Journal of Feline Medicine and Surgery (2009) **11**, 627–632
doi:10.1016/j.jfms.2008.10.008

ELSEVIER

jfms

Clinical outcome of cutaneous rapidly growing mycobacterial infections in cats in the south-eastern United States: a review of 10 cases (1996–2006)

Katie S Horne DVM[a], Gail A Kunkle DVM, DACVD*

Department of Small Animal Clinical Science, College of Veterinary Medicine, University of Florida, Gainesville, FL, USA

Cutaneous infection caused by rapidly growing mycobacteria is a relatively uncommon condition in cats, with variable response rates to surgical debulking and aggressive antibiotic therapy. To date, there have been very few case reports of this disease, especially in the United States. This study reviews a series of cases of cats with rapidly growing cutaneous mycobacterial infections from the south-eastern United States. A majority of the cats were spayed female domestic shorthairs. The median age at onset of clinical signs was 8 years. A majority of cats presented with characteristic lesions in multiple locations, and half of the cats had a known incidence of trauma preceding the development of clinical signs. *Mycobacterium fortuitum* was the most frequently cultured organism. Cats were treated with a variety of antibiotics for a median of 12 months, and half of them underwent surgical debulking of infected tissue. Five out of the 10 cats reached clinical resolution, while five did not. Those that did resolve required a median of 7 months of antibiotic treatment following diagnosis, and had been lesion-free for a median of 24 months at the time this study was completed. Those that did not resolve were treated for a median of 20 months following diagnosis, two of which were still being treated at the time this study was completed.

Date accepted: 13 October 2008

Cutaneous mycobacterial infection caused by rapidly growing mycobacteria is a rarely reported, yet challenging dermatological condition to treat in cats. The disease is characterized by chronic and often refractory infection of the skin and subcutis.[1] Members of the group of rapidly growing mycobacteria are ubiquitous in soil and bodies of water, and have been traditionally thought to cause disease most commonly in warm, humid climates.[2,3]

Management of this condition continues to evolve over time. Currently, aggressive, long-term antimicrobial therapy with or without surgical excision of infected tissues is the most commonly used treatment strategy. However, variation in the extent, severity, and recurrence of lesions among cats remains substantial.[1]

This paper describes culture results, treatment strategies, and clinical course and outcome of disease in a group of cats with cutaneous rapidly growing mycobacterial infections in the south-eastern United States.

*Corresponding author. E-mail: uncdvm@gmail.com
[a]Current address: Wilmington Animal Healthcare, Wilmington, NC, USA.

Materials and methods

The cats with rapidly growing mycobacterial skin disease evaluated in this study were identified from University of Florida Veterinary Medical Center (UF-VMC) microbiology laboratory material. Cats that were initially examined from 1996 to 2006, were tissue culture positive for rapidly growing mycobacterium, and had at least 9 months of follow-up were deemed eligible for inclusion in this study. Adequate information was also required for each case, including signalment, age at onset of clinical signs, general health of the cat, incidence of trauma prior to development of clinical signs (if applicable), location of lesion(s) at presentation, culture and sensitivity information, and duration of and response to all treatments used. For those cases seen by the UF-VMC Dermatology Service, this information was gathered from case records. For those cases not seen by the UF-VMC Dermatology Service, the same information was gathered from the primary care veterinarians who made the diagnosis, via telephone and email communication. Biopsy samples submitted for acid-fast bacteria (AFB) culture at the UF-VMC are cultured on

1098-612X/09/080627+06 $34.00/0

Lowenstein–Jensen agar slants, and mycobiotic agar plates at 37°C for 30 days. At that time, the cultures are finalized, then held for an additional 30 days before being discarded. All mycobacterial cultures submitted to the UF-VMC microbiology laboratory are initially grown and sent to the Mycobacteriology Reference Laboratory at the National Jewish Medical and Research Center in Denver, Colorado for species identification and sensitivity testing. Species identification is performed using high performance liquid chromatography (HPLC) to determine mycolic acid profile, as well as 16S rDNA sequencing, and biochemical testing. Susceptibility testing is performed via microtiter mean inhibitory concentration (MIC) of up to 20 different antibiotics.

For all cases, follow-up information including extent of resolution of lesions and the amount of time from diagnosis to resolution (if achieved) was gathered via telephone and email contact with both primary care veterinarians and owners. Those cases with less than 9 months of follow-up, or for which adequate follow-up information could not be obtained were excluded from this study. After final review, 10 cases of feline rapidly growing mycobacterial infection were deemed appropriate for inclusion in this study.

