Diagnostic Exercise

From The Davis-Thompson Foundation*

ase # **210**; Month: **April**; Year: **2023**

Answer sheet

Title: Atypical mycobacteriosis in a cat

Contributors: Lorena G. R. Ribeiro[1], DVM, MSc, PhD; Lauren W. Stranahan[2], DVM, DACVP, PhD.
[1]Department of Veterinary Medicine - Federal University of Sergipe, São Cristóvão, SE, Brazil. [2]Department of Veterinary Pathobiology - College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, USA
Email: lstranahan@cvm.tamu.edu

Clinical History: A five-year-old, spayed female, American Domestic Shorthair Cat presented with a two-year history of multifocal non-healing, ulcerated areas with serous discharge on the ventral abdomen that responded partially to antibiotics and steroids (Fig. 1). The lesions were biopsied and submitted for culture and histopathology.

Clinical and Histological Images:

Figure 1. Multifocally, ulcerations measuring 0.2 to 1.5 cm in diameter with pale red, serous exudate and surrounding erythematous skin are on the ventral abdomen affecting the inguinal fat pad.

Histologic Findings: Numerous epithelioid macrophages and neutrophils with fewer lymphocytes and plasma cells multifocally infiltrated and effaced the deep subcuticular fat with multifocal extension to the level of the superficial dermis and formed dense, coalescing aggregates (Fig. 2). Inflammatory cells frequently surrounded multifocal round, clear vacuoles lined by a rim of neutrophils. Vacuoles typically contained dense, tangled aggregates of pale basophilic, rod-shaped, filamentous bacteria (Fig. 3). Bacteria were strongly acid-fast (Fig. 4A) and gram-positive (Fig. 4B). GMS also highlighted bacteria and no fungal organisms were observed with this stain (Fig. 4C). The inflammatory infiltrate surrounded and widely separated adnexal units with adjacent hair follicles showing mild to moderate atrophy. The epidermis was mildly and irregularly hyperplastic and exhibited mild, basketweave, orthokeratotic hyperkeratosis. In one of the biopsies, a small focus of pyogranulomatous inflammation surrounded free hair shafts (furunculosis). The adjacent lymph node exhibited moderate lymphoid follicular hyperplasia and sinus histiocytosis.

