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Feline mycobacterial infections

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ABSTRACT

Mycobacteria of feline importance include (1) obligate pathogens (tuberculosis), (2) mycobacteria that are difficult to grow, so the environmental niche is unknown (feline leprosy syndrome), and (3) facultative pathogenic opportunistic saprophytes (non-tuberculous mycobacteriosis). Most cats present with cutaneous disease, although some have systemic involvement. Diagnosis is challenging because there are no pathognomonic histopathological changes and many mycobacteria fail to culture, so molecular diagnostics are required. Treatment can involve extended multidrug therapy and prognosis is variable. This article reviews the microbiology, clinical diagnosis, management and prognosis of feline mycobacterial infections.

Introduction

Mycobacteria of feline importance include (1) obligate pathogens e.g. tuberculosis (TB), (2) mycobacteria that are difficult to grow, with environmental predilections that are currently unknown e.g. feline leprosy syndrome (FLS), and (3) facultative pathogenic opportunistic saprophytes e.g. non-tuberculous mycobacteriosis (NTM). International prevalences vary. For example, FLS and NTM appear to be relatively common in Australia and parts of the USA, while TB (due to *Mycobacterium bovis*), FLS and NTM are regularly diagnosed in New Zealand (Malik et al., 2006). In Great Britain (GB), most definitively diagnosed cases are TB (caused by *M. bovis* and *M. microti*), and disease appears more common than previously thought (Gunn-Moore et al., 2013).

Tuberculosis

Epidemiology and pathogenesis

Feline TB is caused by *M. tuberculosis*, *M. bovis* and *M. microti* (the vole bacillus). Historically, consumption of tuberculous cow's milk often resulted in feline *M. bovis* infections (Jennings, 1949; Snider, 1971). However, declining cattle TB and pasteurisation have resulted in a marked reduction in prevalence (Snider, 1971; Gunn-Moore et al., 2010). Currently, feline TB is recognised infrequently and is almost exclusively caused by *M. microti* or *M. bovis* (Gunn-Moore et al., 2011a). Infection with *M. tuberculosis* is very rare, probably because cats are naturally resistant (Smith, 1965).

Most infected cats hunt small rodents (Gunn-Moore et al., 1996). In GB, wild rodents can be infected with *M. microti* (Cavanagh et al., 2002), and *M. bovis* (Delahay et al., 2007), while in New Zealand, *M. bovis* is endemic in the common brushtail possum, which can be a source of infection for cats (de Lisle et al., 2002). The spoligotypes of *M. bovis* and *M. microti* in cats are the same as those in cattle, badgers (with *M. bovis*) and small rodents from the same geographical area (Monies et al., 2006; Delahay et al., 2007; Smith et al., 2009). Cutaneous disease probably arises from infected bite, fight and, rarely, surgical wounds, or from haematogenous dissemination (Jennings, 1949; Smith, 1965; Isaac et al., 1983; Gunn-Moore et al., 2010). Infections can also occur via environmental contamination, as *M. bovis* can survive for extended periods outside a host (Morris et al., 1994). Nosocomial spread of *M. bovis* between cats has been suspected (de Lisle et al., 1990).

TB is potentially zoonotic (Une and Mori, 2007); there is a single report where diseased colony cats infected an attendant with *M. bovis* (Isaac et al., 1983) and there are anecdotal reports that a small number of people in GB have been infected by their *M. bovis*-infected cats (unpublished data). It is recommended that local health authorities should assess humans exposed to M. bovis-infected cats, especially cats with discharging lesions. *M. microti* is less zoonotic and no cat to human spread has been documented. *M. tuberculosis* and *M. bovis* can cause anthrozoonosis and human to cat transfer has been uncommonly observed.

Predisposition

Feline *M. bovis* infection occurs worldwide, including GB (particularly the South-West of England, co-incident with areas of cattle, badger and rodent *M. bovis* infections), mainland Europe, USA, Japan, Australia and New Zealand (Isaac et al., 1983; de Lisle, 1992; Kaneene et al., 2002; Gunn-Moore, 2010). While *M. microti*

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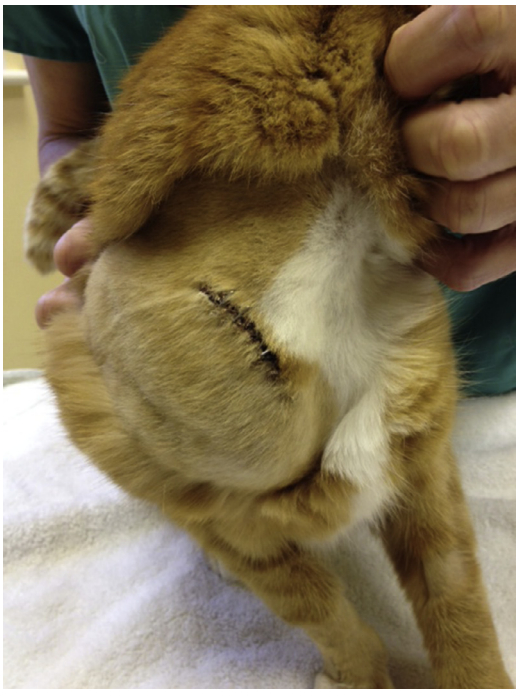

Fig. 1. Large subcutaneous pre-scapular mass (post-biopsy), *M. bovis* (tuberculosis, TB; courtesy of Emma Coles).

infects many different species throughout the world (Cousins et al., 1994; Kremer et al., 1998; Xavier Emmanuel et al., 2007), feline infections occur mainly in GB (especially in the South-East and North of England and the South of Scotland, coincident with *M. microti*-infected rodents; Gunn-Moore et al., 1996; Xavier Emmanuel et al., 2007; Gunn-Moore et al., 2011a), and mainland Europe, including Switzerland (Rüfenacht et al., 2011) and The Netherlands (Huitema and Jaartsveld, 1967; Kremer et al., 1998).

