

Cutaneous Nocardiosis in a Cat

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ABSTRACT. A 4-year-old spayed female domestic shorthair cat was presented to us for swelling of all foot pads. The skin lesions were histopathologically diagnosed as suppurative pyogranulomatous panniculitis. The lesions did not respond to cephalexin, prednisolone or itraconazole. However, complete resolution of the skin lesions was obtained with doxycycline. A littermate living in the same household developed similar skin lesions that were also successfully treated with doxycycline. Polymerase chain reaction analysis detected the 16S ribosomal RNA gene of *Nocardia* spp. in DNA extracted from lesion pus, and direct nucleotide sequencing analysis revealed 100% homology with *Nocardia elegans*. We diagnosed this case as nocardiosis.

KEY WORDS: feline, nocardiosis, suppurative granulomatous inflammation.

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Nocardiosis is a rare infectious disease in dogs and cats that develops when *Nocardia* spp., soil saprophytes, are inadvertently inoculated into a skin puncture wound or inhaled into the lungs [8]. Nocardiosis can be classified into three clinical presentations, pulmonary, systemic or disseminated and cutaneous [5]. Among these three presentations, cutaneous nocardiosis is the most common form and usually causes suppurative pyogranulomatous inflammation. Cutaneous nocardiosis manifests as localized nodules, cellulitis and abscesses, with ulcerations and fistulous tracts that drain a serosanguineous discharge. Skin lesions are usually formed on the extremities, inguinal area and neck [5].

A 4-year-old spayed female domestic shorthair cat was presented to the Kagoshima University Veterinary Teaching Hospital with a 6-month history of non-healing swelling of all foot pads. On physical examination, the cat was obese with a body condition score of 5/5 [3] and had distended foot pads that were partially ulcerated and discharging pus (Fig. 1). Fever (40.4°C) and lethargy were observed. A complete blood cell count and serum chemistry revealed leukocytosis ($22.6 \times 10^9/l$) and mild hyperglycemia (232 mg/dl), respectively. Tests for feline leukemia virus antigen and feline immunodeficiency virus antibody produced negative results with a commercially available kit (SNAP FIV/FelV Combo Test; IDEXX Laboratories, Tokyo, Japan). Since the skin lesions were extremely unusual, we decided to take a skin biopsy from one of the feet. Histopathological examination revealed that the lesion consisted of suppurative pyogranulomatous panniculitis. Sulfur granules that were aggregates of bacterial colonies and inflammatory cells were not observed. No fungal bodies were detected in periodic acid-Schiff stained specimens. A nonfermenting

gram-negative bacillus that was resistant to amoxicillin was obtained from bacterial culture of discharge pus from the lesion.

The cat was treated with cephalexin (20 mg/kg, PO, q12h) to rule out bacterial infections. Although the bacterial culture results were negative after 30 days of treatment, the clinical symptoms did not improve. Treatment with prednisolone (1.7 mg/kg, PO, q24h) was initiated with concurrent enrofloxacin (2.7 mg/kg, PO, q24h) because immune-mediated etiologies were suspected. After 2 weeks, the lesions on the foot pads deteriorated, and subcutaneous abscesses with fistulous tracts were formed in the ventral neck and thorax (Fig. 2-A and B). The cat showed fever, depression, anorexia and progressive weight loss. Prednisolone was withdrawn, and itraconazole treatment (3 mg/kg, PO, q12h) was initiated to rule out fungal infections. In addition, we performed a fungal culture for one of the skin lesions and polymerase chain reaction (PCR) analysis to amplify the conserved region of fungal ribosomal DNA [1, 9] using DNA extracted from the pus. However, both exam-



Fig. 1. Swollen footpads at the first presentation. The lesion is partly ulcerated and discharging pus.

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Fig. 2. Deteriorated lesion after prednisolone treatment. (A) The instep of the hind paw is seriously ulcerated. (B) Subcutaneous abscesses with fistulous tracts are seen in the ventral neck.

