aim of this review is to highlight the importance of urinary capillariosis in dogs. Since the health care of wild and domestic carnivores is extremely important, this review provides information about the morphology, biology and epizootiology of the *C. plica* nematode. Due to the importance of this disease for clinicians and increased disease prevalence during the last decade in many countries, this review presents the latest information on the pathogenesis, clinical signs, diagnosis, treatment and prevention of this infection.

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Key Findings and Conclusions. Capillariosis is usually accidentally diagnosed due to the nonspecific clinical signs and there is no treatment of choice. Practitioners should consider latent urinary capillariosis infection as a possible cause while examining for urinary tract diseases.

Key Words: *Capillaria plica*, dog, urinary bladder, urine analysis

INTRODUCTION

Urinary capillariosis is a parasitic disease of wild and domestic carnivores and is widespread around the world. Infection is caused by the nematode *C. plica* (syn. *Pearsonema plica*) which is located in the urinary bladder and lower parts of the urinary tract in primary hosts (Rossi et al., 2011; Whitehead, 2009; Davidson et al., 2006; Senior et al., 1980).

Foxes play an important role in the epidemiology and spread of this parasite to domestic and hunting dogs and domestic cats (Bork-Mimm and Rinder, 2011). Ecological changes, an effect of global warming, are resulting in significantly increased numbers of foxes and increases in the density of stray dog and cat populations (Ilić et al., 2016a). These circumstances have created preconditions for the occurrence, maintenance and spread of some parasites in domestic dogs and cats (Ilić et al., 2017a; Hadži-Milić et al., 2016b; Ilić et al., 2009; Tasić et al., 2008). Increased urbanization has also caused spread of city areas to locations that were erstwhile fox habitat (Ilić et al., 2016c). Fox juxtaposition with urban areas is now more frequent in many European countries (Sréter et al., 2003), and this has enabled their closer contact with dogs and increased the probability of *C. plica* infection in domestic carnivores (Mariacher et al., 2016).

Aetiology

The causative agent of urinary capillariosis in carnivores was first described in 1819 and named *Capillaria plica*, but in 1982, it was suggested it be renamed *Pearsonema plica* (Moravec, 1982). Both genus classifications are used in the literature nowadays. In dogs, wolves and foxes, the relevant organism is *C. plica* (Davidson et al., 2006), while in cats, both *C. plica* and *C. feliscati* occur (Levine, 1968).

Female *C. plica* are 30 to 60 mm in length, while males are 13 to 30 mm in length (Osborne and Delmar, 1995). This parasite is 0.048 to 0.090 mm wide. *C. plica* eggs are 55-67 × 26-29 μm, grey in colour, with a thick capsule, oval, and with caps on both poles (Petersen et al., 2018; Senior et al., 1980). Considering their specific weight, *C. plica* eggs are classified as light helminthic eggs, and based on their morphological characteristics, they belong to the Trichuridea type.

In adult forms of female parasites, the oesophagus is 10.08 to 10.98 mm long. The vulva is located directly after the oesophagus, 10.35 to 11.52 mm from the front end of the parasite. The cylindrical aperture of the vulva is surrounded by cubicula formations

that resemble small lips. In males, the cloaca is located subterminally and possesses a peaked extension in the shape of a tail. A small, undeveloped bursa, in the form of a ribless membrane, wraps the dorsal part of the end of the tail like eaves. At the front end, there are two smaller growths, finger shaped and with a shallow cylindrical notch that partially splits the bursa into two parts, each wafer-like. The spicule is 2.83 to 3.87 mm long. The proximal end of the spicule is thicker, ends aslope, and as it thins, going to the distal end, it finishes with a small widening. The surface area of the spicule contains four transversal stripes oriented forwards with their needle-like cogs. They are conspicuous only on the distal quarter of the spicule (Skrjabini and Petrov, 1964).

After mating, females lay eggs in the host's urinary bladder, from which eggs are eliminated to the environment. At the moment of laying, eggs are not embryonated and not infectious (Bowman, 1999). Eggs must be ingested by an earthworm, the intermediate host (Bowman, 1999; Osborne and Delmar, 1995; Senior et al., 1980), thereby allowing development of first stadium larvae (L1).

