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Tetrathyridiosis in a domestic shorthair cat

Dorothee Dahlem[1], Berit Bangoura[2], Eberhard Ludewig[3], Nicole Glowienka[4], Katrin Baldauf[5], Frank Stoeckel[6] and Iwan Burgener[7]

Abstract

Case summary This report describes the clinical and parasitological findings in a domestic shorthair cat with isolated thoracic tetrathyridiosis. The cat was a stray from Malta that had lived in Germany for several years since as an indoor-only cat. Therefore, the process of infection remains very unusual. In this case it must be considered that the cat had been infected years previously while in Malta, and had lived at least 4 years without any clinical signs. It was possible to diagnose this uncommon disease and initiate an effective treatment with fenbendazole, praziquantel and supportive care. Clinical signs, as well as radiographic findings, were regressive with this treatment.

Relevance and novel information Tetrathyridiosis is a rare finding in cats, especially in Germany, but it seems to be a potential differential diagnosis of pleural effusion. *Mesocestoides corti*, which was the causative parasite in this case, has not previously been isolated in Germany. Because tetrathyridiosis is only diagnosed post mortem in most cases, little is known about effective therapeutic options. Furthermore, clinical signs of this disease can be absent for several years and can potentially be triggered by neoplastic conditions or immunosuppression. Tetrathyridiosis seems to be a treatable disease that can be controlled by adequate antiparasitic therapy.

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Introduction

Tapeworms are common parasites in the intestine of carnivores. *Mesocestoides* species live as adult worms in the small intestine of carnivores as definitive hosts. In Europe, *Mesocestoides lineatus*, *Mesocestoides leptothylacus* and *Mesocestoides litteratus* are most prevalent.[1–3] The life cycle of *Mesocestoides* species is not known in detail but a cycle including two intermediate hosts and one definitive host is generally assumed.[4] Wild carnivores, especially red foxes (*Vulpes vulpes*) are known as an important worldwide reservoir of *Mesocestoides* species.[3] Arthropods are incriminated as the first intermediate hosts. Vertebrates, including mammals, are potential second intermediate hosts, in which the infective larval stages (tetrathyridia) develop in serosal body cavities and different organs.[5] Tetrathyridia might be able to perform asexual and sexual reproduction.[6] Mammals like dogs and cats, and also humans, are infected by consumption of the organs of these intermediate hosts and therefore act as definitive hosts.[7]

Tetrathyridiosis is a rare finding in dogs and cats in Europe. There are several case reports of this disease in dogs.[8–11] Only a few reports exist about *Mesocestoides* infection in cats.[12–15] Most of these reports of dogs and cats concern peritoneal tetrathyridiosis.[8,12,13,16,17] Thoracic involvement of tetrathyridiosis seems to be an extremely rare finding in dogs and cats.[15,18] Furthermore, tetrathyridiosis is a disease

[1]Division of Small Animal Internal Medicine, Faculty of Veterinary Medicine, Justus-Liebig-University, Giessen, Germany
[2]Department of Parasitology, Faculty of Veterinary Medicine, University of Leipzig, Leipzig, Germany
[3]Division of Diagnostic Imaging, Faculty of Veterinary Medicine, University of Leipzig, Leipzig, Germany
[4]Veterinary Practice, Magdeburg, Germany
[5]Division of Small Animal Internal Medicine, Faculty of Veterinary Medicine, University of Leipzig, Leipzig, Germany
[6]Veterinary Practice Waltenhofen, Waltenhofen, Germany
[7]Division of Small Animal Internal Medicine, Faculty of Veterinary Medicine, University of Utrecht, Utrecht, the Netherlands

Corresponding author:
Dorothee Dahlem Dr Med Vet, Division of Small Animal Internal Medicine, Faculty of Veterinary Medicine, Justus-Liebig-University, Frankfurter Straße 126, 35392 Giessen, Germany
Email: dorothee.p.dahlem@vetmed.uni-giessen.de

