

## Case Report

# Giant kidney worm: novel report of *Diocotophyma renale* in the kidney of a dog in Greece

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### Summary

*Diocotophyma renale* is the largest nematode that infects domestic mammals and is the aetiologic agent of a serious renal disease, diocotophymatosis. It has an indirect life cycle with carnivores serving as final hosts and earthworms as intermediate hosts. The parasite can infect humans with significant zoonotic potential. The pathogenesis of diocotophymatosis is mainly associated with the extent of renal atrophy caused by the parasites, the risk of bilateral renal infestation and the location of the parasite (extrarenal cases). Clinical diagnosis is challenging, and the only treatment option is nephrectomy or nephrotomy to remove the adult nematode. A 6-year-old female crossbreed dog presented with tachypnea, tachycardia and severe hematuria, but died shortly after presentation. Postmortem examination found the right kidney was enlarged and two adult nematodes were found in the renal pelvis. The left kidney was normal. The nematodes were collected and submitted for identification. The two specimens were identified as *D. renale* using specific identification keys. Herein we present the first case of renal parasitosis by the nematode *D. renale* in a dog from Greece. This case highlights the need for investigation of the actual prevalence of the parasite and the use of measures for the control of its expansion aiming the protection of dogs and public health.

**Keywords:** *Diocotophyma renale*; kidney; nematode; dog; Greece

### Introduction

*Diocotophyma renale* (Goeze, 1782), is a parasitic nematode that belongs to the order of Ascaridida and the family of Diocotophymatidae (Bowman, 2014). This parasite has a wide distribution and is also known as the giant kidney worm due to the “gigantic” dimensions of the adults; a female may measure more than 60 cm length and 1 cm diameter. It is the largest nematode that infects domestic mammals and is the aetiologic agent of a serious renal disease, diocotophymatosis. *D. renale* has been described in many different mammalian species as well as humans, highlighting the zoonotic

importance of this parasite (Norouzi *et al.*, 2017; Venkatrajaiiah *et al.*, 2014). The most frequent definitive hosts are mustelids (especially minks), although there are also other wild carnivores such as otters, martens and raccoons that may be infected. Among domestic mammalian hosts, dogs are most frequently affected, but it has been also reported in other domestic animals, such as felines, swine, cattle and horses (Bowman, 2014; Ribeiro *et al.*, 2009; Verocai *et al.*, 2009).

*D. renale* has a complex life cycle and requires two intermediate hosts. The prepatent period is approximately 155 days and the entire life cycle can take up to two years to complete (Dyer, 1998;

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Ferreira *et al.*, 2010). The adult nematodes parasitize, mature and produce eggs in the renal pelvis of the final mammalian host. Eggs are passed through urine into the environment and they are ingested by the first intermediate host, an aquatic oligochaete annelid (e.g., *Lumbriculus variegatus*) (the common mud worm). The eggs hatch inside the intermediate host and start the development of the first and second larval stages. From this stage on, there are three potential routes of transmission. In the first case, the development and maturation to the third and fourth stage larva (the infective stage) takes place inside the same intermediate host, the aquatic oligochaete annelid and mammalian hosts become infected when they ingest the infected intermediate hosts. In the second case scenario, annelids containing the second stage larvae may be ingested by a fish or a frog, where the larvae develop into the final infective stage and encyst in the tissues of these hosts. In this case the mammalian hosts acquire the infection by consuming fish or frogs infected with the fourth-stage larvae. The third potential route of transmission is when the infected annelids parasitize on a cray fish (*Cambarus* spp.) and they are ingested by a fish or a frog. However, some investigators propose that fishes and frogs may act more likely as mechanical vectors or transporters rather than actual intermediate hosts (Dyer, 1998). In each of the above-mentioned scenarios, the definitive host becomes infected by ingesting the fourth-(infective) stage larvae. Inside the definitive host, the *Diocotophyma* larva penetrates the intestinal or duodenal mucosa, enters the peritoneal cavity and migrates to the kidney, where it develops and matures into the adult form (Bowman, 2014; Pedrassani *et al.*, 2017). Adults are able to live up to 3 years in the definitive host and the fertilized eggs that are shed into the environment may survive for up to 5 years (Radman *et al.*, 2017). *D. renale* nematodes are most commonly found inside the renal pelvis where they mature, however they can also be encysted within the abdominal cavity, the uterus, ovary, mammary gland, urethra, subcutaneous tissues of the inguinal region and in the mesenteric lymph nodes (Bowman, 2014; Nakagawa *et al.*, 2007). Most cases have unilateral renal colonization, most frequently the right kidney, due to the anatomic proximity to the duodenum (Bowman, 2014). Diocotophymatosis in dogs is a parasitic disease that results in compressive atrophy of the renal parenchyma of the infected kidney, dilation of the renal pelvis and ureteral obstruction due to the size of the parasite colonizing the renal pelvis space. However, the main pathologic finding is the progressive destruction and atrophy of the renal parenchyma, resulting in a cystic structure containing the adult worms in a hemorrhagic exudate with only a thin capsule remaining of the original renal parenchyma (Nakagawa *et al.*, 2007; Soler *et al.*, 2008). Renal failure may not be evident when only the one kidney is affected, due to adequate compensation by the unaffected kidney, although gross or microscopic hematuria may be detectable. Rarely if bilateral infection occurs, clinical renal failure is inevitable, resulting in end stage kidney disease and death. If the parasite establishes an extrarenal location within the abdominal cavity, ab-