Results

Of the 10 cases in this study, six were spayed females, one was an intact female, one was a castrated male, and the remaining two were intact males. Eight of the 10 were domestic shorthair (DSH) cats, one was a Siamese cat and one was a Maine Coon cat (Table 1).

Age at onset of clinical signs of infection ranged from 1 to 14 years. Median age at onset was 8 years (Table 1).

Upon presentation, lesions were located in the following regions of the body: inguinal, perineum, ventral abdomen, flank, hip, axilla, lateral thigh, lateral thorax, dorsum, and tail base. Areas infected were extensively involved, and characteristic lesions included subcutaneous and dermal nodules or plaques, areas of cellulitis and discoloration, and draining tracts or ulcerations that often connected different nearby areas of lesions. Actively draining wounds exuded serosanguinous fluid. In all but four cats, lesions were present in more than one location. The flank was the most common site of lesions, followed by the ventral abdomen, then the inguinal region; thus, the lesions reported in this study were primarily truncal, and concentrated ventrally (Table 1).

In 5/10 cats, there was known trauma prior to development of clinical signs of infection. Types of trauma included cat bites in two cases, puncture and bite wounds of unknown origin in two cases, and in another case trauma caused by a suspected animal attack in which the other species of animal(s) was unknown. In 2/10 cases trauma was not reported prior to onset of clinical signs. In 3/10 cases, it was unknown if any prior trauma had occurred.

Blood work at the time of diagnosis or at the time of referral was available from nine of the cats. All nine tested negative for feline leukemia virus. Eight cats had hemograms and chemistries recorded at least once during the early course of the condition: all cats had normal total white blood cell count with one cat each manifesting mild neutrophilia, lymphocytosis, and eosinophilia. Another cat with the condition chronically had mild anemia and mild hyperglobulinemia. All other chemistry values were within normal limits. No underlying immunosuppressive conditions or administration of drugs considered to be immunosuppressive was identified in any of the nine cats for which there was early data.

Mycobacterium fortuitum was cultured from 6/10 cases in this study. *Mycobacterium abscessus* was cultured from two cases, and *Mycobacterium goodii* was cultured from one case. One case grew a group IV mycobacterium, for which species identification was not pursued due to owner financial constraints (Table 1).

Multiple antibiotics were used in the treatment of these cats (Table 2). Marbofloxacin was the most frequently prescribed antibiotic in treating the cases in this study, followed closely by clarithromycin,

Table 1. Case details of cats with rapidly growing mycobacterial infections

	Sex	Breed	Age at onset (years)	Location of lesion(s) at presentation	Culture organism
Case 1	FS	DSH	8	Inguina, cranioventral abdomen	*M fortuitum*
Case 2	FS	DSH	14	Inguina, perineum, left flank	*M abscessus*
Case 3	FS	Siamese	2	Right hip	*M abscessus*
Case 4	MC	DSH	1	Ventral abdomen	*M fortuitum*
Case 5	FS	DSH	8	Right axilla, ventrum	*M fortuitum*
Case 6	ME	DSH	4	Ventral abdomen	*M fortuitum*
Case 7	ME	DSH	10	Inguina, thigh, and perineum	*M fortuitum*
Case 8	FE	DSH	6	Left flank	Group IV *Mycobacterium* species
Case 9	FS	DSH	8	Dorsum, left flank, right lateral thorax	*M fortuitum*
Case 10	FS	Maine Coon	8	Tail base, left flank	*M goodii*

FS = female spayed; FE = female entire; MC = male castrated; ME = male entire; DSH = domestic shorthair.

doxycycline, and minocycline. No drug, either alone or in combination with another antibiotic, was used for less than 19 days. This included all cases in which antibiotics were discontinued due to adverse effects except one, in which enrofloxacin was discontinued after 3 days due to the development of abnormal behavior and possible neurological signs. In 6/10 cases, two antibiotics were used in combination at least once during the treatment period; two of these cases eventually resolved. In one case, only one antibiotic was used at a time throughout the entire treatment period; this case resolved. The remaining three cases were treated with only one antibiotic for the entire treatment period, two of which resolved with treatment (Table 2). The reasons for discontinuing an antibiotic included lack of clinical improvement and the development of adverse side effects. In one case, antibiotic therapy was discontinued because the cat developed renal insufficiency. Both reasons for discontinuing a drug were demonstrated equally in this study.