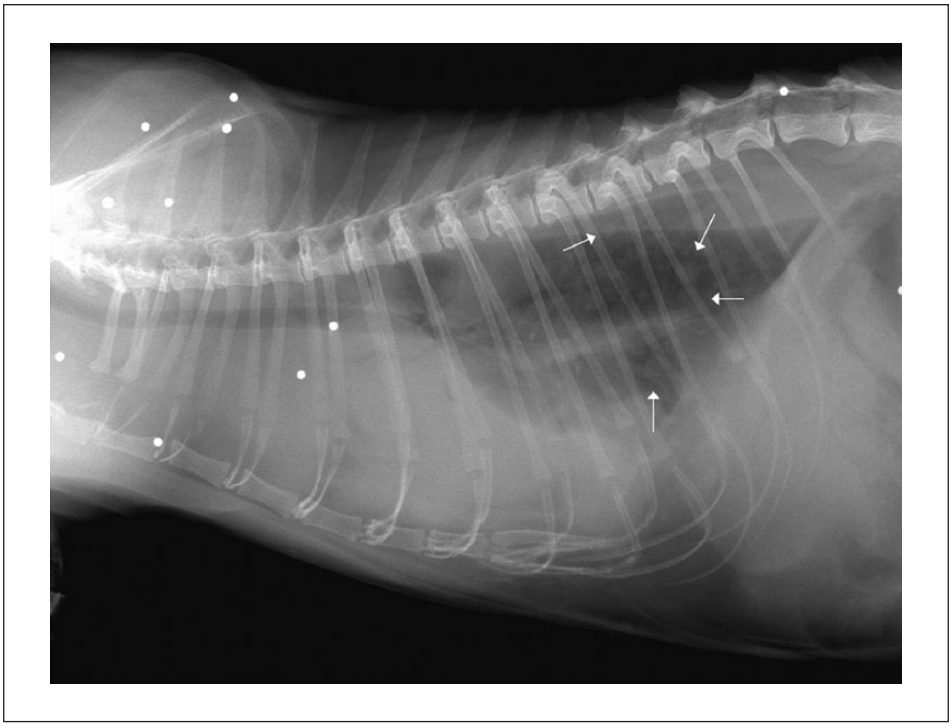

Figure 1 Lateral thoracic radiograph. A large volume of pleural fluid obscures the heart silhouette and other soft tissue structures. Only part of the dorsocaudal lung remains visible. Here, severe pulmonary nodules can be identified (arrows). The bullets can be localised in the thoracic wall and the neck

primarily described in southern European countries such as Italy, Turkey and Spain.[10–16,18] To our knowledge, there is only one reported case of tetrathyridiosis in a dog in Germany.[17] In many cases the diagnosis of tetrathyridiosis is made post mortem.[11,12,15,18] Following the rare diagnosis of tetrathyridiosis no consistent therapeutic recommendations exist and little is known about potential therapy in dogs and cats.[19–21] Praziquantel and fenbendazole seem to be effective against *Mesocestoides* species infections in dogs and cats.[21,22] Nothing is known about treatment duration and combination therapy, especially with regard to long-term outcome.

Based on the geographic history of the cat discussed herein, a long asymptomatic period after infection with tetrathyridia must be suspected. Another interesting finding is the possible relationship between the tetrathyridiosis and the late diagnosis of concurrent anaplastic lymphoma.

Case description

A 6-year-old domestic shorthair cat was presented with dyspnoea to the emergency service of the Small Animal Hospital of the Veterinary Faculty of the University of Leipzig. The owner had noted laboured breathing the evening before presentation.

The cat was female and had been neutered 4.5 years earlier in Malta. It had been moved from Malta to Germany about 6 months after neutering. Since then, it lived as an indoor-only cat together with 11 other cats. Furthermore, the right pinna had been partially resected owing to a squamous cell carcinoma 3 years previously. When the cat was hospitalised to resect the carcinoma, chest radiographs showed various subcutaneous bullets distributed over its body. The cat had been vaccinated recently, but dewormed irregularly and the last time was several years previously.

The cat had been treated repeatedly for ulcerative dermatitis. Immediately before presentation it was treated with ciclosporin (6 mg/kg bodyweight q48h PO) because of these dermatological signs.