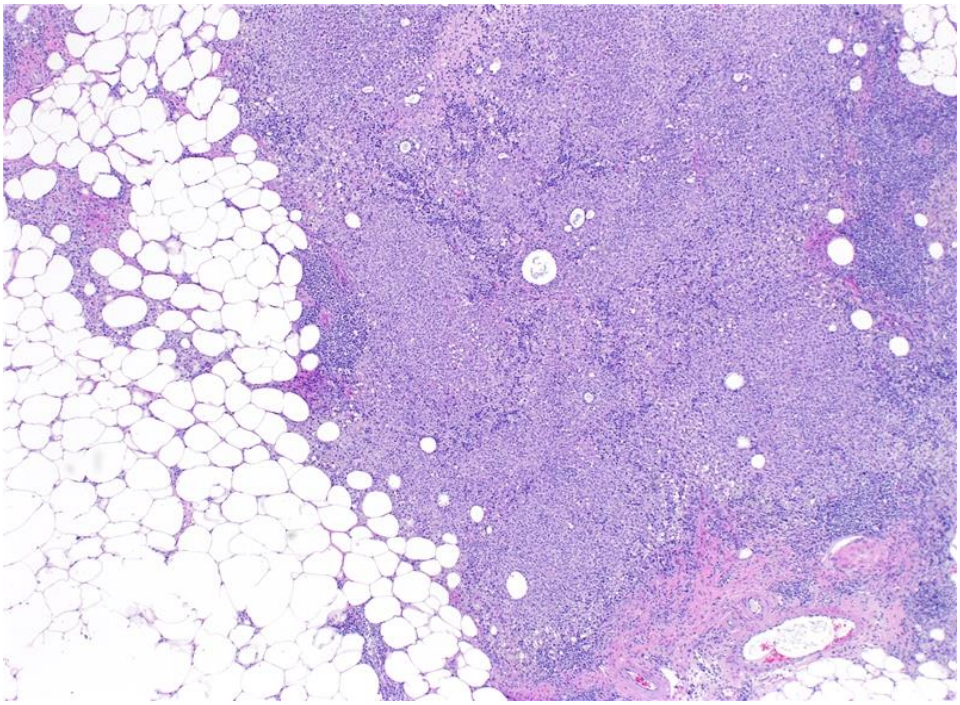

Figure 2. The subcuticular fat is partially effaced by multifocal to coalescing, dense inflammatory cell infiltrates. Hematoxylin and eosin stain (H&E), 10x.

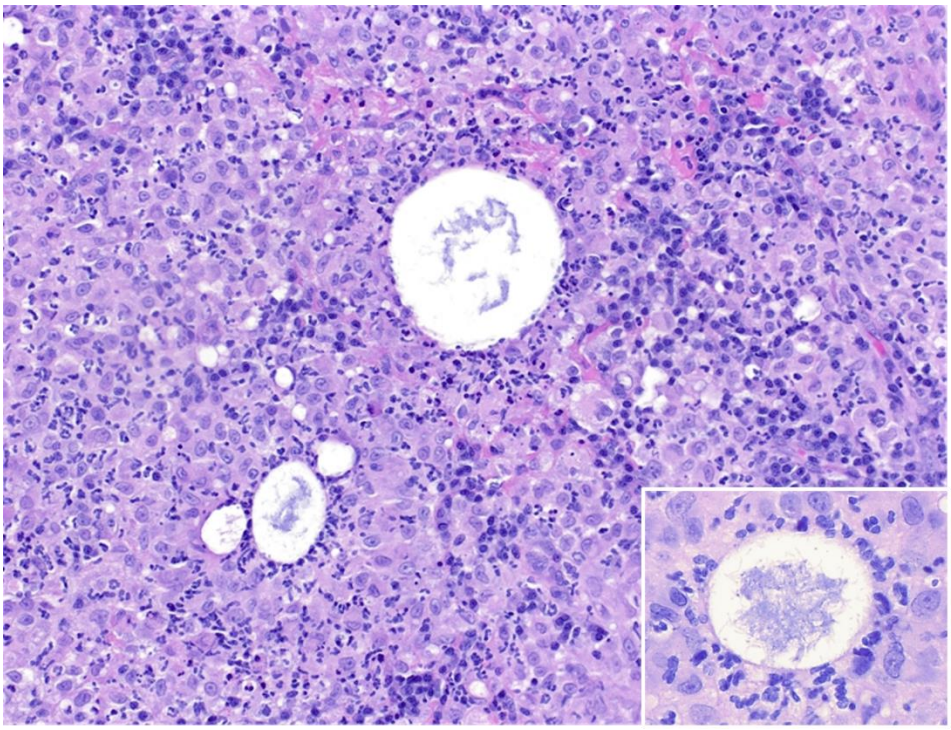

Figure 3. Marked inflammation composed of numerous epithelioid macrophages and neutrophils with fewer lymphocytes and plasma cells surround multifocal round, clear vacuoles containing dense tangled aggregates of basophilic, rod-shaped bacteria (inset), H&E, 20x and 40x.

