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Spontaneous remission of *M. fortuitum*-associated abdominal lymphadenitis in a British Shorthair cat

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Summary

We present the first case of a gastrointestinal *Mycobacterium (M.) fortuitum* infection in a cat, characterized by anorexia and abdominal lymphadenitis. After failed treatment with amoxicillin and clavulanic acid, we performed diagnostic laparotomy to procure lymph node biopsies. Histology including Haematoxylin-Eosin- and Ziehl-Neelsen-staining was negative but PCR confirmed an infection with *M. fortuitum*. We initiated a multimodal antibiotic regimen including clarithromycin, amikacin and enrofloxacin but stopped it after 48 hours due to inadequate owner-patient compliance. Six months post-diagnosis, without further treatment, the cat remained asymptomatic and the lymph nodes showed no pathological abnormalities.

Abbreviations: FeLV = feline leukaemia virus; FIV = feline immunodeficiency virus; NTM = non-tuberculous mycobacteria /mycobacterioses; RI = reference interval; SAA = Serum Amyloid A

Zusammenfassung

Spontane Remission einer *M. fortuitum* – assoziierten, abdominalen Lymphadenitis bei einer Britisch-Kurzhaar Katze

Wir präsentieren den ersten beschriebenen Fall einer *Mycobacterium fortuitum*-Infektion bei einer Katze mit gastrointestinalen Symptomen, Anorexie und abdominaler Lymphadenitis. Nachdem eine Behandlung mit Amoxicillin und Clavulansäure erfolglos war, wurde eine diagnostische Laparotomie zur Lymphknotenbiopsie vorgenommen. Die histologische Untersuchung, einschließlich der Hämatoxylin-Eosin und der Ziehl-Neelsen Färbung, ergab keine Bakteriennachweise; mit einer PCR wurde allerdings *M. fortuitum* nachgewiesen. Eine multimodale Antibiotikatherapie mit Clarithromycin, Amikacin und Enrofloxacin wurde eingeleitet. Die Therapie musste aber nach 48 Stunden, wegen ungenügender Compliance des Tierhalters abgebrochen werden. Die Katze zeigte sechs Monate nach der Diagnose, und ohne zwischenzeitliche Behandlungen, keine Symptome und die Lymphknoten zeigten keine pathologischen Veränderungen.

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Introduction

Mycobacterial infections continue to pose significant challenges worldwide, with *Mycobacterium tuberculosis* among the top 10 infectious causes of death in humans. The prevalence and impact of these infections emphasize the importance of ongoing research, diagnostic advancements and effective treatment strategies to address this global health concern (WHO 2019). Mycobacteria are not confined to humans and can also infect animals, including dogs and cats (Munro et al. 2021).

Mycobacterium spp. are divided into obligate pathogens, e.g. *Mycobacterium tuberculosis* (TB); mycobacteria that are difficult to grow, with environmental predilections that are currently unknown, e.g. *M. lepraemurium*; and non-tuberculous mycobacteria (NTM) (Appleyard & Clark 2002; Munro et al. 2021). NTM consist of a large number of mycobacterial species that can be classified into many groups based on growth ability in culture (slow-growing, rapid-growing or non-growing) and on pathogenicity (absolute, facultative or saprophyte pathogens) (Chuenngam & Chermprapai 2025). Mycobacterial infections generally cause cutaneous lesions in dogs and cats and are associated with feline leprosy syndrome. Non-tuberculous mycobacteria can cause disease, particularly in individuals with compromised immune systems (Gunn-Moore 2014). Prominent members of this group of organisms include *Mycobacterium avium*, *M. fortuitum*, *M. chelonae*, *M. smegmatis*, *M. abscessus* and *M. thermoresistibile* (Malik et al. 2000). The diverse nature and the certain zoonotic potential of mycobacteria makes it crucial for accurate diagnosis to understand these categories and underlines the need for tailored approaches to address the specific challenges posed by each subgroup. They are common in the environment, including soil and water, and are able to survive in amoeba and protozoal organisms (Krajewska-Wędzina et al. 2019). As NTM are typically found in soil, water and decaying vegetation, NTM infections are also believed to be secondary to wound contamination (Horne 2009).