The cat showed laboured breathing with a respiratory rate of 68 breaths per minute during the clinical examination. Over the caudal aspects of the lungs the respiratory sounds were exacerbated; over the cranial aspects the sounds were muffled. The rest of the clinical examination was unremarkable.

After the initial stabilisation of the cat with oxygen supplementation, thoracic radiographs were taken (Figure 1). A large amount of pleural and potentially mediastinal fluid obscured the heart silhouette and other soft tissue structures. Within the ventilated part of the lung well-delineated structures were identified. Because of these findings, neoplasia involving both lung and pleural cavity was a very likely differential diagnosis.

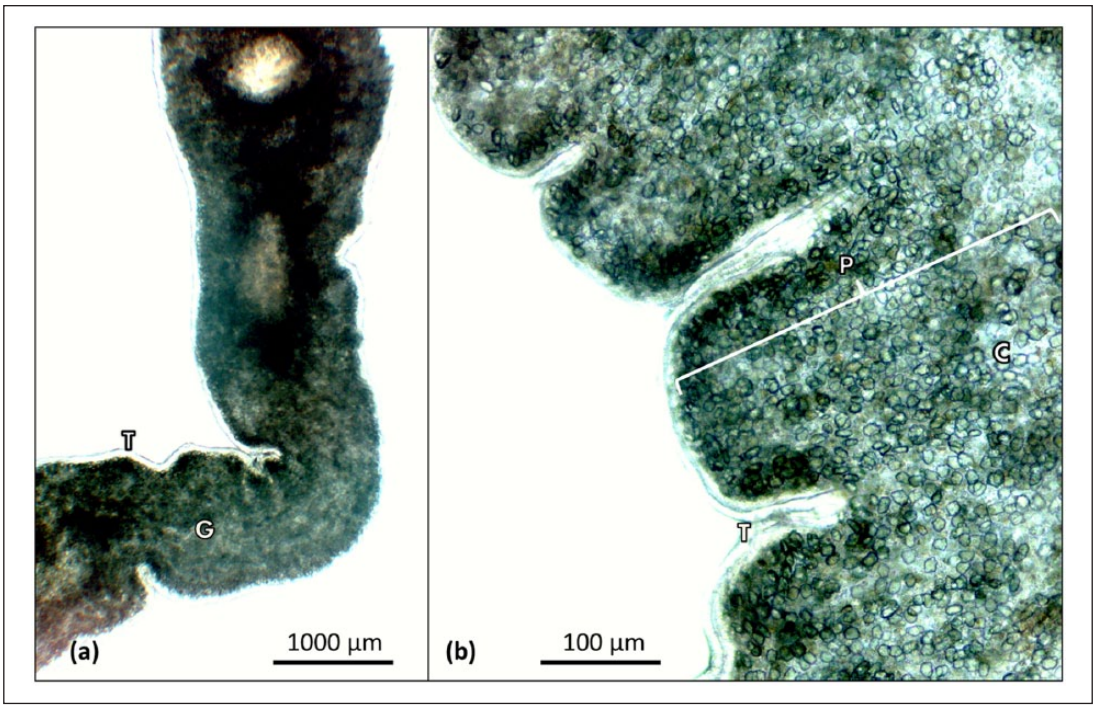

Figure 2 (a) Flat contractile tetrathyridium with unsegmented body, filled with dense granula (G), and a smooth clear tegumental border (T; × 40 magnification); (b) tegument (T) and parenchyma (P) with numerous calcareous corpuscles (C; × 400 magnification)

Despite the potentially guarded prognosis the owner was willing to perform further diagnostics and therapy, and the cat was hospitalised. The cat had to be sedated for thoracocentesis. Only 70 ml of the effusion could be evacuated from the chest because the needle was repeatedly blocked with white, filamentous structures. These structures could only be partially removed from the chest. The thoracocentesis was continued under ultrasonographic control and an echocardiographic examination was performed simultaneously. No abnormal findings could be gathered and the pleural effusion was considered to be of extracardiac origin.

Further analysis of the effusion revealed a reactive inflammatory exudate (6850 cells/µl, protein content 47 g/l, specific gravity 1.034). Microscopically, the white filamentous structures had a small granular appearance and moved in a meandering pattern. Because of the suspected parasitic origin the samples of the pleural effusion, as well as faecal samples, were sent to the Institute of Parasitology for further examination.