Infection of a primary host occurs by ingestion of an earthworm which contains infectious L1 larvae. Adult forms of parasites fixate themselves onto the primary hosts' urinary bladder mucosa. Occasionally they can be found in host ureters and the renal pelvis (Bork-Mimm and Rinder, 2011). The prepatent period lasts for about eight weeks (Bork-Mimm and Rinder, 2011), but in foxes it is slightly shorter (Low, 1999; Meadway and Skelley, 1961).

Epizootiology

C. plica is a common parasite of red foxes (*Vulpes vulpes*) in Europe, with prevalences of 3% in Croatia (Rajković-Janje et al., 2002), 40% in Spain (Segovia et al., 2004), 52% in Hungary (Sréteret et al., 2003), 53% in Norway (Davidson et al., 2006), 57% in Italy (Magi et al., 2014), 78% in Germany (Bork-Mimm and Rinder, 2011), 80% in Denmark (Saeed et al., 2006) and 93% in Lithuania (Bruzinskaite-Schmidhalter et al., 2012). In Italy, *Capillaria* was first reported in foxes 29 years ago (Iori at al., 1990), and afterwards, the parasite was detected in cats (Rossi et al., 2011). In dogs, the presence of this parasite is related to the occurrence of glomerular amyloidosis (Callegari et al., 2010). The fact that *C. plica* were found in wild carnivores in surrounding countries (Hungary, Italy, Croatia, Bosnia and Herzegovina) indicates it is possibly present in dogs, cats and foxes in Serbia.

Infection is also described beyond Europe. The first case of urinary capillariosis was diagnosed in a cat in 2008 in Brazil (Pagnoncelli et al., 2011). In spite of therapy, the cat died with symptoms of dysuria, incontinence and eosinophilia. In Canada, a case was described in a four-year-old cat with symptoms of haematuria, a large number of amorphous crystals and the presence of *C. plica* eggs (Bédard et al., 2002).

Increasing attention from the clinical-parasitological aspect is being dedicated to nematodes from the *Capillariidae* family, which parasitize dogs and cats. *Capillaria aerophila* was, for a long time, considered as a low pathogenicity parasite that causes

sporadic respiratory infections in dogs and cats. Consequently, it was not afforded much importance until its zoonotic potential and the menace it poses to human health was proved (Ilić et al., 2015). Until recently, *C. plica* was not a challenge for clinicians because of the often-asymptomatic infections it causes. There is now growing interest in scientific circles in this parasitosis, considering the spread of the causative agent outside of its endemic areas, and it being a novelty in the aetiopathogenesis of canine urinary infections.

Pathogenesis and pathomorphological signs

This nematode's life cycle is indirect. Primary hosts (domestic and wild carnivores) excrete *C. plica* eggs into the external environment (Anderson, 2000), where from intermediate hosts (*Annelida* type earthworms) ingest them (Bowman, 2014; Taylor et al., 2007).

The primary host excretes eggs via its urine. After the eggs are ingested by the intermediate host earthworm, the L1 larvae form in the worm's bowels, and these larvae pass through the intestinal wall and form cysts in nearby connective tissues. Infection of the primary host occurs via ingestion of earthworms that contain infectious L1 larvae. L1 larvae progress to L2 larvae in the wall of primary host's small intestines, and remain there eight to ten days after infection. L3 larvae then migrate to the glomeruli, and then to the ureters and urinary bladder. It is assumed the larvae arrive in the urinary bladder *via* blood vessels. In the urinary bladder, L3 and L4 larvae can be found 33 days after the onset of infection, and these larvae mature to adult forms and fixate onto the urinary bladder mucosa (Callegari et al., 2010). The adult then reproduces in the urinary bladder, in which the females excrete eggs. Thereafter, around day 60, eggs are eliminated through urine. Eggs can be isolated from the urine of primary hosts about two months after ingestion of infected earthworm (Rossi, 2011).

The life cycle of this parasite continues when a primary host ingests earthworm containing infectious larva. It is assumed that an alternative path of infection can be ingestion of soil contaminated with larvae, originating from decomposed earthworms (Pagnoncelli et al., 2011).

Callegari et al. (2010) indicated *C. plica* could contribute to the occurrence of glomerular amyloidosis in dogs. A consequence of the infection could be deposition of amyloids and stimulation of an inflammatory response over long times (Callegari et al., 2010). Infection of an eight-year-old hunting terrier was described in Italy. Pathohistological examination showed chronic interstitial nephritis and glomerular amyloidosis, with chronic inflammation of the urinary bladder and renal pelvis, and with mononuclear cells infiltrating the submucosa (Callegari et al., 2010). Mariacher et al. (2016) found disseminated fields of tubular necrosis.

