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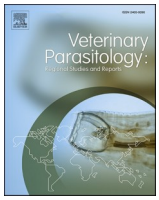

Case Report

Case report: Infection with *Dicrocoelium dendriticum* in a Japanese Chin dog

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ABSTRACT

Dicrocoelium dendriticum is a trematode colonising the bile ducts of herbivores. Coproscopic findings in dogs are usually considered gastrointestinal passages of eggs after ingestion of unheated liver tissue or infected ruminant faeces. Here, a Japanese Chin presented with diarrhoea and weight loss. Eggs comparable to *D. dendriticum* were detected in faeces and infection was confirmed via PCR and by ruling out differential diagnoses. Egg excretion continued for a period of 10 months. Praziquantel (50 mg/kg body weight [BW]) was administered orally for four consecutive days. Egg excretion 10 days after treatment entailed further treatments with 100 mg/kg BW, again for four days. Faecal samples were negative ten days and four weeks afterwards, diarrhoea resolved, and the dog gained weight. In cases of repeated coproscopic positivity for *D. dendriticum*, an infection with dogs acting as definitive hosts should be considered. Treatment with praziquantel at a higher dosage may be required.

1. Introduction

Dicrocoelium dendriticum (Trematoda, Dicrocoeliidae) is a parasitic trematode with a worldwide distribution. A variety of mammal species, predominantly herbivores, have been identified as definitive hosts. Occasionally, pigs, dogs, and humans can be affected (Nesvadba, 2006; Capucchio et al., 2009; Jeandron et al., 2011). In Switzerland, *D. dendriticum* is a common parasite of cattle and small ruminants (Schweizer et al., 2003; Eichenberger et al., 2013). Adult stages of *D. dendriticum* live in the bile ducts and gall bladder of the definitive host. Infections often are subclinical or may be accompanied by mild clinical signs. In aberrant hosts such as humans, although rare, infections with *D. dendriticum* have been associated with abdominal pain, vomiting, weight loss, and chronic diarrhoea (Singh Rana et al., 2007; Cengiz et al., 2010;). In dogs, Nesvadba (2006) reported anorexia, weight loss, vomiting, diarrhoea, and reduced performance. Here, we report a case of infection with *D. dendriticum* in a Japanese Chin dog acting as accidental definitive host.

2. Case presentation

A two year old female Japanese Chin dog with a body weight (BW) of 2.3 kg presented with a history of weight loss and intermittent, mucous, occasionally bloody diarrhoea. The dog was kept with a companion dog of the same breed in a household located in a rural environment with abundant small ruminant husbandry. Both dogs were fed a conventional, processed, canned diet based on goat mono-protein. Anthelmintic treatments had not been carried out on a regular basis. A faecal sample was submitted for coproscopic, parasitological examination and resulted in the detection of trematode eggs of the *D. dendriticum* type. Gastrointestinal passage of parasite eggs ingested via coprophagy of ruminant faeces appeared most likely. Yet, differential diagnosis included a potential infection with trematodes such as *Dicrocoelium* spp., *Metorchis* spp., or *Opisthorchis* spp. Moreover, gastrointestinal passage of parasite eggs from the aforementioned diet was considered. A comprehensive anamnestic interview with the owner revealed no history of access to aquatic life such as fish, frogs and others, ruling out infection with *Metorchis* sp. or *Opistorchis* sp. Since canned pet food undergoes heat treatment and sterilisation (EC Regulation, 2002; Roberts et al., 2005; Zicker, 2008), and with lack of history of feeding raw liver, these alternative sources of trematode eggs could be ruled as a cause for gastrointestinal passage.

To further exclude gastrointestinal passage of eggs, faecal samples of the dog were collected over four consecutive days. During this period, owner compliance was very high: the dog was not unleashed when walked, did not have unsupervised time outside and could not ingest anything other than its own food. Faecal samples were subjected to a combined sedimentation-flotation procedure using saturated sodium-chloride solution with a specific weight of 1.2 g/cm^3 (Deplazes et al., 2021). Thus, the presence of trematode eggs resembling *D. dendriticum* with a size of 44 µm × 50 µm was confirmed in every single faecal sample (two faecal samples per day) of the four days collection period

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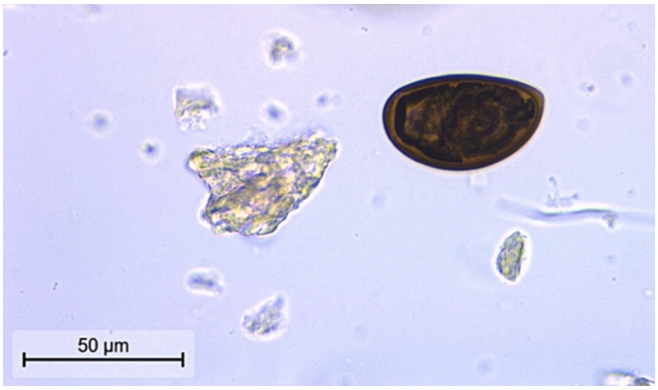

Fig. 1. Trematode egg confirmed as *Dicrocoelium dendriticum* (44 µm × 50 µm).