Simultaneous blood examination showed leukopenia (3.7 G/l [reference interval (RI) 6–11 G/l]) with lymphocytopenia (0.41 G/l [RI 1–6 G/l]) and thrombocytopenia (78 G/l [RI 150–550 G/l]). All parameters of the biochemistry profile were within the RIs. Blood testing for feline leukaemia virus via SNAP-test (IDEXX) and PCR analysis was negative. Furthermore, an ultrasonographical examination of the abdomen revealed no pathological findings.

The structures found in the pleural effusion were examined microscopically. Drops of the pleural fluid were screened at a magnification of × 40 (Figure 2). Motile tubes were observed, which showed contracting movements. A faecal sample was tested for parasitic stages, especially for cestode proglottids and eggs, by a combined sedimentation flotation method.[23]

The aspirate was centrifuged (2000 × *g*, 5 mins) and the DNA extracted from two parasitic tissue samples of the sedimented structures using the QIAamp DNA Mini Kit (Qiagen) according to the manufacturer's instructions for tissue samples. A cestode-specific PCR was performed based on the mitochondrial 12S rRNA gene, as previously described.[24,25] DNA samples of *Echinococcus equinus* and *Echinococcus multilocularis* were amplified as positive controls. PCR products were run on a 1.5% agarose gel, stained with ethidium bromide and the bands visualised by ultraviolet light. The PCR products underwent sequencing (Interdisziplinäres Zentrum für Klinische Forschung, University of Leipzig, Germany) followed by BLASTN analysis (NCBI Basic Local Alignment Search Tool, Nucleotide BLAST 2.2.26).[26]

The faecal samples were tested negative for any parasitic stage, including cestode proglottids and eggs. All DNA samples of the pleural effusion and particles tested positive for cestode DNA (product length approximately 370 base pairs). Sequencing of the samples revealed a high homology to the amplified sequence of the

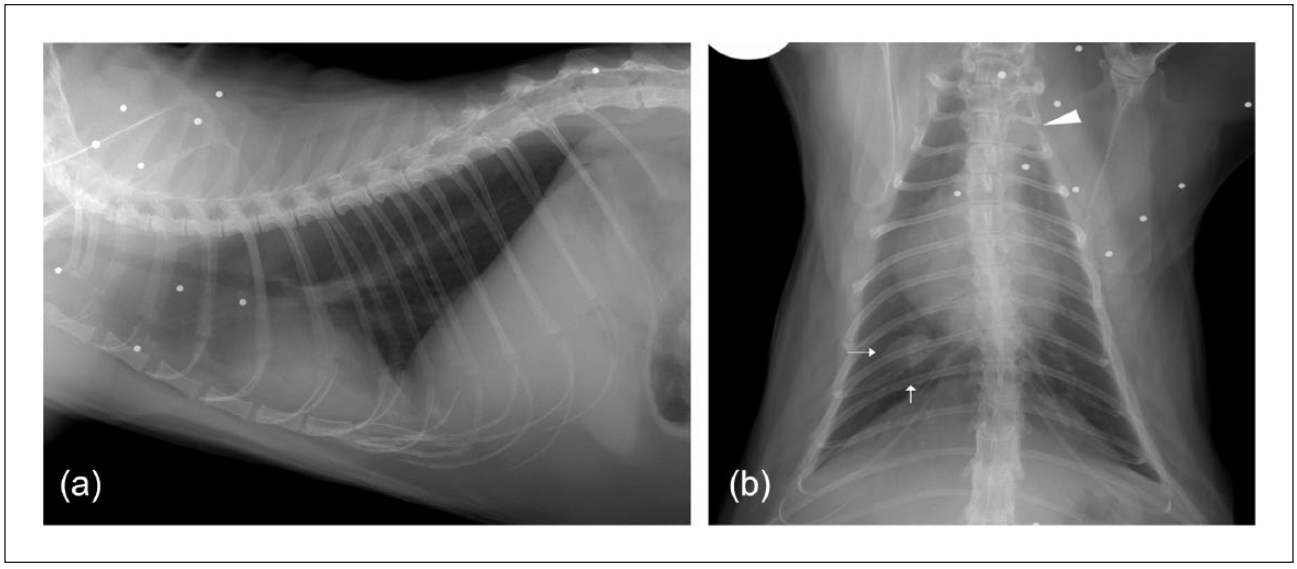

Figure 3 (a,b) Thoracic radiographs taken 8 weeks after discharge. A small amount of pleural fluid can be recognised on the left side (closed triangle in [b]). A nodule not previously seen is present in the right caudal lung hemithorax (arrows in [b])

