

Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: Month: April Year: 2018

Answer Sheet

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Clinical History: Two 5-week-old male Sprague Dawley research rats, housed in the same cage, were euthanized on the same day due to "infected cuts on their front fingers" (history per contributor). Bacterial cultures of joint fluid had no growth.

Necropsy Findings: On necropsy, both rats had variable swelling of the front feet and digits with purulent discharge and crusted ulcers (Figure 1).

Gross and Microscopic Images:

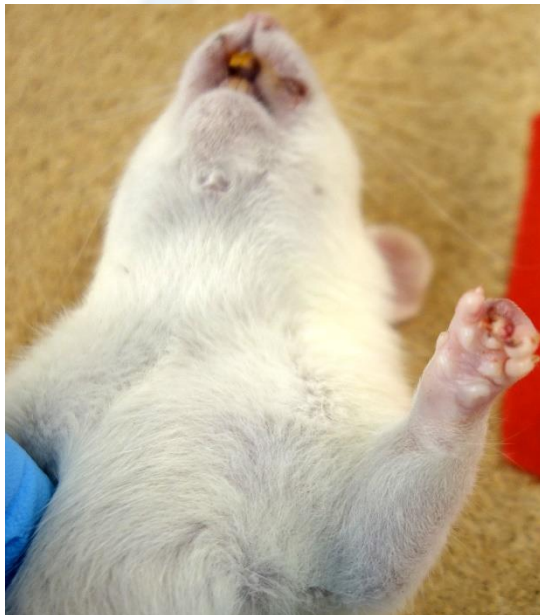


Figure 1. Left paw, Gross image

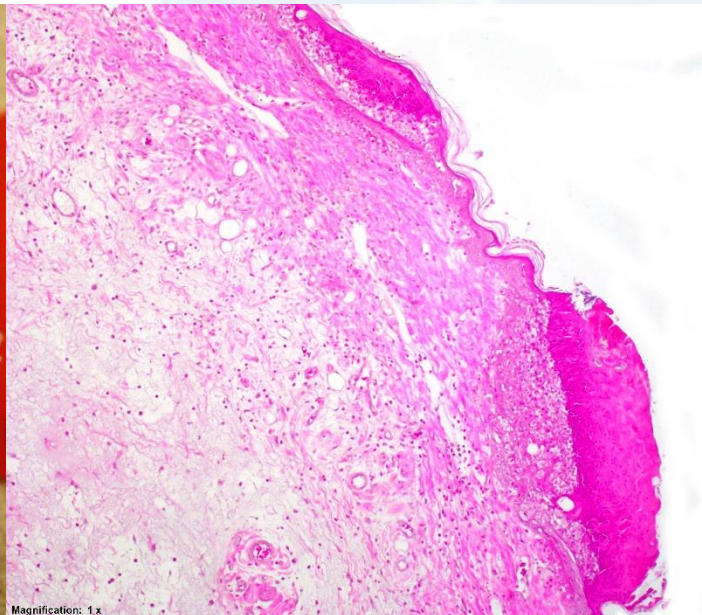


Figure 2. Paw, haired skin, H&E stain, 100X

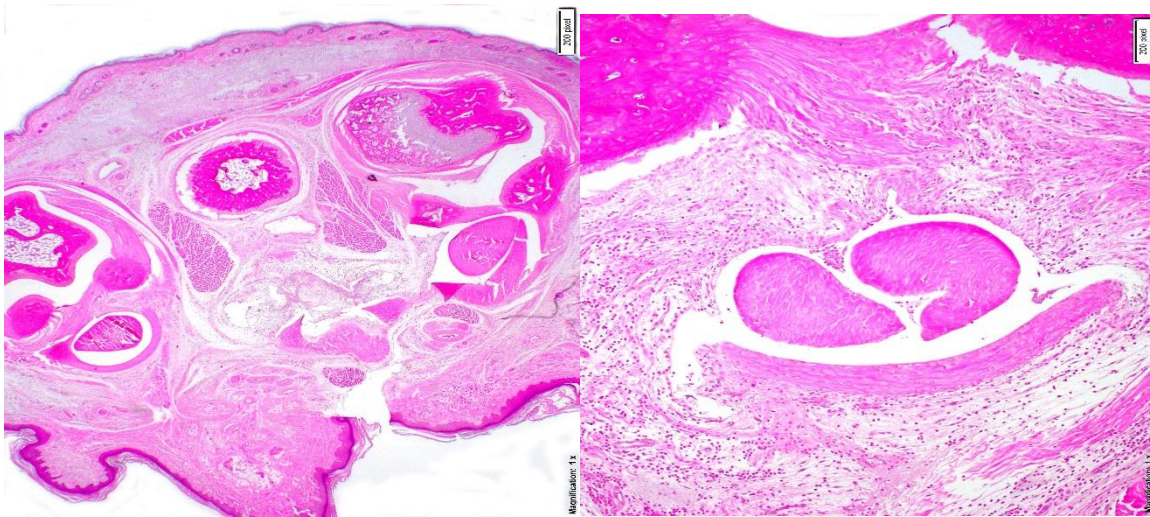


Figure 3. Left front paw, cross section H&E stain, 20X

Figure 4. Tendon, H&E stain, 100X

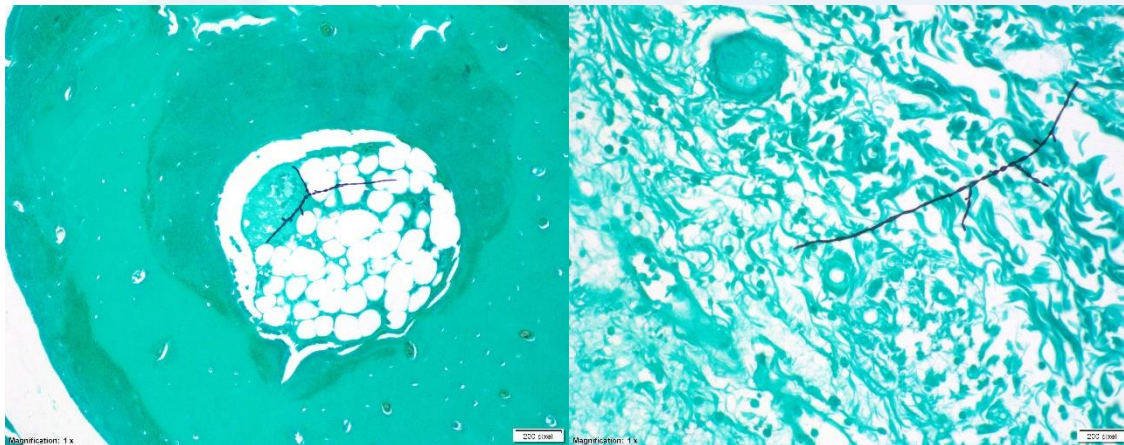


Figure 5 & 6. Intraosseous and intradermal fungal hyphae, GMS stain, 200X and 400X

Gross Morphologic Diagnosis and Possible Causes:

The gross (Figure 1) and histologic (Figure 2) findings in this case are consistent with ulcerative pododermatitis that extended to multiple deep tissues and resulted in cellulitis (Figure 3), ligament, and tendon involvement (Figure 4), etc. Few intradermal bacteria are present on GMS (bacteria did not photograph well so were not included), but GRAM stains were essentially negative. Rare fungal hyphae are observed in the deeper tissues of both rats (Figures 5 & 6), which explain the lack of growth on bacterial cultures.

The colloquial term of this condition is "Bumblefoot". It typically occurs on the rear hocks and heel portions of the feet but, in this case, the front feet were affected. Lesions result when any of the epidemiologic triad factors (host, agent, environment) tip out of balance. Tissue can become abraded from pressure, trauma, excess weight, immobility, etc. A small pustule develops, fills, and ruptures. If caught and treated at this early stage, then prognosis is good.

If left untreated, secondary bacterial and fungal infections occur when the wound is exposed to normal skin flora, soiled bedding, or cages with accumulated urine-soaked feces.

Chronic wounds that are left untreated can spread to the lymphatic system, to the bone causing osteomyelitis, or travel to the blood causing bacteremia and sepsis (this case represent deeper tissue involvement). If there is secondary or a primary bacterial etiology, then *Staphylococcus aureus* is the bacterium most often cultured; however, other pathogens can be involved.

