



Diagnostic Exercise

From The Davis-Thompson Foundation*

Case **202**; Month: **December**; Year: 2022

Answer Sheet

Title: Equine multinodular pulmonary fibrosis.

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Clinical History: A 16-year-old warmblood gelding was presented with a two-month history of fever and weight loss. Complete blood count revealed moderate neutrophilic leukocytosis, mild lymphopenia, and mild hyperfibrinogenemia. Pulmonary nodules were seen on diagnostic imaging test. Treatment with antibiotic, antiviral, and anti-inflammatory medications yielded some initial improvement; however, the horse was euthanized due to intractable fever and clinical decline.

Necropsy Findings: The lung had numerous firm, pale tan, solid nodules (Fig. 1). Nodules ranged from <1 cm in diameter to 6.5 x 6 x 3.5 cm. The right pulmonary lobes was more severely affected, and the majority of nodules were in the caudal lobes. Approximately 220 mL of dark red watery fluid was present in the pericardial sac.

Gross and Microscopic Images:

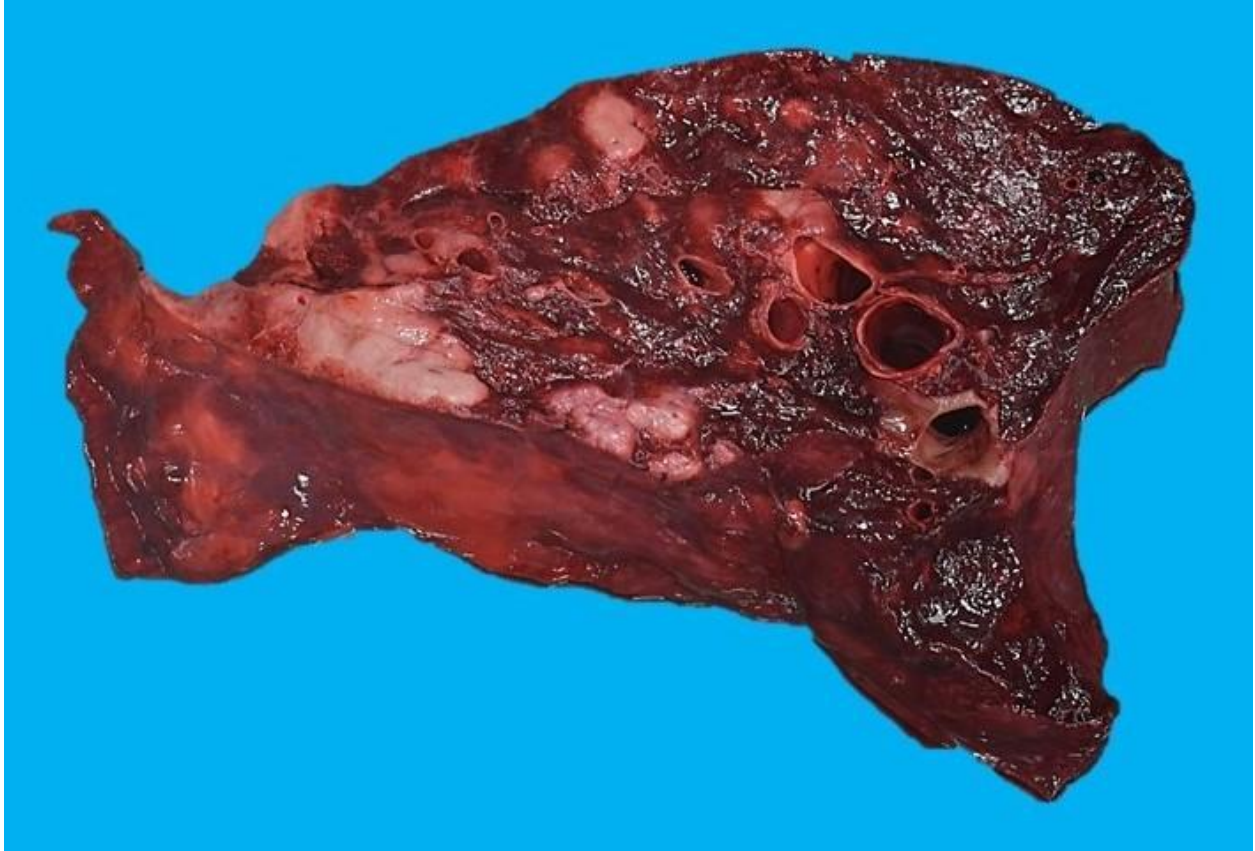


Figure 1. Horse, equine multinodular pulmonary fibrosis. The lung contains variably sized, pale tan, firm, nodules.