Mesocestoides corti 12S ribosomal RNA gene (GenBank: HM011122.1; homology level: 98%).

The cat received fenbendazole (50 mg/kg q24h PO) and praziquantel (5 mg/kg PO) as an antiparasitic treatment. In addition, supportive treatment (infusions, theophylline [4 mg/kg q8h IV]) and amoxicillin/clavulanic acid (14 mg/kg q8h IV) were given.

Shortly after starting the therapy the dyspnoea disappeared. The leukocyte, as well as thrombocyte count, returned to normal.

Unfortunately, the cat showed dyspnoea again 2 days later. The respiratory sounds were muffled, especially ventrally on both sides of the chest. An ultrasonographical examination of the chest showed marked amounts of effusion. Therefore, chest tubes were placed on both sides under general anaesthesia. Various tetrathyridia could be evacuated through these tubes. Overall, about 250 ml of pleural effusion was removed.

Contrast-enhanced computed tomography of the thorax revealed the presence of multiple pulmonary nodules with diameters ranging from 3–7 mm. The pulmonary nodules did not show enhancement after the administration of iodinated contrast medium (Iomeprol; 600 mg iodine/kg). A moderate amount of both pleural and mediastinal fluid was seen. Further, lymphadenomegaly of the mediastinal and tracheobronchial lymphnodes were present.

Three days later the chest tubes were removed owing to minimal residual fluid load. The cat was discharged after 1 week of hospitalisation.

Fenbendazole (50 mg/kg q24h PO) was administered continuously for 4 weeks and praziquantel (5 mg/kg PO) was repeated three times at an interval of 14 days.[21,22,27]

Two weeks after discharge the cat was presented for follow-up examination. At this time, the cat was in good general condition. Radiographs revealed a smaller volume of fluid in the pleural space and a marked widening of the mediastinum. Pulmonary nodules were present. However, those identified in the first examination decreased in size.

Six weeks later (9 weeks after initial presentation), the cat was re-presented to the emergency service of the hospital because of the sudden onset of anorexia and lethargy. The clinical examination revealed an elevated body temperature of 40.2°C. Thoracic radiographs showed regressive pleural effusion and a decreased width of the mediastinum. Pulmonary nodules were no longer visible. Nonetheless, a nodule in the right caudal lung lobe was seen that was not obviously present in the previous radiographs (Figure 3a,b).

The most recent blood samples showed pancytopenia with marked leukopenia and marked thrombocytopenia (leukocytes 0.45 G/l [RI 6–11 G/l], thrombocytes 3.7 G/l [RI 150–550 G/l] and haematocrit 22% [RI 28–45%]). Because of the pancytopenia a bone marrow aspirate was taken. An anaplastic lymphoma with high-grade replacement of bone marrow was diagnosed. Owing to the poor prognosis, the owner decided to have the cat euthanased.

Discussion

Mesocestoides species infections are quite uncommon in German domestic animals – the prevalence of patent infections is <0.1% in cats and dogs.[28] In other countries the prevalence is distinctly higher; for example, 7.1% of Iranian stray cats harbour adult *M lineatus*.[29] Most case