Five of the 10 cases in this study reached clinical resolution. Two of these five cats had surgery to debulk infected tissue mass in addition to antibiotic therapy. Of the remaining three that did not undergo surgery, one resolved with treatment with only one antibiotic for the entire duration of treatment, while the other two were treated with at least two antibiotics, either in combination or succession. Two of these cases were receiving clarithromycin at the time of resolution. One case was receiving trimethoprim-sulfa, while another was receiving minocycline at the time of resolution. The last case resolved while receiving both marbofloxacin and sulfadimethoxine−ormetoprim. Of those that did not resolve, three had surgery to debulk infected tissue in addition to treatment with at least two antibiotics either in combination or succession, as did one case that did not undergo surgery. One case was treated with only one antibiotic for the entire treatment period (Table 2).

Duration of treatment following diagnosis of all cats ranged from 3 to 60 months, with a median of 12 months. The cats that resolved required a median duration of treatment of 7 months, with range of 3−21 months. Three of the 10 cats were still being treated at the time this paper was completed, including one case that resolved. This particular cat had been lesion-free for 19 months at the time this study was completed, but the owner insisted on continuing treatment. Duration of treatment following diagnosis of those cases which did not resolve ranged from 7 to 60 months, with a median of 20 months (Table 2).

At the time this study was completed, the amount of time that the resolved cases had remained lesion-free ranged from 13 to 75 months, with a median of 24 months (Table 2).

Discussion

This study reviewed the case details and clinical outcome of 10 cases of feline cutaneous rapidly growing mycobacterial infections in the south-eastern United States. Of the 10 cases, five resolved with treatment and five did not.

Similar to what has been illustrated in previous studies, there was an over representation of spayed female cats in our study. Malik has hypothesized that spayed female cats are more likely to become obese and to have significant fat deposits that can serve as potential growth media for mycobacteria following inoculation through the skin.[4] However, of the five cases that resolved, three were spayed females, suggesting that while a predisposition to obesity may very well make developing a rapidly growing mycobacterial infection more likely, it may not necessarily affect how likely the case is to resolve with treatment. On the other hand, the sex of the five cases that failed to resolve did not appear to have any significance; both neutered and intact males and females were present in this group (Tables 1 and 2). The age range at onset of clinical signs in this study did not differ from what has been observed in the past, nor did location of lesions at presentation.[4,5] In addition, age did not appear to correlate with response to therapy, as the median age of onset for both responders and non-responders was 8 years (Table 1).

The species of mycobacterium, on the contrary, differed between the cases that resolved and those that did not resolve. Four of the five cases that did not resolve were infected with *Mycobacterium fortuitum*, while *M fortuitum* was the cause of only 2/5 cases that did resolve. It should be noted that the mycobacterium species was not identified in 1/5 cases that resolved. A study conducted in Australia showed that *M fortuitum* strains were more commonly resistant to multiple antibiotics than other strains[4]; however, in our study, cases of *M fortuitum* infection were susceptible in vitro to more antibiotics than cases caused by any other species (Table 3). It has also been suggested that *M fortuitum* may be a more common cause of disease than other species of mycobacteria in North American cats.[1,6,7] As *M fortuitum* was cultured from 6/10 cases in this study, this appears to be the more reasonable explanation for the over representation of unresolved cases due to this species.

Interestingly, while it is currently thought that cutaneous rapidly growing mycobacterial infections occur following organism inoculation resulting from some type of trauma,[3,8] two cases in our study had no history of any type of trauma prior to development of infection; one case cleared and the other did not. As it is considered impossible for rapidly growing mycobacteria to cause disease without a break in normal defense mechanisms,[2,3,8] it can be presumed likely that either these cats had undergone some unnoticed trauma, or some type of wound was present that became contaminated with environmental organisms.

No underlying conditions or drugs that might have led to immunosuppression were identified in these cats. A recent Mayo Clinic study of 63 human patients with skin and soft tissues infections from rapidly growing mycobacteria[9] concluded that these infections are

Table 2. Treatment and resolution information for cats with rapidly growing mycobacterial infections

	Antibiotics used following biopsy for culture and sensitivity testing	Surgical debulking	Duration of treatment following diagnosis (months)	Resolution	Antibiotic being used at time of resolution	Time since resolution (months)
Case 1	Clarithromycin minocycline, trimethoprim-sulfa	No	40+	Yes	Trimethoprim-sulfa	19
Case 2	Clarithromycin	No	4.5	Yes	Clarithromycin	47
Case 3	Doxycycline, clarithromycin	No	7	Yes	Clarithromycin	24
Case 4	Minocycline, doxycycline, trimethoprim-sulfa, marbofloxacin, moxifloxacin, clarithromycin	Yes	50	No		
Case 5	Marbofloxacin	Yes	20+	No		
Case 6	Enrofloxacin, ciprofloxacin, minocycline, amoxycillin−clavulanic acid, marbofloxacin, cefadroxil	Yes	60	No		
Case 7	Clarithromycin, doxycycline, marbofloxacin, sulfa-ormetoprim	Yes	13	Yes	Marbofloxacin, sulfa-ormetoprim	13
Case 8	Minocycline	Yes	3	Yes	Minocycline	75
Case 9	Minocycline, marbofloxacin, doxycycline	No	7	No		
Case 10	Marbofloxacin, doxycycline	No	11+	No		

+ Indicates patient was still being treated with antibiotics at the time this study was completed.