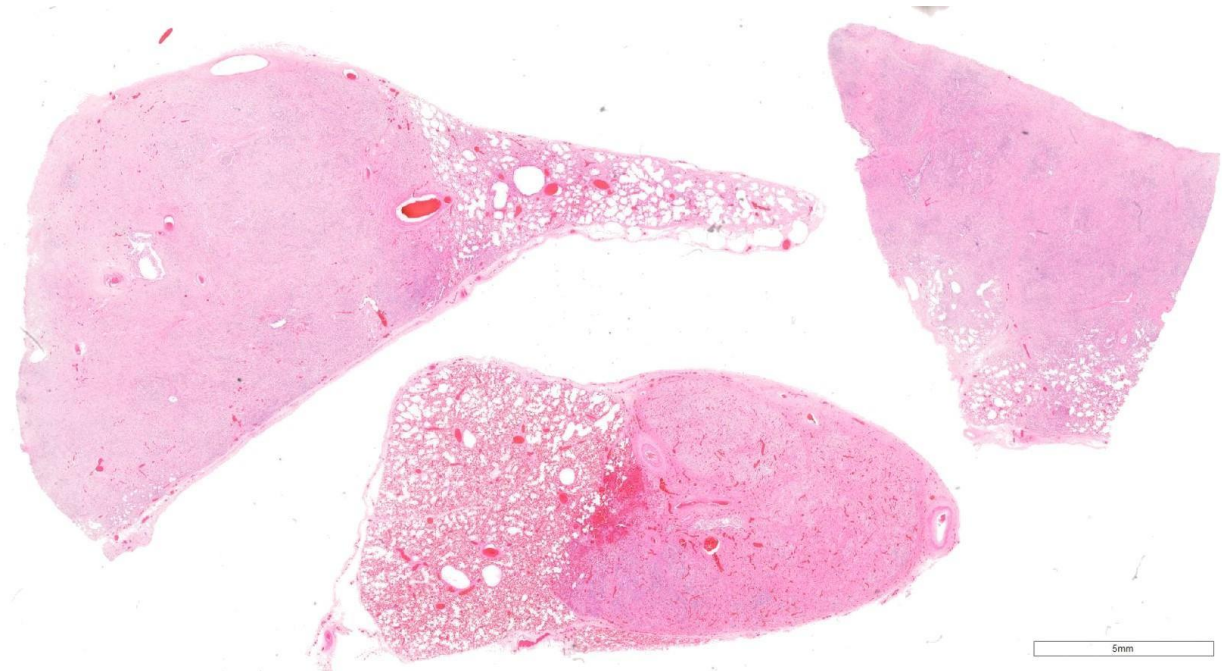


Figure 2. Horse, equine multinodular pulmonary fibrosis. Three sections of lung containing fibrotic nodules.