Clinical signs

Infection is mostly asymptomatic and remains unnoticed, which is why there is a small number of reported cases in dogs and cats (Basso et al., 2014). The reasons behind this are the parasite's life cycle and the fact that making a correct diagnosis within the patient's lifetime is complicated. The infection is self-limiting, and over time there is a reduction in the number of eggs excreted until they can no longer be detected in the urine, i.e. after about 2.5 months (Senior et al., 1980; Engik, 1950). The absence of clinical signs can be an after-effect of a small number of parasites in the urinary tract or their superficial fixation on mucosa of the urinary bladder (Bowman et al., 2002; Kruger and Ozborne, 1993).

In dogs and cats with clinical symptoms, pollakiuria, dysuria, haematuria, polydipsia, incontinence and fever can be present (Basso et al., 2014; Rossi et al., 2011; Senior et al., 1980; Meadway and Skelley, 1961). The literature data about infection in cats shows a connection between urinary capillariosis with clinical signs such as abdominal pain, fever, incontinence, dysuria and cystitis, which require adequate symptomatic therapy, as well as anthelmintic treatment (Pagnocelli et al., 2011; Rossi et al., 2011; Whitehead, 2009). Clinical cases of urinary capillariosis in dogs were documented in the USA (Senior et al., 1980; Kirkpatrick and Nelson 1987) France (Cazelles et al., 1989), Switzerland (Basso et al,. 2014; Spillman and Glardon, 1989), Netherlands (van Veen, 2002), Poland (Studzińska et al., 2015) and Italy (Maurelli et al., 2014; Callegari et al., 2010).

Pets that have limited contact with the environment are rarely exposed to infection, as opposed to hunting dogs. The main risk factor for dog infections is hunting, and the main source of infections is the fox. In foxes (Fernandez-Aguila et al., 2010), cystitis was found with haematuria and possible pyelonephritis caused by secondary bacterial infection, anorexia, dysuria and slow growth (Bowman, 1999). In silver foxes, cystitis with hyperaemic, thickened urinary bladder mucosa and reproductive disorders was reported (Watkins and Harvey, 1942; Volkmar, 1930).

Diagnosis

Diagnosis of urinary capillariosis in dogs is generally set as an accidental finding; urine sediment examination can show many struvite crystals, red and white blood cells, bacteria and parasite eggs (Studzińska et al., 2015). Considering that female parasites only periodically excrete eggs, it is not always possible to set a diagnosis this way, despite the presence of infection (Kirkpatrick and Nelson, 1987). Since egg excretion varies and the sensitivity of the urine sediment examination is low, more than one urine sediment examination is recommended (Knaus et al., 2014). Definite diagnosis is set through endoscopy, or more often *via* detection of eggs in the urine sediment (Basso et al., 2014).

Urine analysis is performed only in cases with clinical signs present that indicate infection. Suspicion can be raised by symptoms connected with urinary bladder

inflammation, sporadic kidney dysfunction, haematuria, dysuria or pollakiuria (Callegari et al., 2010; van Veen, 2002), increased numbers of epithelial cells in urine sediment, or ultrasound or radiological examination. Urine analysis can show slight proteinuria, while microscopic examination can show haematuria and an increased number of transitional epithelial cells (Bowman, 1999; Wilson-Hanson and Prescott, 1982; Senior et al., 1980).

False negative results are possible even in cases of symptomatic infections due to the long prepatent period, irregular excretion of eggs, small number of eggs, and difficulties in detecting immature or atypical eggs (Basso et al., 2014; Maurelli et al., 2014; Rossi et al., 2011; Senior et al., 1980).

From a diagnostic aspect, novel, highly sensitivity techniques include flotation solutions (FLOTAC and Mini-FLOTAC). They are considered important diagnostic methods for egg detection of gastrointestinal parasites in dogs (Lima et al., 2015; Cringoli et al., 2010), and those techniques were used for detection of *C. plica* eggs in dogs in Italy (Maurelli et al., 2014). Lima et al., (2016) indicated that FLOTAC could increase the probability of correct diagnosis of urinary capillariosis in dogs. Mini-FLOTAC has shown better results than the classical sedimentation technique and could be used instead of FLOTAC in laboratories that cannot centrifuge urine (Lima et al., 2016).