NTMs are not usually transmitted from animals to humans, although there are some reports of human infection by cat and dog bites and from surgical procedures (Jang et al. 2002). Clinical manifestations involve cutaneous nodules with or without ulceration, granulomatous panniculitis and regional lymphadenitis (Gunn-Moore et al. 2011). Pneumonia is a rarely described manifestation (Gunn-Moore 2014). Nonspecific generalized symptoms including mesenteric and intrathoracic lymphadenitis are primarily seen in infections with *M. avium* and *M. xenopi* (Gunn-Moore 2014). Figure 1 shows a classification of Mycobacteria.

We describe the first case of *Mycobacterium fortuitum* infection in a cat presenting with gastrointestinal symptoms and intraabdominal lymphadenopathy.

Case Report

A one-year-old neutered male British Shorthair cat was admitted to our clinic with a history of reduced general behaviour over the past ten days and weight loss. The cat was regularly vaccinated and dewormed and had occasional outdoor access. The referring veterinarian had initiated treatment with amoxicillin and clavulanic acid 22 mg/kg p.o. q12h and meloxicam p.o. q24h. Clinical examination revealed a mildly elevated body temperature of 39.6 °C, a mildly decreased skin turgor and abdominal pain upon palpation. Haematology, blood biochemistry and electrolyte analysis indicated a mild normochromic, normocytic non-regenerative anaemia (PCV 29 %; reference interval (RI) 30.3–52.3 %, reticulocytes 12.7 K/µl; RI 3.0–50.0 K/µl), mild hyperproteinaemia (9.6 g/dl; RI 5.7–8.9 g/dl), mild hyperglobulinaemia (6.9 g/dl; RI 2.8–5.1 g/dl) and an abnormal feline pancreatic lipase snap test (Idexx Laboratories). Abdominal ultrasound showed multiple enlarged abdominal lymph nodes with a mean size of 2.5 x 2.2 cm (Fig. 2). We performed an ultrasound-guided fine-needle aspiration of the mesenterial lymph nodes and sent the sample to the laboratory for further diagnostics to differentiate between neoplastic and reactive enlargement. Cytology indicated a reactive state and neutrophilic inflammation; there was no evidence of malignant neoplasia.

The cat was hospitalized for four days. Treatment at our facility included intravenous fluids (Ringer's solution 4 ml/kg/h), omeprazole (Nexium, Grünenthal Pharma, Mitlödi, Switzerland) 1 mg/kg i.v. q24h, sucralfate (Sucralan, G.L. Pharma GmbH, Lannach, Austria) 2.5 ml p.o. q12h, maropitant (Vominil, VETVIVA Richter, Wels) 1mg/kg i.v. q24h, metamizol (Novasul, Richter Pharma AG, Wels, Austria) 25 mg/kg i.v. q12h and buprenorphine (Bupaq, VETVIVA Richter) 0.01 mg/kg i.v. q6h and amoxicillin clavulanic acid (Curam, Sandoz, Novartis, Basel, Switzerland) 22 mg/kg i.v. q8h.

During hospitalization, the cat improved clinically and began eating on its own and after four days of symptomatic treatment it was discharged in good clinical condition. One month later, the cat presented with anorexia, vomiting and reduced general behaviour. Bloodwork revealed mild leucocytosis (22.88 K/µl; RI 2.87–17.02 K/µl), mild neutrophilia (16.72 K/µl; RI 2.30–10.29 K/µl), mild hyperproteinaemia of 10.2 g/dl (RI 5.7–8.9 g/dl), moderate hyperglobulinemia and elevated serum amyloid A (SAA) levels of 7.4 g/dl (RI 2.8–5.1 g/dl). Ultrasound examination revealed persistent mesenterial lymphadenopathy. Treatment with amoxicillin and clavulanic acid 22 mg/kg twice daily was extended for two weeks. Fourteen days later, the cat's general condition improved and clinical examination was unremarkable, although SAA levels were still elevated (40.9 mg/l; RI 0–1.5 mg/l) and mesenterial lymph nodes were still enlarged, which led to further extension of the antibiotic treatment for an additional two weeks. A diagnostic