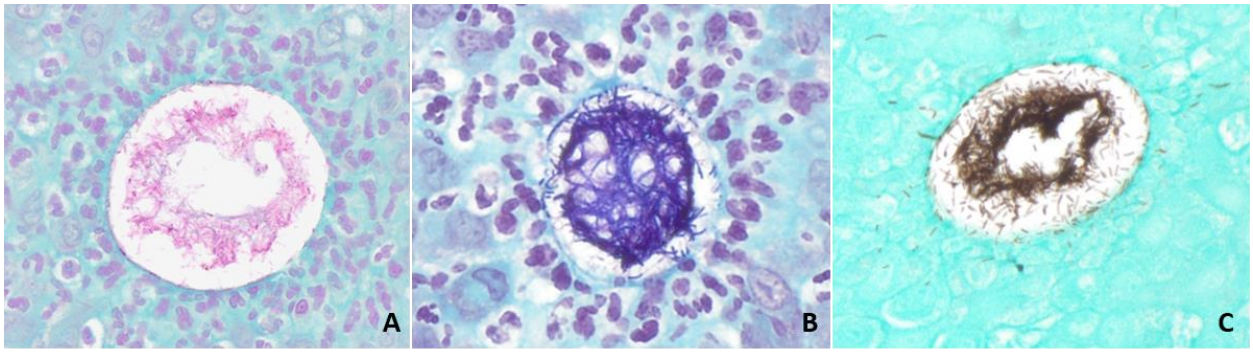

Figure 4. Special stains highlight the dense, tangled bacilli within vacuoles. **A.** Fite's-Faraco acid-fast stain **B.** Gram stain **C.** Grocott Methenamine Silver (GMS) stain; 40 x.

Follow-up questions:

1. Morphologic diagnosis: Marked, multifocal to coalescing, chronic, pyogranulomatous dermatitis and panniculitis with intralesional gram-positive and acid-fast bacteria.
2. Etiological diagnosis: Bacterial dermatitis and panniculitis.
3. Condition: Atypical mycobacteriosis
4. Possible causative agent(s): non-tuberculous mycobacteria (*M. fortuitum, M. chelonae, M. smegmatis*), *Nocardia* spp., *Actinomyces* spp.

Ancillary test results:

- Aerobic culture grew *Staphylococcus pseudintermedius* and *Leclercia adecarboxylata*.

- Fungal culture was negative**.**

Comments:

The clinical and histologic findings are consistent with atypical mycobacteriosis. Pathogenic mycobacteria are divided into the Mycobacterium tuberculosis complex (MTC) formed from species that cause tuberculosis, such as *Mycobacterium bovis*, *M. microti*, and *M. tuberculosis*; the *Mycobacterium leprae*, that cause feline leprosy syndrome in cats, characterized by pyogranulomatous nodules; and the non-tuberculous Mycobacteria (NTM). The NTM, which are associated with atypical mycobacteriosis in cats, are facultative, saprophytic organisms distributed ubiquitously in nature that can be isolated frequently from the soil, fresh water, and poorly sanitized medical equipment (3,7-8).

The NTM are divided into two categories depending on their growth in culture: the slow-growing species, such as *Mycobacterium avium,* that take several weeks to months and rapid-growing Mycobacteria (RGM) that take 7 to 30 days to grow (5,9-10). RGM can cause a clinical syndrome characterized by chronic infection of the subcutis and skin of cats, denominated feline mycobacterial panniculitis (7). The most common RGM isolated include *M. fortuitum, M smegmatis, M. chelonae,* and *M. abscessus* with rare reports of *M. thermoresistibile* and *M. setense* in cats (1,7,9).

Feline atypical mycobacteriosis may be associated FeLV, FIV, toxoplasmosis, immunosuppressive drugs, or idiopathic CD4+ T-lymphopenia, although in many cases, including the present one, immunosuppression is not documented (5). The route of infection is presumably via open wounds and/or penetrating trauma, and the higher frequency of this condition in cats compared with other domestic mammals is suspected to be due to their tendency to hunt or fight (7). The infection has an insidious onset and typically begins in the inguinal fat pad through wounds or previous sites of a puncture, bite, or surgical incision. Resulting pyogranulomatous inflammation with ulceration and fistulous draining tracts expand to the lateral and ventral abdominal adipose tissue, progressing to large ulcerated and non-healing areas (2,4). In severe cases, the entire ventral abdomen with adjacent flanks or limbs may be involved. Occasionally, atypical mycobacteriosis may present as cutaneous or subcutaneous nodules with variable lymph node involvement (1,5). Interestingly, the NTM have a tropism for lipid-rich tissue, accounting for the predilection of these bacteria for the inguinal fat pad in cats. It is thought that triglycerides not only support NTM growth, but also allow the organism to evade the host immune response and resist the action of antibiotics (6-7).