(Fig. 1). Eggs from the flotate were filtrated, DNA was extracted using the QIAmp® Fast DNA Stool mini kit (Quiagen, Hilden, Germany) starting with alkaline lysis (Mathis et al., 1996; Stefanić et al., 2004), after which the kit's manufacturer's instructions were followed. A *D. dendriticum*-specific PCR (primers: DdmtDNA For 5′ GGTGTCCCGAAAGGTAGTGA 3′; DdmtDNA Rev. 5′ TCACCAATCACCTCAAAGCA 3′) was conducted amplifying a sequence of 170 base pairs as part of the Cox1 gene (Martínez-Ibeas et al., 2011; Mitchell et al., 2017). The amplicons were purified using the MiniElute PCR Purification Kit (Qiagen, Hilden, Germany), the DNA was quantified with Nanodrop (Thermo Fisher Scientific) and sequenced unidirectionally using Sanger technology (Microsynth AG, Balgach, Switzerland). All obtained sequences were compared with the ones in the GenBank™ nucleotide database, using BLAST search (http://www.blast.ncbi.nlm.nih.gov). After comparison with GenBank™ accession number JF690758.1 an agreement of 100% could (170/170 bp) be yielded which confirmed an infection with *D. dendriticum*.

The owner decided not to treat the dog in the first place. However, after an apparent improvement of the clinical signs, after 10 months the dog again presented with the aforementioned symptoms. Blood chemistry and liver enzyme analyses did not reveal abnormalities. Parasitological examination as described above, instead, re-confirmed the presence of *D. dendriticum* eggs and a corresponding infection. Accordingly, the dog was treated orally with praziquantel 50 mg/kg BW (Caniquantel Plus S®, Gräub AG, Bern, Switzerland) over four consecutive days as suggested by Nesvadba (2006). Since the dog still excreted eggs ten days after termination of treatment, a second round of oral praziquantel at a dosage of 100 mg/kg BW was initiated for four days which resulted in resolution of egg excretion ten days and four weeks after termination of treatment. Furthermore, clinical signs disappeared.

3. Discussion

D. dendriticum has been confirmed in a variety of host species (Nesvadba, 2006; Capucchio et al., 2009; Jeandron et al., 2011). Reports of infections in dogs yet have been very scant and the detection of *D. dendriticum* eggs has mainly been regarded as gastrointestinal passage following raw liver ingestion or coprophagy of infected ruminant faeces (Burger et al., 2006; Nesvadba, 2006). Yet, dogs often ingest grass and therefore a risk of infection is plausible. In the present case, gastrointestinal passage seemed most probable in the first instance. Due to exclusion of these options through high owner compliance ensuring no ingestion of material potentially containing eggs, we verified this dog being infected with *D. dendriticum,* especially given the fact that the dog remained coproscopically positive ten months after initial diagnosis. Furthermore, clinical problems resolved after the second successful round of anthelmintic treatment. Coproscopic positivity for eggs after the first round of treatment could also have been due to protracted excretion of eggs stored in the gall bladder being intermittently released via the bile rather than the oral dosage of 50 mg/kg BW of praziquantel not being efficacious.

In herbivores, clinical signs of dicrocoeliosis can be absent even in cases of high infection levels (Rojo-Vázquez et al., 1981). In the present case, the dog suffered from diarrhoea and weight loss which have also been observed by Nesvadba (2006).

Since reports on dicrocoeliosis in dogs were limited, we initially decided to align with Nesvadba (2006). The dog was then negative after the second round of treatment with a higher dosage of the compound. In this context it is important to evidence the off-label use of praziquantel for an administration for four consecutive days and at doses of 50 mg/kg BW or 100 mg/kg BW, respectively. Praziquantel is usually well tolerated, but trematode infections require high doses for effective treatment. For example, a dose of 50 mg/kg BW has commonly been used in *D. dendriticum* infections in south American camelids (Dadak et al., 2013). Moreover, praziquantel has been proven an effective compound in other trematode infections (Kirkpatrick and Shelly, 1985; Ouldabdallahi et al., 2013) and in general is characterised by a high therapeutic tolerance and a very low level of acute toxicity. In dogs, toxicity at most might translate into occasional vomiting at a dosage of 50–200 mg/kg BW (Murmann et al., 1976; Shmidl et al., 1981; Andrews et al., 1983). As for the present case, it is important to be aware that praziquantel was not available as a monopreparation for the use in dogs in Switzerland, in contrast to camelids where it can be applied as a highly concentrated monopreparation (Dadak et al., 2013). Therefore, a formulation also containing fenbendazole was chosen for treatment. Given the aforementioned treatment regime, the dog hence also received a very high dose of fenbendazole, i.e. ten times the amount of praziquantel in the used formulation. Fenbendazole has a high therapeutic index: for instance, Willesen et al. (2007) observed mild side effects related to the gastrointestinal tract, i.e. vomiting or diarrhoea in dogs treated with fenbendazole at a dose of 25 mg/kg BW for 20 days. In the present case, the patient showed no side effects of treatment except for slightly loose faeces on the last day of the four day administration regime. Regardless, a thorough clinical surveillance is recommended in patients receiving high dosages of anthelmintic compounds or off-label use as described in the present case.

As prolonged egg excretion despite successful treatment cannot be ruled out completely, for future cases starting anthelmintic treatment with 50 mg/kg BW of oral praziquantel for four consecutive days may be recommended, with the option to increase the dosage in case of persistent infection.

4. Conclusions

D. dendriticum is rarely detected in dogs, despite broad use of flotation solution with higher (> 1.3) specific gravidity (i.e., zinc choride or zinc sulfate). Accordingly, little is known regarding the frequency of clinical signs in infected dogs. In the present case, blood chemistry and analysis of liver enzymes were not indicative for liver damages, but clinical signs related to the gastrointestinal tract were supporting an infection with this parasite. Comprehensive clinical evaluation should be conducted in confirmed infections with *D. dendriticum* in dogs to identify affected organs and prevent more severe outcomes.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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