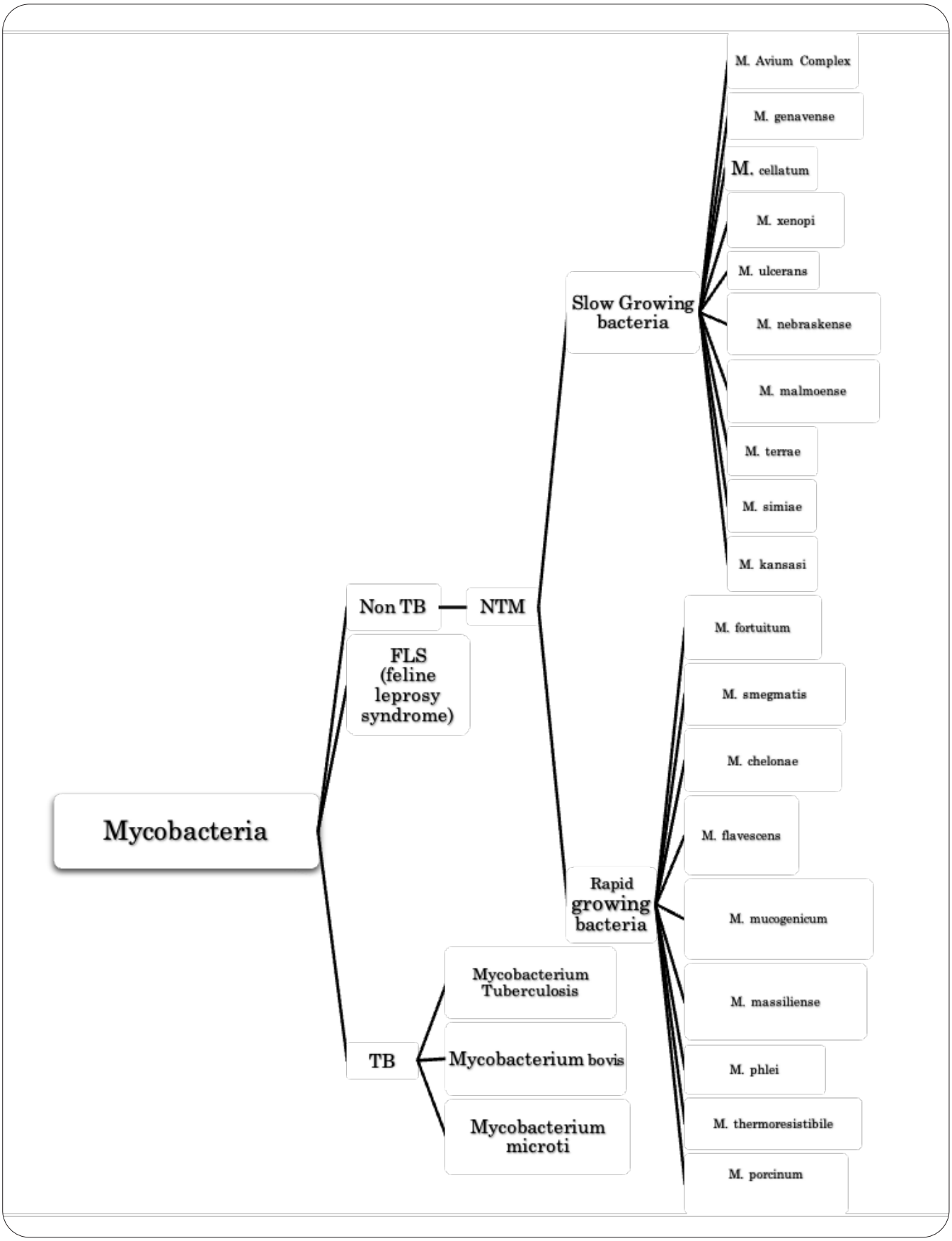

Fig. 1: Classification of Mycobacteria (adapted from: Gunn-Moore 2014) / Klassifizierung der Mykobakterien (nach: Gunn-Moore 2014)