Table 3. Culture and sensitivity information for cases of rapidly growing mycobacterial infection

		Amikacin	Kanamycin	Tobramycin	Gentamicin	Cefoxitin	Ceftriaxone	Cefepime	Cefotaxime	Imipenem	Doxycycline	Minocycline	Ciprofloxacin	Gatifloxacin	Moxifloxacin	Clarithromycin	Azithromycin	Trimethoprim-sulfa	Linezolid	Augmentin	Sulfamethoxazole	Tigecycline	Erythromycin
Case 1	*M fortuitum*	S	I	R	S	S	R	R	R	I	I	S	S	S	S	S	S	S	S	R	NT	NT	NT
Case 2	*M abscessus*	S	S	I	R	S	R	R	R	I	R	R	R	R	R	S	S	R	R	R	NT	NT	NT
Case 3	*M abscessus*	S	S	R	R	S	R	R	R	S	R	R	R	R	R	S	S	R	R	R	NT	NT	NT
Case 4	*M fortuitum*	S	S	R	I	S	R	R	R	S	S	S	I	S	S	I	R	S	I	I	S	S	R
Case 5	*M fortuitum*	I	R	R	S	S	R	R	R	S	R	I	S	S	S	S	S	S	I	R	NT	S	NT
Case 6	*M fortuitum*	S	S	S	S	I	NT	NT	NT	S	NT	S	S	NT	NT	R	R	NT	NT	S	R	NT	R
Case 7	*M fortuitum*	S	S	S	S	I	R	R	R	S	S	S	S	S	S	S	S	S	S	I	NT	S	NT
Case 8	Group IV *Mycobacterium* species	S	S	I	S	S	NT	NT	NT	S	NT	S	S	NT	NT	R	R	NT	NT	S	R	NT	R
Case 9	*M fortuitum*	S	S	I	S	I	R	R	R	S	S	S	S	S	S	I	R	S	I	I	NT	S	NT
Case 10	*M goodii*	S	S	S	S	I	R	R	R	S	S	S	S	S	S	R	R	S	R	S	NT	S	NT

S = organism susceptible to antibiotic; I = organism had intermediate susceptibility to antibiotic; R = organism resistant to antibiotic; NT = susceptibility to antibiotic not tested; NA = information not available. All sensitivity tests performed at the Mycobacteriology Reference Laboratory at the National Jewish Medical and Research Center in Denver, Colorado.

often associated with systemic disease and/or immunosuppressive medications. However, patients with *M fortuitum* infections were likely to be younger, generally had a prior invasive surgical procedure at the site and were much less likely to be immunocompromised than those with *Mycobacterium chelonae* or *Mycobacterium abscessus*. Although we did not identify immunocompromise in our cats it is certainly possible that we failed to identify a medical reason for the infection and/or the slow response to treatment.

It has been suggested that some cases of cutaneous rapidly growing mycobacterial infection are so severe that complete resolution is practically impossible without surgical debulking of infected tissues down to a level of infection more effectively managed by systemic antibiotics.[3,5] Surgical debulking was performed in half the cases in our study, but only two of these cases eventually resolved. It is indeed possible that those which did not resolve were severe enough that removal of infected tissue was not sufficient to result in cure with subsequent antibiotics. Or, it could be hypothesized that the infected tissue may not have been as effectively removed in the cases that did not resolve as it was in the two cases that did resolve. Regardless, with case numbers so small there is not sufficient evidence from this study to support the opinion that surgical debulking is the best chance for cure of extensive infections.

Previous studies of feline rapidly growing mycobacterial infections, conducted in Australia, concluded that treatment of these infections often requires courses of antibiotics 3–6 months in length. In these studies, a total of 19 cats were treated first with either doxycycline or a fluoroquinolone for several weeks, followed by radical surgical debulking of infected tissues[10] with intra- and perioperative intravenous gentamicin. This was followed by treatment with doxycycline or a fluoroquinolone. In all cases resolution was achieved in less than 6 months. Resolution was defined as absence of disease recurrence for years after treatment was stopped.[4,5] In contrast, the cases that resolved in our study required a median duration of treatment following diagnosis of 7 months, with a range of 3–21 months. In addition, the cases that did not resolve were treated for a median of 20 months, with a range of 7–60 months (Table 2).