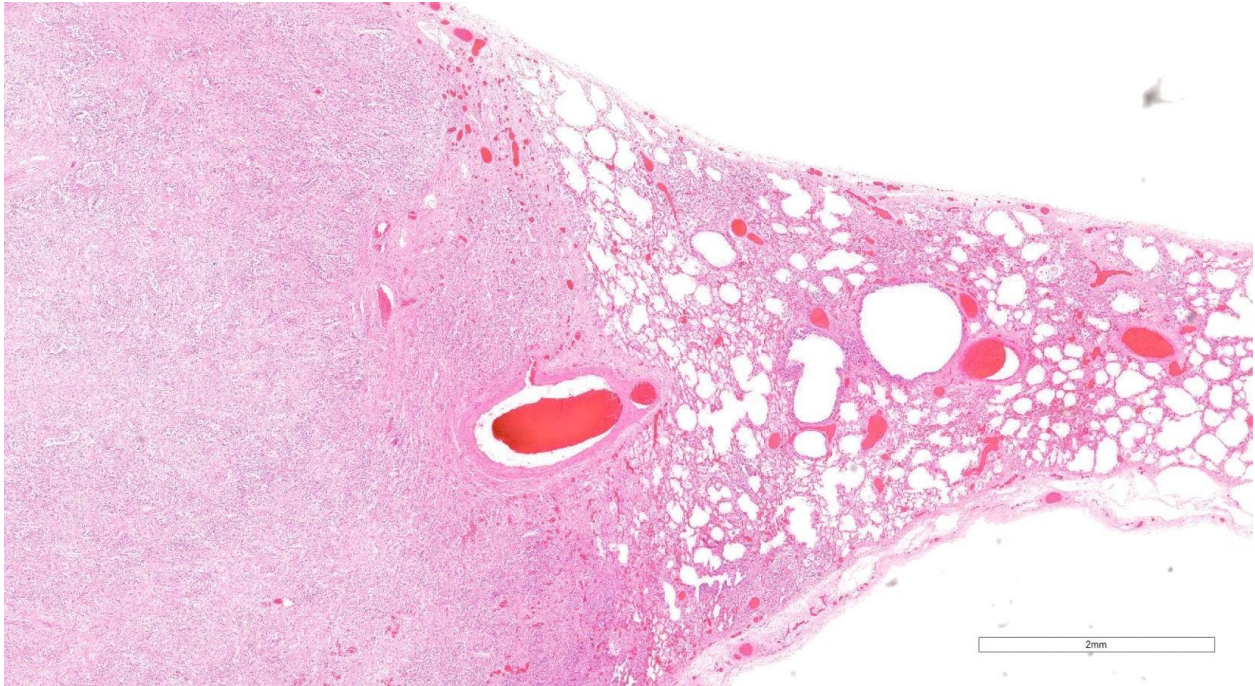


Figure 3. Horse, equine multinodular pulmonary fibrosis. Nodules are sharply demarcated from normal pulmonary parenchyma.

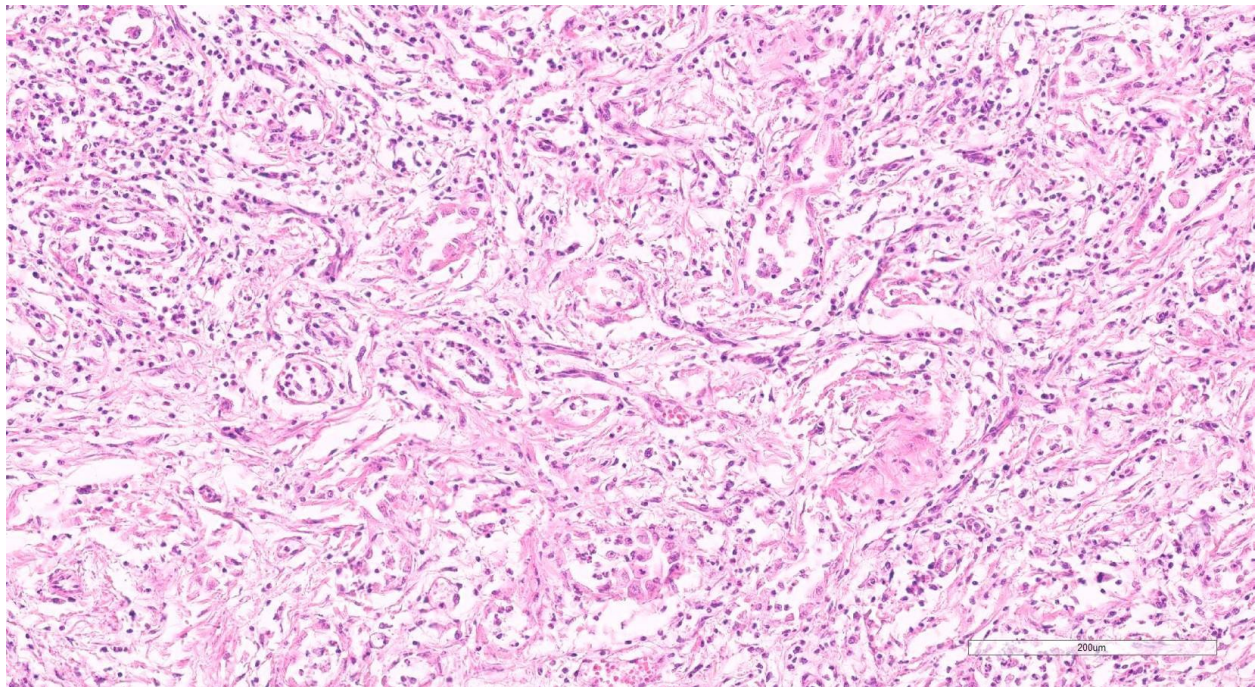


Figure 4. Horse, equine multinodular pulmonary fibrosis. There is marked interstitial fibrosis. Thickened alveolar septa contain variably dense collagen, numerous fibroblasts, and moderate numbers of neutrophils. Alveolar lumen is often lined by cuboidal type II pneumocytes and contain neutrophils, macrophages, and sloughed epithelial cells.