laparotomy was scheduled to obtain lymph node biopsies for further examination. Surgical exploration revealed no pathological findings other than enlarged lymph nodes. Pathological examination of the lymph nodes disclosed a high-grade, multifocal, chronic, pyogranulomatous lymphadenitis, accompanied by high-grade, chronic, follicular and paracortical hyperplasia. To investigate the cause, we performed immunohistochemical staining with antibodies against feline coronavirus (FIP), which gave negative results. We also carried out the periodic acid-Schiff reaction and Ziehl-Neelsen-staining, both of which produced negative findings. In view of the marked pyogranulomatous inflammation on histopathological examination, were used additional molecular diagnostics to investigate potential infectious agents. An initial pan-fungal PCR assay was negative, effectively excluding a fungal aetiology. Subsequent sequencing of the amplified DNA confirmed infection with *Mycobacterium fortuitum*. All molecular analysis, including PCR assays and sequencing of amplified DNA, was performed by an external laboratory.

The selected treatment regimen, based on prior case reports, involved a multi-drug approach consisting of fluoroquinolones, macrolides and aminoglycosides (Malik et al. 2000; Bercovier & Vincent 2001; Morgado et al. 2022). Our therapeutic decision involved the administration of clarithromycin (Klacid, Viatris Healthcare, Bad Homburg, Germany) 10 mg/kg q12h, trimethoprim sulphonamides (Cotrim, Ratiopharm, Ulm, Germany) 12 mg/kg q12h and pradofloxacin (Veraflox, Bayer, Leverkusen) 3 mg/kg q24h. This tailored combination was the treatment of choice to address the *Mycobacterium fortuitum* infection, considering its efficiency in cases of cutaneous *Mycobacterium fortuitum* infections (Malik et al. 2000; Morgado et al. 2022). Regular monitoring of the cat's response to the regimen and any potential side effects ensured optimal therapeutic outcomes.

After two days of the prescribed antibiotic treatment, the owner opted to discontinue the antibiotics, pointing out clinical improvement in the cat's general condition and challenges in administering the medication. Five weeks after the initial diagnosis, the cat returned for a follow-up. Remarkably, it had gained 400 g weight since the last appointment and exhibited an increase in appetite and overall improved behaviour. Ultrasound examination revealed a significant reduction in the size of the abdominal lymph nodes (0.5 x 0.5 cm) and serum