Histologically, the lesions consist of pyogranulomatous dermatitis and panniculitis with intralesional acid-fast bacteria classically noted extracellularly within clear vacuoles. Unlike lesions caused by tuberculous mycobacterial species, the inflammation in atypical mycobacteriosis shows rare to no multinucleated giant cells (2,4). Confirmatory diagnosis can be achieved through culture or PCR (4-5). Special care must be taken in the process of culturing mycobacterial species, which likely accounts for the lack of mycobacterial growth in aerobic culture in this case. Differential diagnoses include other high-order bacteria such as *Nocardia* spp., which are gram-positive and variably acid-fast, as well as *Actinomyces* spp. or *Streptomyces* spp., which are both gram-positive and acid-fast negative (1). If bacteria are not visible in histologic sections, additional differentials must include fungal infection and sterile nodular panniculitis. Prognosis for feline atypical mycobacteriosis is fair to guarded with treatment typically consisting of surgical

debridement and long-term antimicrobial therapy (5). After two months of antibiotic therapy, the cat of the present case has demonstrated significant improvement of the lesions, although few draining tracts are still present.

References:

1. Apostolopoulos N, Prenger-Berninghoff E, Wildermuth B, Moser I, Hillemann D, Nobach D, Herden C, Ewers C, Thom N. *Mycobacterium setense* isolated from a cat with atypical mycobacterial panniculitis. Tierarztl Prax Ausg K Klientiere Heimtiere 2021;49: 390–6.
2. Davies JL, Sibley JA, Myers S, Clark EG, Appleyard GD. Histological and genotypical characterization of feline cutaneous mycobacteriosis: a retrospective study of formalin-fixed paraffin-embedded tissues. Vet Dermatol 2006;17: 155-62.
3. Franco-Paredes C, Marcos LA, Henao-Martínez AF, Rodríguez-Morales AJ, Villamil-Gómez WE, Gotuzzo E, Bonifaz A, Heredia C. (2018). Cutaneous Mycobacterial Infections. Clin Microbiol Rev 2018;32: 1-25.
4. Gross TL, Ihrke PJ, Walder EJ, Affolter VK. Infectious nodular and diffuse granulomatous and pyogranulomatous diseases of the dermis. In: Gross TL, Skin Diseases of the Dog and Cat: Clinical and Histopathologic Diagnosis. 2nd ed. Oxford, UK: Blackwell Science; 2005. p. 283-7.
5. Gunn-Moore DA. Feline mycobacterial infections. Vet J. 2014;201: 230-8.
6. Johnson MM, Odell JA. Nontuberculous mycobacterial pulmonary infections. J Thorac Dis 2014;6: 210-20.
7. 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.
8. Pekkarinen H, Airas N, Savolainen LE, Rantala M, Kilpinen S, Miuku O, Speeti M, Karkamo V, Malkamäki S, Vaara M, Sukura A, Syrjä P. Non-tuberculous Mycobacteria can Cause Disseminated Mycobacteriosis in Cats. J Comp Pathol 2018; 160:1-9.
9. Vishkautsan P, Reagan KL, Keel MK, Sykes JE. Mycobacterial panniculitis caused by *Mycobacterium thermoresistibile* in a cat. JFMS Open Rep 2016;2: 1-7.
10. Winburn B, Sharman T. Atypical mycobacterial disease. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2022.

The Diagnostic Exercises are an initiative of the Latin Comparative Pathology Group (LCPG), the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. - Consider submitting an exercise! - A final document containing this material with answers and a brief discussion will be posted on the CL Davis website.

Associate Editor for this Diagnostic Exercise: Raquel Rech
Editor-in-chief: Claudio Barros