This report agrees with another United States report[7] of six cats with rapidly growing mycobacteria in which treatment with antibiotics and/or surgery was usually unsuccessful. Although laboratory testing and antibiotic choices may be better today, the prognosis for cure in the United States is still not good.

There are many possible explanations for the disparity between our findings and those that are currently described. For example, there could be a difference in the mycobacterial species responsible for the infections in each study. From all but 2/17 cases that cured in the Australian study, *M smegmatis* was cultured and was susceptible to a wider range of antibiotics than the *M fortuitum* cultured from the other two.[4,5] In contrast, *M fortuitum* was cultured more frequently than any other species in our study, both from cases that cleared and those that did not (Table 1), and it was susceptible to a wider range of antibiotics than the other species cultured (Table 3). This evidence suggests that not only does there appear to be a difference in the more commonly recovered species of organism, which has been suggested in the past,[4,6,7] but the same organism appears to behave differently depending on the geographic area of the cat from which it is cultured. As these organisms are saprophytic and ubiquitous in the environment, differences in temperature, humidity, and amount of precipitation between areas of the south-eastern United States and areas of Australia could possibly affect the biological and/or physical characteristics of the mycobacteria.

The different findings could also be attributed to differences in drug dosing, dosing intervals, combinations and order of drugs administered, treatment intervals, drug formulation, compounding pharmacies, and owner compliance. However, no correlation was found between type of treatment strategy used and resolution among the cases in our study (Table 2). In addition, clarithromycin was determined by the Australian study to be a very effective drug in treating this type of infection.[4,5] This was supported by the two cases that resolved while being treated with clarithromycin in our study (Table 2).

The objective of this study was to gather and report data on feline cases of cutaneous rapidly growing mycobacterial infections in an attempt to report prognosis for this condition in the south-eastern United States. Because only half of the cases in this study resolved, one can justify a guarded prognosis in cases of feline rapidly growing mycobacterial infection in the south-eastern United States.

Acknowledgements

We thank the many veterinarians and owners that provided information on the cats in this study; they were an integral part of this study. We also recognize the Microbiology Laboratory and the Medical Records Department at the University of Florida Veterinary Medical Center; their patience and assistance were greatly appreciated.

References

1. Malik R, Martin P, Wigney D, Foster S. Infections caused by rapidly growing mycobacteria. In: Winkel A, Stringer S, eds. Infectious diseases of the dog and cat, 3rd edn. St Louis: Saunders Elsevier, 2006: 482–7.
2. Pedersen NC. Atypical mycobacteriosis. Feline infectious diseases. Golete: American Veterinary Publications, 1988: 197–200.
3. Wilkinson GT, Mason KV. Clinical aspects of mycobacterial infections of the skin. In: August JR, ed. Consultations in feline internal medicine. Philadelphia: Saunders, 1991: 129–36.

4. Malik R, Wigney DI, Dawson D, Martin P, Hunt GB, Love DN. Infection of the subcutis and skin of cats with rapidly growing mycobacteria: a review of microbiological and clinical findings. *J Feline Med Surg* 2000; **2**: 35–48.
5. Malik R, Hunt GB, Goldsmid SE, Martin P, Wigney DI, Love DN. Diagnosis and treatment of pyo-granulomatous panniculitis due to *Mycobacterium smegmatis* in cats. *J Small Anim Pract* 1994; **35**: 524–30.
6. Kunkle GA, Gulbas NK, Fadok V, Halliwell REW, Connelly M. Rapidly-growing mycobacteria as a cause of cutaneous granulomas: report of five cases. *J Am Anim Hosp Assoc* 1983; **19**: 513–21.
7. White SD, Ihrke PJ, Stannard AA, et al. Cutaneous rapidly-growing mycobacteria in cats. *J Am Vet Med Assoc* 1983; **182**: 1218–22.
8. Street ML, Umbert-Millet IJ, Roberts GD, Su WP. Nontuberculosis mycobacterial infections of the skin. Report of fourteen cases and review of the literature. *J Am Acad Dermatol* 1991; **24**: 208–15.
9. Uslan DZ, Kowalski TJ, Wengenack NL, Virk A, Wilson JW. Skin and soft tissue infections due to rapidly growing mycobacteria. *Arch Dermatol* 2006; **142**: 1287–92.
10. Hunt GB. Skin-fold advancement flaps for closing large sternal and inguinal wounds in cats and dogs. *Vet Surg* 1995; **24**: 172–5.