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Non-tuberculous Mycobacteria can Cause Disseminated Mycobacteriosis in Cats

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Summary

Mycobacteriosis caused by non-tuberculous mycobacteria (NTM) is a rising concern in human medicine both in immunocompromised and immunocompetent patients. In cats, mycobacteriosis caused by NTM is considered mostly to be a focal or dermal infection, with disseminated disease mostly caused by *Mycobacterium avium*. We describe three cases of disseminated mycobacteriosis in cats, caused by *Mycobacterium mageritense*, *Mycobacterium branderi/shimoidei* and *M. avium*, with no identified underlying immunosuppression. In all cases, extracellular mycobacteria were seen in the pulmonary epithelium, intestinal lumen and glomerular tufts, which could affect the shedding of the organism. The present study highlights the importance of mycobacteriosis as a differential even in immunocompetent animals. Considering the close relationship of owners and pets and the potential presence of free mycobacteria in secretions, cats should be considered as a possible environmental reservoir for mycobacteria.

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Introduction

Mycobacteria are acid-fast, aerobic, non-spore forming rod shaped bacteria that range from obligate pathogens to environmental saprophytes. Mycobacteria can be divided into three groups based on the disease they cause: *Mycobacterium leprae* and *Mycobacterium lepromatosis* cause leprosy in man. The *Mycobacterium tuberculosis* complex (MTC) is formed from species that cause tuberculosis in man and animals, such as *M. tuberculosis*, *Mycobacterium bovis* and *Mycobacterium microti*. In human medicine the word ‘tuberculosis’ is reserved for infections caused by the MTC species (Esteban and Muñoz-Egea, 2016).

The rest of the mycobacterial species are grouped as non-tuberculous mycobacteria (NTM), which are mostly opportunistic environmental pathogens (Koh, 2017). Most mycobacteria have a particular host preference, but some can cause infections in other species, including man (Quinn *et al.*, 2011).

Human leprosy is caused by either *M. leprae* or the more recently discovered *M. lepromatosis*, with varying skin lesions and peripheral nerve thickening and occasionally with systemic or mucosal involvement (Renault and Ernst, 2010). It was at first presumed that these species infected only man, but both species have also been found in Eurasian red squirrels (*Sciurus vulgaris*) (Avanzi *et al.*, 2016) and *M. leprae* is known to infect nine-banded armadillos (*Dasypus novemcinctus*) (Balamayooran *et al.*, 2015).

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Tuberculosis can cause organ-specific infections, systemic infections or classical granulomatous pulmonary infections (Fitzgerald *et al.*, 2010; Pesciaroli *et al.*, 2014). MTC species are closely related to each other with a high sequence similarity (Esteban and Muños-Egea, 2016) and all of them have an established zoonotic potential (Thirunavukkarasu *et al.*, 2017). *M. tuberculosis* is the most common cause of tuberculosis in man, but *M. bovis* has been found in 5–10% of cases (Esteban and Muños-Egea, 2016) and *M. microti* has been described in over 20 human cases (Esteban and Muños-Egea, 2016). In man, most MTC species cause a disease similar to classical tuberculosis (Esteban and Muños-Egea, 2016). In animals, the most common cause of tuberculosis is *M. bovis*, which has been described to affect, with varying degree, all common domestic mammals (Pesciaroli *et al.*, 2014).

The *Mycobacterium avium* complex (MAC) is the most common NTM in man (Daley, 2017; Koh, 2017), but a multitude of NTM species are known to cause disease (Koh, 2017; Thirunavukkarasu *et al.*, 2017). NTM infections affect both immunocompromised and immunocompetent patients (Koh, 2017) and the incidence of NTM isolates in human samples has been rising (Shah *et al.*, 2016). Infections in people are classified into four distinct clinical syndromes: chronic pulmonary disease, lymphadenitis, cutaneous disease and disseminated disease (Koh, 2017). In animals MAC species are generally considered to be the most important NTM (Quinn *et al.*, 2011) and these include *M. avium*, causing avian tuberculosis, and *M. avium* subspecies *paratuberculosis*, causing paratuberculosis or Johne's disease. Other NTM species are described to cause mostly sporadic, non-specific infections in several species (Thirunavukkarasu *et al.*, 2017).

There are few data on the prevalence of mycobacterial infections in domestic cats. In the UK, a recent publication studying histopathological samples reported typical lesions with acid-fast bacteria in approximately 0.3% of all cases examined, with the most common mycobacteria isolated being *M. bovis* and *M. microti* (Gunn-Moore *et al.*, 2013). Broughan *et al.* (2013) reported *M. bovis*-positive cultures in 16% of feline samples over a period of 7 years when examining microbiological samples submitted to the Animal Health and Veterinary Laboratories Agency, UK, for confirmation of suspected mycobacteriosis. Cats with access to wildlife reservoirs or bovine milk infected with mycobacteria are predisposed to mycobacterial infections (Gunn-Moore, 2014; Pesciaroli *et al.*, 2014) and there might be an increased risk associated with immunosuppressive diseases, especially with NTM infections (Gunn-Moore, 2014).

Tuberculosis in cats usually presents as a localized cutaneous disease or, less commonly, as a disseminated or systemic respiratory or alimentary disease (Gunn-Moore *et al.*, 2011a; Gunn-Moore, 2014; Pesciaroli *et al.*, 2014). NTM infections cause mostly cutaneous or subcutaneous nodules or granulomatous panniculitis with variable lymph node involvement (Gunn-Moore *et al.*, 2011a; Gunn-Moore, 2014). The 'feline leprosy syndrome', a leprosy-like ulcerative and nodular skin disease especially affecting the head and limbs (Gunn-Moore, 2014), is also part of the NTM group of infections. Of the NTM species, a few cases of disseminated or systemic disease have been reported with *M. avium* (Morfitt *et al.*, 1989; Barry *et al.*, 2002; Griffin *et al.*, 2003; Knippel *et al.*, 2004; Baral *et al.*, 2006; De Groot *et al.*, 2010; Rivière *et al.*, 2011), two cases with *Mycobacterium xenopi* (MacWilliams *et al.*, 1998; Meeks *et al.*, 2008) and single cases with *Mycobacterium heckeshornense* (Elze *et al.*, 2013), *Mycobacterium simiae* (Dietrich *et al.*, 2003) and *Mycobacterium kansasii* (Lee *et al.*, 2017). Despite the reported cases, systemic mycobacteriosis caused by NTM species is still considered relatively rare, especially outside the MAC species (Lloret *et al.*, 2013; Gunn-Moore, 2014; Mauldin and Peters-Kennedy, 2016).

There is close contact between domestic cats and their owners. Given that the incidence of NTM isolates from human patients is rising and that there are still lingering views that systemic NTM mycobacteriosis rarely affects cats, the aim of this study was to describe the pathological and bacteriological findings in three cases of disseminated mycobacteriosis in cats caused by different NTM species.

Materials and Methods

Animals

Three privately owned cats from urban areas of Southern Finland were subjected to necropsy examination at the Department of Veterinary Biosciences, Faculty of Veterinary Medicine, University of Helsinki, Finland, between December 2014 and November 2016. The cats all had a cytological diagnosis of mycobacterial infection. The cats had tested negative for feline immunodeficiency virus (FIV) and feline leukaemia virus (FeLV) within the 8 months preceding their death by humane destruction. Cats A and B had current vaccinations against feline panleucopenia virus, felid herpesvirus and feline calicivirus at the time of death, while cat C had not been vaccinated for several years.

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