Factors that may play a part in the development of ulcerative pododermatitis are skin trauma, excess weight, neuropathies, minute abrasions, as mentioned above, or rats having a genetic predisposition. It is also thought that the use of pine or cedar shavings used to cover cage flooring may play a part. This is a common finding in pocket pets, such as hamsters, guinea pigs, and rabbits. A sequela would be amyloid deposition in other organs due to the production inflammatory cytokines, such as IL-1, TNF alpha, and IL-6, leading to chronic production of serum amyloid-associated (SAA) protein and consequent deposition of AA fibrils.

Microscopic Morphologic Diagnoses (based on the pictures shown):

1. Haired skin, forepaw, left: Cellulitis, panniculitis, tendonitis, synovitis, and osteomyelitis, lymphoplasmacytic and neutrophilic, focally extensive, subacute, marked, with ulceration, posterior draining tract formation, fibrin, edema, early granulation tissue formation and rare intralesional fungal hyphae.

Possible Cause/s:

Primary differentials for ulcerative pododermatitis in a mouse would be ectromelia (murine orthopox virus), but cytoplasmic inclusions would be present. Also, humidity imbalance (Ringtail) can cause similar appearing lesions. Rats are not affected by Murine Poxvirus; however, they can get Ringtail.

Staphylococcus spp. virulence factors include adhesins; proteases that convert host tissue into nutrients; and evasion from innate and humoral immune response.

Comments:

It is important to be thorough in the diagnostic workup of such a case and perform stains for bacteria (Gram) and fungi (GMS and PAS), since coinfection is possible. Fungi can be the primary etiologic agent and should be suspected when bacterial cultures are negative, especially if deeper tissues are involved. The identification of this fungus was not requested by the investigator. No additional rats were affected. This case served as a good review of foot anatomy since the anatomy of the foot is complex, with all the digits, tendons, ligaments, joints, skeletal muscle, cartilage and bone, and there are limited references available on the rat. Rats are digitigrade, meaning they walk upright on their digits. Their front paws have four well developed digits, and their back paws have five digits when viewing an imprint. When writing a description for board examination, or crafting a morphologic diagnosis, it is also important to remember to use the unique nomenclature for the foot to earn those needed points.

References:

1. Percy D, Barthold SW. Guinea Pig. In: *Pathology of Laboratory Rodents and Rabbits*. 3rd Ed. Ames, Iowa: Blackwell Publishing; 2007: 229.
2. Posesko P, Rajtova V, Horak J. *A Colour Atlas of Anatomy of Small Laboratory Animals: Rat, Mouse, Golden Hamster*. Vol 2. Bratislava, Czechoslovak: Wolfe Publishing; 1992.

*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 (http://www.cldavis.org/diagnostic_exercises.html).

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