reports of tetrathyridiosis originate from Turkey or other southern countries.[10–13,30] In this case, owing to the cat originating from Malta, there is a possibility that it had been infected with tetrathyridia or adult intestinal *Mesocestoides* species before moving to Germany. Moreover, the finding of 98% genetic homology of the amplified DNA fragment to the *M corti* 12S ribosomal RNA gene suggests the presence of tetrathyridia of a *Mesocestoides* species closely related to *M corti* (syn vogae).[31] This species is not known to occur in middle Europe, which corroborates our import theory. This also corresponds to the statement of the owner that the cat received very irregular antiparasitic treatments. Another point supporting the hypothesis of the infection occurring in Malta is that the cat lived only indoors since moving to Germany several years ago. An infestation with *Mesocestoides* species of the other cats could not be excluded. The faeces of these cats were examined several times and parasites were never been detected. Therefore, only a prophylactic treatment with praziquantel was initiated in the other cats. Nevertheless, in case of an in-house reservoir the potential first intermediate host remains unclear because all cats lived as indoor-only cats and infection by direct route is not known in *Mesocestoides* species. According to the owner all the other cats originated in Germany. Owing to the geographical distribution of *M corti*, which is not known in middle Europe, an infection within Germany seems very unlikely.[31]

Based on the available information there is no relation between the previously diagnosed ulcerative dermatitis and the development of tetrathyridiosis. Because of recurrent pruritus the cat previously received a complete dermatological work-up. A typical aetiology of this disease – ectoparasites and allergy – could be excluded. However, the immunosuppressive treatment with ciclosporin could be a predisposing factor for the development of clinically relevant tetrathyridiosis.

There have been several case reports of *Mesocestoides* species tetrathyridiosis in dogs and cats.[8–13] Most authors describe disseminated *Mesocestoides* species tetrathyridiosis with larvae in different organs and cavities.[11] These parasites could migrate through the intestinal wall and take residence as tetrathyridia in body cavities.[32] However, there are known exceptions. Avci et al reported a cat with an infected mammary gland without further affected tissues.[14] Jabbar et al reported a pleural larval mesocestoidiasis in a cat,[15] which was diagnosed post mortem and was probably the reason for high-grade dyspnoea. As in our case, the reason for this local presentation remains unclear. The diagnosis in the reported cases were often made by necropsy.[11,17] Therefore, little is known about therapeutic options in this disease. Previous studies in mice described a good efficacy of mebendazole against *Mesocestoides* species larvae,[19] while praziquantel is known to be effective against all stages of feline cestodes in general.[20] The combination of both drugs was chosen owing to the limited amount of data available and the severity of disease in the present case. The long-term therapy was effective in terms of a significant reduction in the larval burden and resolving the clinical signs, together with the symptomatic treatment.[7] Crosbie et al did not experience success when using a combination therapy of albendazole and praziquantel, but described fenbendazole as very effective against tetrathyridiosis in dogs.[22] Papini et al,[21] however, observed inefficacy of therapy with fenbendazole alone. Repeated treatment with praziquantel was also successful in eliminating peritoneal tetrathyridia in a dog. Based on these partially contradictory treatment reports we decided to treat the cat in this report with long-term (4 weeks) fenbendazole in combination with repeated praziquantel administration.[7,21] Unfortunately, it is not known if there were larvae left after completion of the therapy. The thoracic nodule, seen in the last follow-up radiographs, might be a sign of recurrent parasitic colonisation. However, the owner did not allow a puncture or a necropsy.

Tetrathyridiosis in cats is not well studied with regard to its clinical importance. Asymptomatic infections are described.[33] In the present case, the concurrent anaplastic lymphoma could have promoted the development of clinical tetrathyridiosis. However, via the first cytological evaluation of pleural effusion no evidence of lymphoma was found. Additionally, the cat had been immunosuppressed with ciclosporin, which could be a predisposing factor for development of tetrathyridiosis. To our knowledge, neither fenbendazole nor praziquantel, in contrast to ciclosporin, seem to be risk factors for inducing neoplastic conditions such as lymphoma.[34]

Conclusions

Although very rare, tetrathyridiosis has to be considered as a differential diagnosis in cats presenting with respiratory signs due to pleural effusions and pulmonary nodules. The presence of these radiological findings alone does not prove the diagnosis of neoplastic disease. Compared with pleural effusion of neoplastic origin, tetrathyridiosis is a treatable disease, which can be controlled by adequate antiparasitic therapy. Furthermore, clinical signs of this disease can be absent for several years and can potentially be triggered by neoplastic conditions or immunosuppression.

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