inations produced negative results. A bacterial culture for *Nocardia* spp. was attempted under aerobic conditions, but no growth was observed on blood agar, chocolate agar or BTB agar at 37°C for 48 hr. One month culture on Sabouraud's dextrose agar also failed to induce any growth of microbes. Itraconazole treatment did not improve the symptoms or skin lesions. The antibiotic regimen was changed to doxycycline (5 mg/kg, PO, q12h). Subsequently, obvious reductions in lesion size and recovery of the clinical symptoms were observed within 2 weeks. The ulcers on the feet and subcutaneous abscesses in the ventral neck and thorax disappeared completely after 2 months of doxycycline treatment. Withdrawal of doxycycline caused two relapse, and improvement was seen after restart of doxycycline administration. Since doxycycline-responsive bacterial infections were suspected, PCR analysis to amplify the 16S ribosomal RNA gene of *Mycobacterium* spp. [7] was performed using DNA extracted from the pus. An approximately 540-bp DNA fragment was amplified, and direct nucleotide sequencing analysis (Texas Genomics Japan, Tokyo, Japan) revealed 100%, 99.4% and 99.1% homology with the 16S rRNA genes of *Nocardia elegans*, *Nocardia transvalensis* and *Nocardia farcinica*, respectively. This DNA fragment showed 97.2% homology with *Nocardia asteroides*, which is the most commonly isolated species in cats. Small numbers of acid-fast bacilli that were approximately 3 μ m long were identified by Ziehl-Neelsen acid-fast staining in the skin biopsy sample obtained at the first presentation (Fig. 3). These bacilli were smaller than those of previous reports [5, 6]. This case was ultimately diagnosed as cutaneous nocardiosis based on the PCR analysis and Ziehl-Neelsen staining results.

At 3 months after resolution of the skin lesions, one littermate living in the same household developed subcutaneous abscesses in the back, and the lesion improved after doxycycline treatment. Although PCR analysis was not performed, nocardiosis was highly suspected.

Nocardiae are soil saprophytes belonging to the family Actinomycetales and are ubiquitously present in the envi-

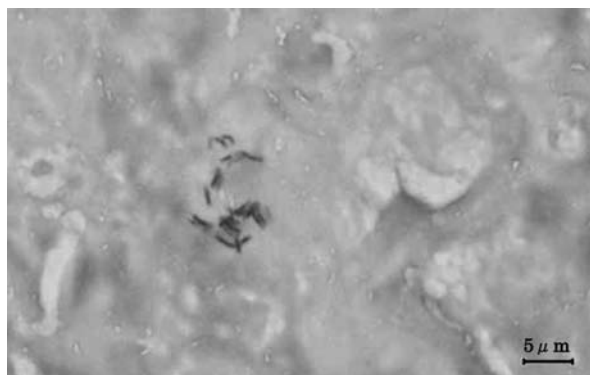


Fig. 3. Ziehl-Neelsen staining of the skin biopsy sample at the first presentation. The center of the granulomas contains acid-fast filamentous organisms.

ronment, especially in soil and plants. *Nocardia* spp. are gram-positive, aerobic and partially or variably acid-fast bacteria that form branching filamentous rods [10]. *N. asteroides* is the most commonly isolated *Nocardia* species in human and animal patients, and there have been few reports of infections by other *Nocardia* species in cats [5]. *N. elegans* was first isolated from a human patient as a causative agent of pulmonary nocardiosis in Germany [11]. Infection of cats with *N. elegans* has not previously been reported.

It was difficult to diagnose nocardiosis in the present case because the pathogen was not identified by either histopathological examinations or bacterial cultures for *Nocardia* spp. However, diagnosis was finally achieved by 16S rRNA gene sequencing analysis. Owing to the species-specific drug susceptibility patterns of *Nocardia* spp., it is important to rapidly identify nocardial species and select appropriate antibiotics. Sequencing analysis of the 16S rRNA gene is a rapid and reliable method for diagnosing nocardiosis and to identifying *Nocardia* species [4]. Although the drug susceptibilities of *N. elegans* have not been reported, doxycycline was effective in the present case.

Even though immunosuppressive conditions, such as acquired immune deficiency syndrome, transplantation and corticosteroid administration, can be major risk factors for infections in humans [2], the two cats in the present report were clinically immunocompetent. Although the routes of infection could not be identified in these cats, there are several possibilities. These include the possibility that there were some infectious sources of *Nocardia* spp. in the soil around the cat owner's home. It is also possible that the two cats may have been more susceptible to *Nocardia* spp. than the other two cats living in the household that did not present clinical symptoms of nocardiosis. Finally, it is possible that the first cat transmitted cutaneous nocardiosis to the second cat, but there are no previous reports of such transmission from cat to cat.

Doxycycline treatment was continued for 7 months after the two episodes of relapse and then withdrawn. The cat has remained free of relapse for 4 months since withdrawal of

doxycycline.

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