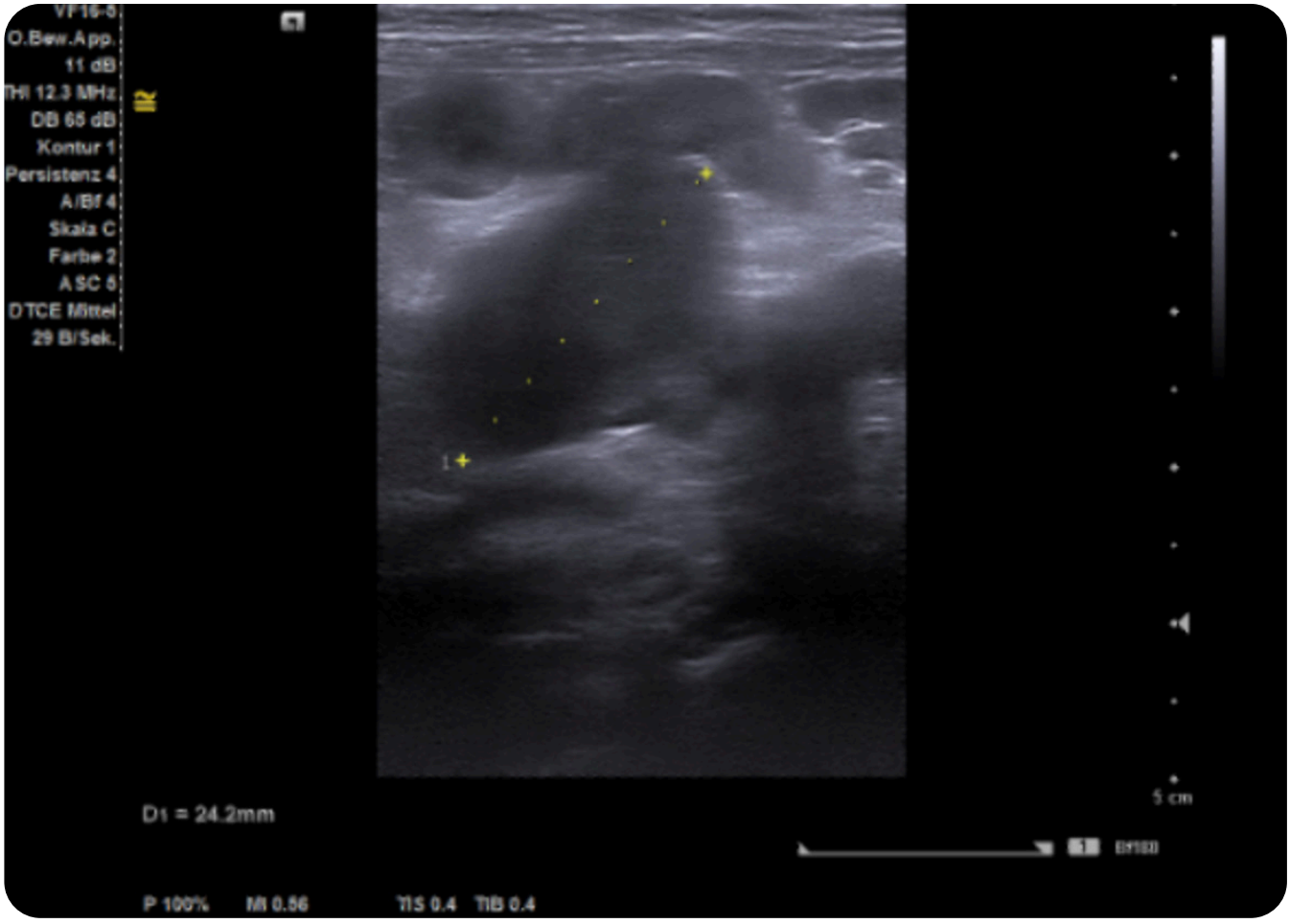

Fig. 2: Ultrasound images on initial presentation showing enlarged lymph nodes. The thick yellow dots indicate the dimensions of the lymph nodes / Ultraschallbilder bei der Erstvorstellung des Patienten, mit vergrößerten Lymphknoten. Die dicken gelben Punkte markieren die Größe der Lymphknoten.