The high prevalence of foxes with urinary capillariosis in Europe and their colonization in urban areas increases the probability of infection in domestic dogs and cats, so in cases of urinary pathology, the possibility of infection with *C. plica* should be considered in differential diagnosis (Basso et al., 2014). This disease has importance in small animal practice and clinicians should include it in differential diagnosis of carnivore diseases of urinary aetiology.

In differential diagnosis, the nematode *Dioctophyma renale* (giant kidney worm) must be excluded, as this can also be found in the dog urinary tract and is a commonly detected species (Mesquita et al., 2014). It is important to bear in mind that this parasite rarely occurs in dogs in Central Europe. It is possible to differentiate *D. renale* and *C. plica* eggs through microscope examination. *D. renale* eggs are elliptical with a thick, rough membrane and apparent bipolar, symmetrically lined plugs. Egg colour varies from transparent to brownish-yellow and dimensions are 60-84 × 39-52 μm (Lima et al., 2016).

After manifestations of oliguria and dysuria, some symptomatically similar diseases should be excluded, such as acute and chronic renal insufficiency, urolithiasis, prostate hyperplasia, feline urological syndrome (FUS), cystitis with other aetiology (for example bacteriological) etc. Mariacher et al. (2016) pointed out the importance of urinary capillariosis in differential diagnosis of chronic and recurrent diseases of the lower urinary tract and kidneys.

Clinicians should be careful and bear in mind the possibility of false negative results, which can occur on urine sediment examination of a symptomatic patient. Reasons for this are the low method sensitivity and the parasite's biology. Since asymptomatic

infection can occur, routine urine sediment examination is recommended for all suspicious dogs, regardless of symptoms.

In infected dogs, ultrasound examination can show a hyperechoic and thickened urinary bladder wall, and endoscopy of the urinary bladder can detect parasites fixated to mucosa (Basso et al., 2014). However, for correct diagnosis and urinary capillariosis monitoring, techniques with higher sensitivity will need to be developed and adopted in the future (Mariacher et al., 2016).

Clinicians in rural areas should include *C. plica* in their differential diagnosis of suspect dogs, considering these patients are exposed to the risk of direct contact with red foxes (Ilić et al., 2017b). This is similar to the principle by which cardiopulmonary metastrongilosis is included in differential diagnosis for dogs that live in rural areas (Ilić et al., 2017b).

Treatment

The treatment of choice for this nematode is not yet determined, but there are reports of one-time treatments with the following medications: fenbendazole (Deplazes et al., 2013; Rossi et al., 2011; Deplazes et al., 2006; van Veen, 2002; Brown and Prestwood, 1986), albendazole (Deplazes et al., 2006; Senior et al., 1980), levamisole (Bowman et al., 2004) and ivermectin (Deplazes et al., 2006; Kirkpatrick & Nelson, 1987).

Treatment with fenbendazole is not always successful, as was documented in the case of a dog that, after unsuccessful use of fenbedazole, was successfully treated with ivermectin afterwards (Studzińskaet al., 2015). Literature data confirms fenbendazole (50 mg/kg) and ivermectin (0.2 mg/kg) as an effective treatment for dogs with urinary capillariosis, with mandatory urine sediment control examinations and repetition of treatment depending on results shown by urological diagnostics (Basso et al., 2014). Basso et al. (2014) stated that treatment with fenbendazole and ivermectin caused short-term improvement, while levamizole, metabolites of which are excreted by the urine in 94% of cases, was more effective (Studzińska et al., 2015).

Knaus et al. (2014) studied the treatment effectiveness of a drug combination: fipronil 8.3% (w/v), methoprene 10% (w/v), eprinomectin 0.4% (w/v) and praziquantel 8.3% (w/v) for treatment of cat urinary capillariosis (Studzińskaet al., 2015). The study involved sixteen shorthaired European cats (5 male, 11 female) in which urine *C. plica* eggs were diagnosed before treatment (Knaus et al., 2014). Every cat in the treated group received the combined treatment (10 mg fipronil + 12 mg methoprene + 0.5 mg eprinomectrin + 10 mg praziquantel per kilogram of body weight), in a minimal therapeutic dose of 0.12 ml/kg of body weight. Cats that did not receive treatment maintained *C. plica* eggs in their urinary bladders (4-12 parasites). In all eight cats treated with the drug formulation, parasites were not found, showing this combination of drugs was 100% effective for treatment of urinary capillariosis in cats (Knaus et al., 2014). This drug combination is the first containing macrocyclic lactones (eprinomectrin) with proven effectiveness in cat urinary capillariosis under