dominal distension, pain and peritonitis may be develop. However, most of the reported canine diocotophymatosis cases were asymptomatic (Ferreira *et al.*, 2010).

Several clinical diagnostic methods for the detection of *D. renale* infection are available. The analysis of urine sediment is most commonly used to detect *D. renale* eggs, which is a low-cost with high sensitivity and specificity technique. Other reported diagnostic techniques include advanced imaging techniques (Nakagawa *et al.*, 2007; Soler *et al.*, 2008) and enzyme-linked immunosorbent assay (ELISA) for the detection of anti-*Diocotophyma renale* antibodies (Pedrassani *et al.*, 2015). However as many cases are asymptomatic, most of the reported cases rely on postmortem diagnosis of canine diocotophymatosis (Ferreira *et al.*, 2010). Treatment of canine diocotophymatosis remains challenging for veterinary practitioners. Surgical removal of the nematodes is recommended with ureteronephrectomy for unilateral infection or bilateral nephrotomy for bilateral infections (Ferreira *et al.*, 2010). At the current time, there has been no report of canine diocotophymatosis in Greece, and only one confirmed case of human infection (Katafigiotis *et al.*, 2013). The primary aim of this case report is to present the first confirmed case of renal parasitosis by the nematode *D. renale* in a dog from Greece and secondly to highlight the zoonotic potential of this infection in countries where it has not been previously reported and is unlikely to be detected ante-mortem.

## Case report

A 6-year-old female mixed breed dog of 27 kg body weight was presented with a history of lethargy, muscle weakness and severe hematuria to a veterinary clinic in the city of Xanthi, northern Greece. The owners reported weight loss and hematuria. The dog lived in a farmhouse located in the sub-rural area of Xanthi and was allowed free range activity in the area around the farm but had not travelled outside of Greece. There was a river and water sources in the local vicinity.

At clinical examination the dog presented with tachypnea (60/min), tachycardia (140 – 170/min), and hyperemic oral mucosa (> 2 – 3 min capillary refill time). The dog was slightly pyrexia with a body temperature of 39.2 °C. Following clinical examination, urinalysis, complete blood count (CBC) and serum biochemistry were performed. Urinalysis revealed severe hematuria, but no evidence of bacteriuria or infection. Microscopy of the sediment failed to show any evidence of parasitic infection or ova. Significant serum biochemistry findings were azotemia with serum creatinine of 3.8 mg/dL (reference value: 0.8 – 1.8 mg/dL), serum urea of 49 mg/dL (reference value: 15 – 40 mg/dL), and all other parameters were within normal ranges. The hematologic profile of the patient revealed leukocytosis (> 50 x 10<sup>9</sup> WBC/L) with left shift neutrophilia, microcytosis and anisocytosis. Serological analysis for the detection of the antigen of the nematode *Dirofilaria immitis* and the specific antibodies against the pathogens *Anaplasma platys*/

*phagocytophilum*, *Ehrlichia canis/ewingii* and *Borrelia burgdorferi* were also performed using specific in-clinic rapid enzyme-linked immunosorbent assay (ELISA) kit (SNAP® 4Dx® from IDEXX® Laboratories, Westbrook, Maine, USA), according to the manufacturer instructions. The results of this examination revealed seropositivity only to *D. immitis*.