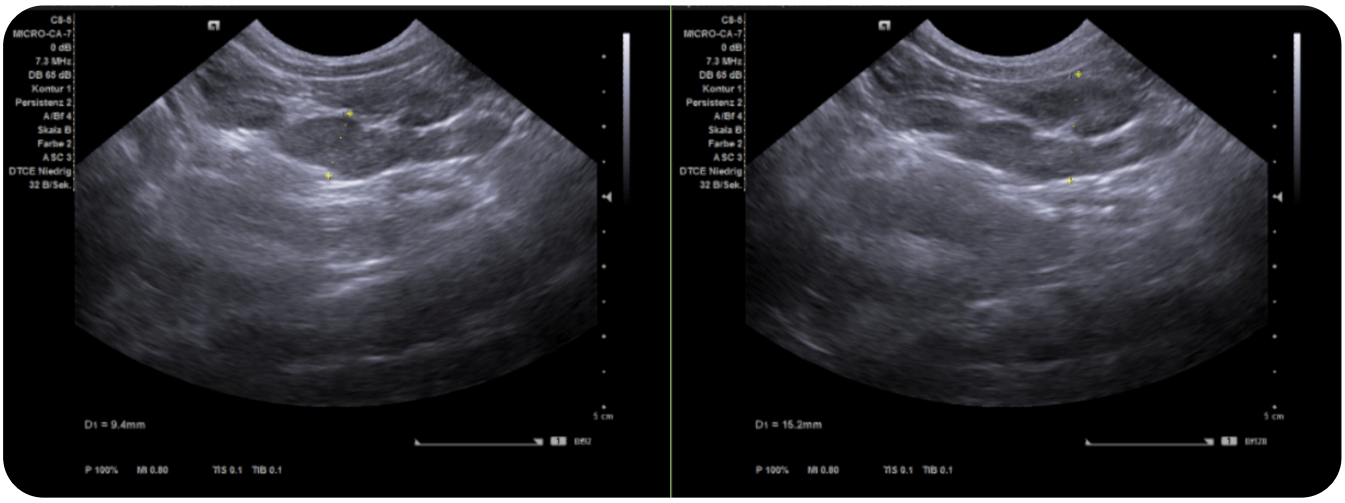

Fig. 3: Ultrasound images eight weeks after presentation, showing abdominal lymph nodes of physiological size. The thick yellow dots indicate the dimensions of the lymph nodes. / Ultraschallbilder acht Wochen nach der Erstvorstellung des Patienten mit abdominalen Lymphknoten in physiologischer Größe. Die dicken gelben Punkte markieren die Größe der Lymphknoten.

amyloid A (SAA) levels were within the normal range (0.0 mg/l; RI 0–1.5 mg/l). Another nine weeks later, at the subsequent follow-up appointment, the cat displayed no clinical abnormalities. The abdominal ultrasound indicated a physiological size of the abdominal lymph nodes (Fig. 3) and SAA levels were within the normal range.

At the time of writing, 6 months after initial diagnosis and without treatment, the cat has gained weight, shows increased appetite and has no clinical manifestations of illness. We are continuing to monitor the cat through regular check-ups every 3 months to ensure its sustained health and well-being. The positive response to the initial treatment and the subsequent stability in the cat's condition are encouraging indicators of a favourable outcome.

Discussion

In cats, infections with non-tuberculous mycobacteria (NTM) typically present as cutaneous lesions, most often resulting from contamination of wounds with soil or debris following trauma or surgical procedures (Webster et al. 2022; Lloret et al. 2013). Reports on infections caused by *Mycobacterium fortuitum* in cats commonly describe manifestations such as panniculitis and ulcerative dermatitis (Krajewska-Wędzina et al. 2019). Once phagocytosed by macrophages, *Mycobacterium* spp. are capable of surviving and replicating within these cells, triggering a granulomatous to pyogranulomatous inflammatory response in the affected tissues. The present case deviates from this pattern, as the cat exhibited no signs of skin disease. Instead, the primary concern was the presence of enlarged abdominal lymph nodes, accompanied by anorexia and elevated serum amyloid A (SAA) levels (Lloret et al. 2013).

The challenge in diagnosing mycobacterial infections lies in their often nonspecific clinical signs. Given the potential public health risk posed by companion animals susceptible to these infections, accurate diagnosis becomes imperative. When mycobacterial infection is suspected, it is crucial to obtain biopsies of the affected tissue for histopathological examination and Ziehl-Neelsen staining should be performed. In some cases, cytological examination of cutaneous or lymph node aspirates can assist in identifying mycobacteria. Fine-needle aspiration is less invasive but less sensitive than biopsies (Greene & Gunn-Moore 2006). In our case, histopathology only revealed severe chronic granulomatous inflammation without any evidence of infectious agents. While histopathology is valuable, culturing remains the gold standard for confirming mycobacterial infections due to its specificity, its ability to provide quantitative data and its capacity for antimicrobial susceptibility testing. The two modalities complement each other in the diagnosis and management of these infections (Greene & Gunn-Moore 2006).

However, culturing has its limitations, including prolonged incubation times (often several weeks), the need for specialized laboratory infrastructure and experienced personnel and a higher risk of contamination. Molecular diagnostic methods such as PCR are therefore also employed in the diagnosis of mycobacterial infections. Although PCR offers advantages including faster turnaround times and the ability to identify species through sequencing, it requires specialized laboratory conditions and trained personnel. Moreover, PCR may have reduced sensitivity, particularly in infections caused by non-tuberculous mycobacteria (NTM). In feline patients, the reduced sensitivity is well recognized and has been attributed to several factors: low bacterial loads in affected tissues (i.e. paucibacillary lesions), the thick lipid-rich cell wall of mycobacteria, which hampers efficient DNA extraction and the wide genetic diversity

of NTM species, which can compromise primer binding in standard assays. The use of formalin-fixed tissue can further decrease PCR performance. To optimize sensitivity, fresh or frozen samples and improved lysis protocols are strongly recommended and sequencing is often necessary to achieve definitive species-level identification. Not all commercial PCR assays can determine the species of mycobacteria when a generic PCR assay yields positive results (Aranaz et al. 1996; Higgins et al. 2011).