TB is typically seen in adult male cats with access to the outdoors. The median age of infected cats is 3 years for *M. bovis* and 8 years for *M. microti* (Gunn-Moore et al., 2011a). No evidence of classical immunosuppression has been demonstrated and infected cats are usually negative for feline immunodeficiency virus (FIV) and feline leukaemia virus (FeLV) infections (Gunn-Moore et al., 1996, 2011a). However, tuberculous cats have low serum vitamin D concentrations, which influences macrophage function (Lalor et al., 2012).

Infection is thought to occur after protracted exposure to infected individuals, so sub-clinical infection might be common (Snider et al., 1971). However, disease and even death can occasionally occur after a single high dose inoculation of *M. bovis* (Francis, 1958; Isaac et al., 1983).

Clinical signs

Depending on the route of infection, affected cats present with localised cutaneous disease, or less commonly, systemic signs of alimentary, and/or respiratory involvement (Jennings, 1949; Gunn-Moore et al., 2011a). Cutaneous lesions often involve the face, extremities, tail base or perineum, and present as firm dermal nodules, ulceration, or non-healing wounds with draining sinuses, often with local or generalised lymphadenopathy (Fig. 1; Snider, 1971; Gunn-Moore et al., 2011a). Extension can involve muscle and/or bone. Occasionally, localised peripheral lymphadenopathy is the only finding (Gunn-Moore et al., 1996, 2011a).

In rare cases of inhaled infection, tubercles arise in the lungs and/or hilar lymph nodes (Jennings, 1949). However, pulmonary infection occurs more frequently via haematogenous spread from cutaneous (or alimentary) sites, so respiratory lesions are typically diffuse and interstitial (eventually becoming bronchial), causing dyspnoea and occasionally coughing (Gunn-Moore et al., 2010; Bennett et al., 2011). In the alimentary form, tubercles arise in the intestines and/or mesenteric lymph nodes, causing weight loss, anaemia, vomiting and diarrhoea (Jennings, 1949; Monies et al., 2006). Occasionally tubercles arise in the tonsils, causing oropharangeal signs (Jennings, 1949).

Disseminated disease can cause hepato-splenomegaly, pleural or pericardial effusion, generalised lymphadenopathy, weight loss and fever (Gunn-Moore, 2010). Lameness might result from bone and/or joint involvement (Gunn-Moore et al., 1996). Ocular and brain involvement have been documented (Formston, 1994; Gunn-Moore et al., 1996).

Feline leprosy syndrome

Epidemiology and pathogenesis

Historically, it was presumed that FLS was caused by *M. lepraemurium* (which causes leprosy in rodents), as this bacterium cannot be cultured using standard techniques (Shrikrishna and Middleton, 1983). However, molecular techniques have demonstrated that FLS is actually caused by a number of mycobacteria, namely, *M. lepraemurium*, *M. visibile*, *Mycobacterium* sp. Tarwin, and novel mycobacterial species, with geographically variable prevalence (Hughes et al., 1997; Appleyard and Clark, 2002; Malik et al., 2002, 2013; Davies et al., 2006; Courtin et al., 2007; Fyfe et al., 2008).

Infection can follow rodent bites (Fyfe et al., 2008), or possibly involve soil contamination of wounds. While there is no known zoonotic potential, molecular diagnostics might provide further information on this.

Predisposition

There is no breed predisposition, but adult male cats with outdoor access are most at risk, probably because of hunting and fighting (McIntosh, 1982; Malik et al., 2002; Courtin et al., 2007; Fyfe et al., 2008). In Australia, older cats with chronic kidney disease or immunosuppressed with FIV appear predisposed to the novel mycobacterial species (Malik et al., 2013). Prevalence is higher in temperate maritime climates e.g. Australia, New Zealand, Europe (GB, Channel Islands, The Netherlands, France, and Greece), Western Canada and the USA (California and Oregon; Poelma and Leiker, 1974; Schiefer et al., 1974; Thompson et al., 1979; McIntosh, 1982; Malik et al., 2002; Courtin et al., 2007).

Clinical signs

FLS is primarily a cutaneous disease presenting as alopecic or ulcerated, non-painful and freely mobile single or multiple nodules, often on the head, limbs and occasionally trunk (Fig. 2; Thompson et al., 1979; McIntosh, 1982; Malik et al., 2002). Rare cases affect the tongue, lips, nose or conjunctivae (Malik et al., 2000, 2002). Regional lymphadenopathy can occur (Poelma and Leiker, 1974; McIntosh, 1982; Malik et al., 2002). Systemic disease is rare, but can be progressive and aggressive (Malik et al., 2002). In Australia, younger cats typically develop rapidly progressing localised, often ulcerated, nodules on the limbs, while older cats develop generalised non-ulcerative skin involvement with a slower clinical progression (Malik et al., 2002). The severity of