Emergency supportive treatment was initiated with intravenous fluid therapy Lactated Ringer's solution (Vioser S.A., Greece) at 10 ml/kg/hr however the dog suffered a cardiac arrest and was not resuscitated. The following day, a postmortem examination was performed. The pleural and the abdominal serosal surfaces appeared normal. In the thorax, the lungs appeared normal, however the heart appeared generally enlarged. Internal examination of the heart found about 45 whiteish nematodes later identified as adults of *D. immitis*, positioned in the right side of the heart from

the right atrium, the caval opening and the apex of the right atrial appendage. On inspection of the abdominal cavity, all the visceral organs appeared normal. However, the right kidney was enlarged and soft on palpation, with a cystic appearance. (Fig. 1). The left kidney was normal. During examination and opening of the left kidney, two large nematodes were found (Fig. 2). The entire renal structure was destroyed and there was a thin outer capsule. The two nematodes were collected and placed in saline solution and sent to the Laboratory of Parasitology and Parasitic Diseases of the Aristotle University of Thessaloniki, Greece. At the laboratory, the two specimens were examined under the stereoscope and identified using specific identification keys (Bowman, 2014). The two nematodes were identified as a pair of female and male *D. renale* measuring 58 cm long and a maximum of 4.2 mm width and 23 cm long and 2.9 mm width maximum respectively.

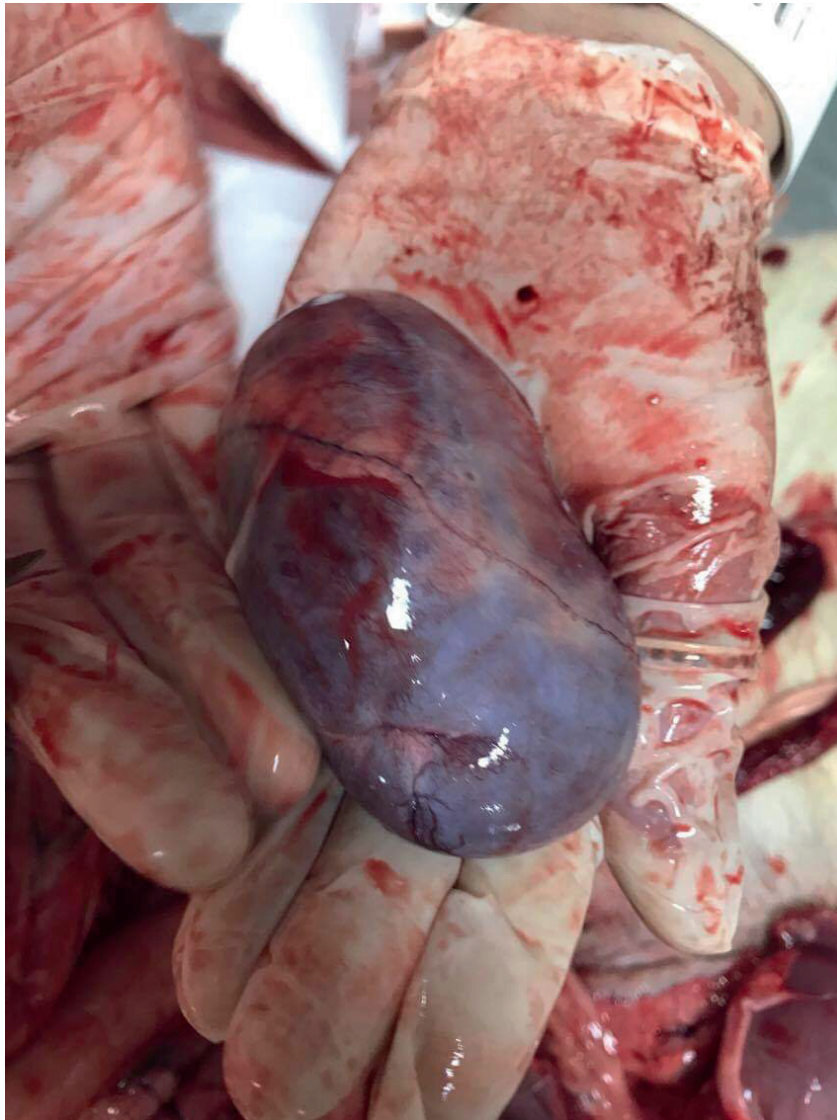


Fig. 1. Enlarged right kidney of the infected dog.





Fig. 2. *Diocotophyma renale* adult parasites recovered at the *post mortem* examination of the right kidney.