A precise diagnosis is vital as the therapeutic approach and the life expectancy in mycobacterial infections depend on the causative species. *Mycobacterium fortuitum* strains have shown resistance to broad-spectrum antibiotics, yet studies suggest susceptibility to aminoglycosides (amikacin, gentamicin), trimethoprim sulfadiazine and macrolides (clarithromycin) (Malik et al. 2000; Greene & Gunn-Moore 2006; Gunn-Moore 2014). Our choice of PCR for diagnosis and sequencing was primarily driven by the need for results as soon as possible.

A limitation of this case is the absence of testing for feline retroviruses (FeLV and FIV). Cats infected with FeLV or FIV have documented immunosuppression and are predisposed to more severe or prolonged infections with opportunistic pathogens. It is important to note that, unlike in humans—where retroviral infections such as HIV are well established predisposing factors for MAC-associated systemic mycobacteriosis—there is no significant association between feline leukaemia virus (FeLV) and/or feline immunodeficiency virus (FIV) infection and mycobacterial disease in cats.

Although this cat showed rapid clinical improvement following antimicrobial therapy, the lack of FeLV/FIV testing represents a diagnostic limitation and should be addressed in future cases to assess the patient's immunological status and any potential relationship between retroviral status and susceptibility to mycobacterial infections (Barry et al. 2002; Munro et al. 2021; Webster et al. 2022).

A further limitation in this case was the absence of bacterial culture following fine-needle aspiration. We decided to continue the antibiotic therapy with amoxicillin-clavulanic acid as it had been initiated the day before by the referring veterinarian and the cat showed initial improvement. While culture remains the gold standard for confirming and characterizing mycobacterial and other bacterial infections, it was not pursued initially as we decided to await the results of the histopathological examination. Following histopathological identification of pyogranulomatous inflammation, PCR was prioritized over culture to expedite diagnosis and reduce turnaround time. Nevertheless, bacterial culture should be considered in such cases to allow antimicrobial susceptibility testing and a more comprehensive characterization of the infectious agent.

This case is also limited by the lack of radiological imaging and antimicrobial susceptibility data from the bacterial examination. Thoracic radiographs were not conducted to assess for pulmonary lesions, as the cat exhibited no signs of dyspnoea or coughing and pneumonia caused by rapidly growing NTMs has rarely been documented in cats. Nevertheless, radiographs should be performed to rule out pulmonary involvement (Greene & Gunn-Moore 2006).

We are aware of only one reported occurrence of spontaneous remission in leprosy in veterinary medicine. In human medicine there have been cases of remission without medical treatment for *Mycobacterium abscessus* and *Mycobacterium* ulcerans (O'Brien et al. 2017; Jo et al. 2020). The present case marks the first reported infection with M. fortuitum where the patient presented with intraabdominal lymphadenitis and gastrointestinal symptoms only and there was clinical improvement without the necessity for any form of multimodal antimicrobial intervention. This emphasizes the intricate nature of Mycobacterial infections and underlines the need for additional research to increase our understanding of their diverse presentations and potential therapeutic responses.

Clinical Relevance

We describe the variability in clinical presentations among various mycobacterial species, emphasizing the necessity for *Mycobacterium* testing in cases of unclear lymph node enlargement, even without cutaneous lesions. There are many potential therapeutic approaches, all based on the combination of multiple antimicrobials, although often with uncertain efficacy. However, this case shows that some patients exhibit improvement even without multimodal treatment.

Fazit für die Praxis:
Mykobakterien können verschiedenste klinische Symptome hervorrufen. Bei Lymphknotenvergrößerungen unklarer Ursache sollte auch bei fehlenden Hautveränderungen an Mykobakterieninfektionen gedacht werden. Es existieren verschiedene Therapieansätze, die alle auf der Anwendung mehrerer Antibiotika beruhen; die Wirksamkeit ist aber nicht immer sicher. Allerdings kann es – wie im gegenständlichen Fallbericht – auch ohne Therapie zu einer Besserung des Zustandes kommen.

Conflicts of Interest: The authors declare no conflicts of interest.

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