controlled conditions. Rehbein et al. (2014) affirmed this combined treatment as being highly effective for capillariosis treatment in cats, finding decreased numbers of eggs excreted *via* feces. The study was conducted in cats from seven European countries, and the authors concluded the Trichuridea type eggs diagnosed in the cats' faeces originated from capillaries located in the respiratory tract but not the urinary bladder.

Prophylaxis

One of the main risk factors for the occurrence of urinary capillariosis in dogs is likely to be hunting. This claim is supported by results of epidemiological studies on foxes in which the prevalence of this nematode ranged from 50% to 80% (Saeed et al., 2006). Therefore, foxes are probably the main source of infection for hunting dogs (Callegari et al., 2010).

For the purpose of prophylaxis, the risk of pet infections with this nematode can be lowered by keeping dogs and cats in enclosed spaces, restricted yards or on a leash. This should limit the possibility of *C. plica* infection *via* earthworms or intermediate or paratenic hosts.

In public dog shelters where urinary capillariosis is an endemic disease, appropriate measures to avoid infections and reinfections from environment must be taken. From an epizootiology point of view, adequate pads raised above ground or sand or grit instead of soil must be provided, so earthworm ingestion is prevented, and the parasite's life cycle is interrupted (Callegari et al., 2010).

CONCLUSION

From the aspect of pet carnivores' health care, it is extremely important to be familiar with basic morphological, biological and epizootiological characteristics of urinary capillariosis in these patients. Considering the evident increased prevalence of this disease in the last ten years in dogs and cats in Europe and worldwide, *C. plica* infection is important for small animal practices, and it is recommended clinicians include it in their differential diagnosis of carnivore diseases with urinary aetiology.

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Authors contributios

IT, RM, GB and AJ were participated in the design of the study, conceived of the study, and participated in its design and coordination and helped to draft the manuscript.

All authors read and approved the final manuscript.

Competing interests

The authors hereby declare that they have no competing interests.

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URINARNA KAPILARIOZA KOD PASA

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Kratak sadržaj

Uvod. Urinarnu kapilariozu pasa uzrokuje *Capillaria plica* (syn. *Pearsonema plica*), ubikvitarna nematoda končastog oblika iz familije *Capillariidae*. Uzročnik parazitira u mokraćnoj bešici kanida, felida i mustelida, a može da se ustanovi u ureterima i bubrežnoj karlici. *Capillaria plica* ima indirektan životni ciklus koji uključuje kišne gliste (*Lumbricina*) kao prelazne domaćine i domaće i divlje životinje (pas, mačka, lisica, vuk) kao prave domaćine. Infekcija pravog domaćina nastaje unošenjem kišnih glista koje sadrže infektivnu larvu prvog stadijuma (L1). Pretpostavlja se da alternativni put infekcije za životinje može da bude ingestija zemljišta kontaminiranog infektivnim larvama poreklom od kišnih glista koje su podlegle procesu dekompozicije. Infekcija je najčešće asimptomatska, a u slučaju ispoljavanja kliničke slike simptomi su polakiurija, disurija, hematurija, polidipsija, inkontinencija urina i groznica

Cilj i pristup. Cilj rada je da pruži informacije o morfologiji, biologiji i epizootiologiji nematode *Capilaria plica* kao i da ukaže na mogućnost postojanja infekcije kod lovačkih

i nevlasničkih pasa. Zbog značaja oboljenja za kliničare i povećanja prevalencije tokom poslednje decenije u zemljama u okruženju, u radu su iznete najnovije informacije o patogenezi, kliničkim simptomima, dijagnostici, lečenju i prevenciji ove nematodoze.

Ključni nalazi i zaključak. Dijagnoza kapilarioze se najčešće postavlja slučajnim nalazom parazita zbog nespecifične kliničke slike. U slučaju sumnje na oboljenja urinarnog trakta, treba diferencijalno dijagnostički isključiti latentnu infekciju ovom nematodom.

Ključne reči: *Capillaria plica*, pas, mokraćna bešika, analiza urina