## Discussion

Canine diocotophymatosis is a rare parasitic disease that poses serious threat for the canine health as well as for public health due to the zoonotic significance. The majority of reported cases come from the cold temperate regions where freshwater is available, as its life cycle requires an aquatic environment. Brazil is the country with the highest number of reported *D. renale* cases in domestic dogs with prevalence rates up to 14.2% (Ferreira *et al.*, 2010; Nakagawa *et al.*, 2007; Pedrassani *et al.*, 2017; Rappeti *et al.*, 2017). Canine diocotophymatosis has also been reported recently in other Latin America countries, such as Colombia (Florez *et al.*,

2018) and Argentina (Radman *et al.*, 2017). Recent studies have also reported *D. renale* in dogs in Iran (Vafae Eslahi *et al.*, 2017; Zolhavarieh *et al.*, 2016). In the European continent, the parasite has been reported sporadically in several countries, i.e. France, Holland, Germany, Bulgaria, Romania, Italy, Poland, Spain and former USSR (Smits *et al.*, 1965; Measures, 2001; Soler *et al.*, 2008).

Until recently, there was no officially reported case of canine *D. renale* infection in Greece. However, in 2013 a scientific team from the University hospital in Athens reported for the first time a rare and life-threatening human case of *D. renale* infection (Katafigiotis *et al.*, 2013). Human infection with *D. renale* is rare and is usually as-

sociated with the consumption of raw fish, however human cases have been reported in China (Yang *et al.*, 2019; Yang *et al.*, 2016), India (Chauhan *et al.*, 2016; Venkatrajaiah *et al.*, 2014), Iran (Norouzi *et al.*, 2017), and the USA (Kuehn *et al.*, 2016).

The present case of canine dirofilariasis presented with severe hematuria and general lethargy, typical symptoms of a *D. renale* infection (Taylor *et al.*, 2017). However, these symptoms are very nonspecific and parasitic infection would not be immediately suspected in countries where the disease is not prevalent. The clinical history was significant in that the animal lived in close vicinity and had free access to fresh water sources that facilitates the transmission route of the parasite. However, this patient also presented with severe tachypnea and tachycardia, clinical symptoms that were more likely to be secondary to the simultaneous infection with *D. immitis*. It is possible that the co-existence of these two pathogenic parasites in this host proved fatal for the animal. The pathogenesis and prognosis of untreated cardiopulmonary dirofilariasis is more severe and acutely life-threatening when compared to dirofilariasis. At the post-mortem examination of the dog, the two giant worms, were retrieved from the right kidney, which was destroyed. As it was expected, the left kidney was normal due to the fact that the right kidney (close vicinity with the duodenum) is mostly infected by the nematodes (Bowman, 2014). At the time of presentation of this dog to the emergency clinic, *D. renale* had not previously been reported in the veterinary literature regarding Greece and therefore treatment efforts were focused on the most likely infection which was dirofilariasis and the renal infection was only identified at postmortem examination. Canine dirofilariasis is a serious disease with poor knowledge of any effective anthelmintic treatment. Surgical excision is the treatment of choice, however the prognosis is very poor, and the majority of animals, if symptoms appear, die soon after the etiological diagnosis. The only known prophylaxis consists of avoiding consumption of fresh-water fish or the other hosts (Beugnet *et al.*, 2018).

Finally, it is of concern that, according to the owner, the dog had no history of travelling outside the country or living in close vicinity with dogs imported from other countries, confirming the autochthonous character of this infection. Similarly, the human case that was previously reported in Greece (Katafigiotis *et al.*, 2013) was also described as autochthonous. Consequently, these cases have a significant importance in terms of epidemiology as they both support the hypothesis that this parasite circulates within the Greek canine or wildlife population, which is extremely important with respect to public health.

## Conclusion

Dirofilariasis is a life-threatening disease with severe clinical manifestations and guarded prognosis in dogs as well as in humans. The presence of this nematode infection both in dogs and humans in Greece stresses its zoonotic importance in terms of public health. Veterinary and medical practitioners should be

aware of this disease and include it in the differential diagnosis in cases presenting with hematuria. A large-scale epidemiological study must be conducted in the country in order to estimate the accurate prevalence of this parasite and address possible risk factors that are associated with it.

## Ethical Approval and/or Informed Consent

For this study formal consent is not required.

## Conflict of Interest

Authors state no conflict of interest.

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