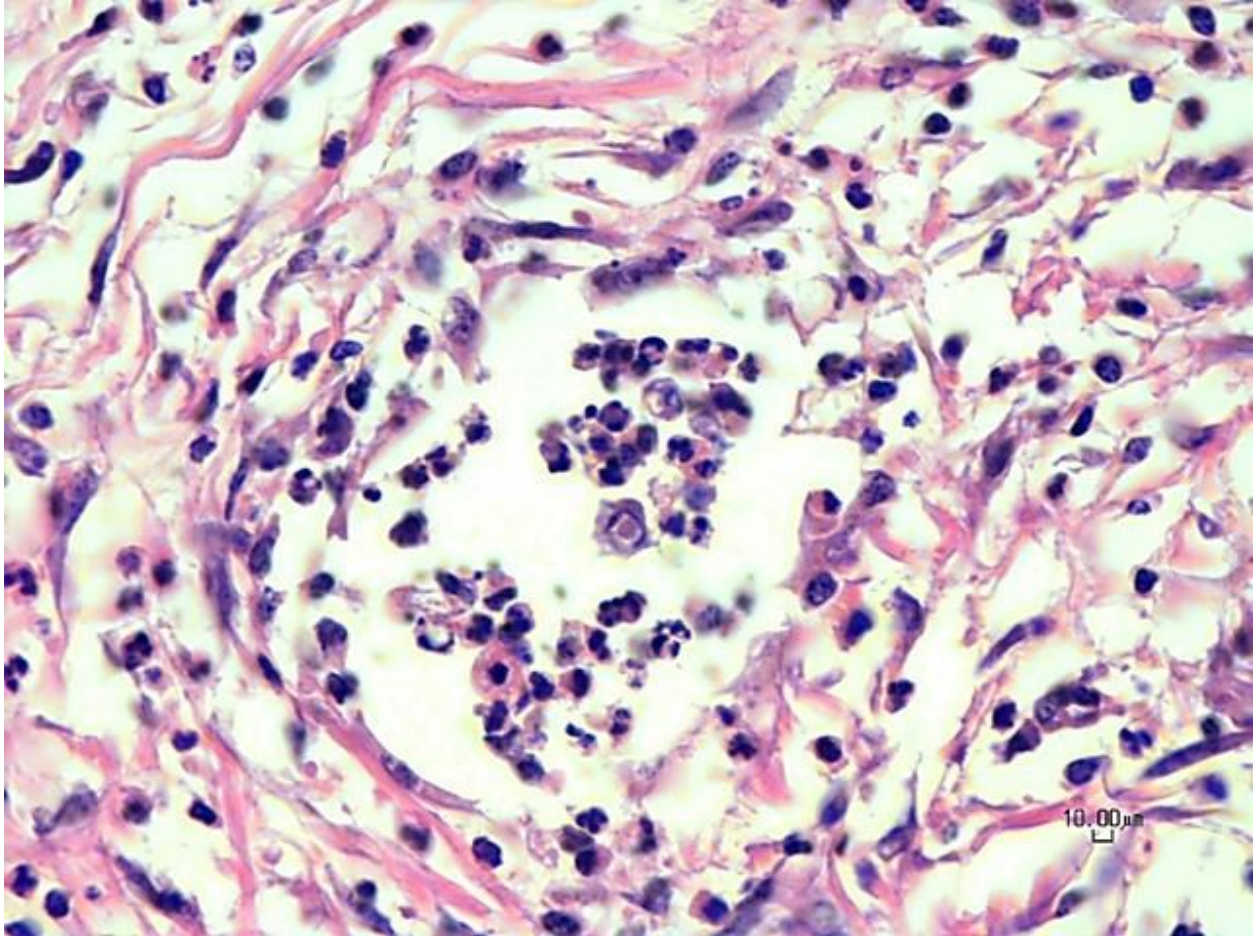


Figure 5. Horse, equine multinodular pulmonary fibrosis. Macrophages rarely contain a eosinophilic intranuclear inclusion body (4-6 μm in diameter) that causes nuclear enlargement and chromatin margination.

Microscopic Description: Lung: The pulmonary interstitium is expanded by increased amounts of mature collagen (interstitial fibrosis). Areas of fibrosis affect up to 80% of a section and form discrete nodules with sharp demarcation from the surrounding normal pulmonary parenchyma. Thickened alveolar septa contain variably dense collagen, numerous fibroblasts, moderate numbers of neutrophils, and congested capillaries. Alveolar lumen are often lined by cuboidal type II pneumocytes and contain neutrophils, macrophages, and sloughed epithelial cells. Macrophages rarely contain a eosinophilic intranuclear inclusion body (4-6 μm in diameter) that causes nuclear enlargement and chromatin margination. There is mild expansion of the pleura by increased fibrous connective tissue in which there are small numbers of neutrophils.

Morphologic Diagnosis: Lung: Nodular interstitial fibrosis, multifocal, chronic, severe with intrahistiocytic intranuclear viral inclusion bodies.

Associated Infection: Gammaherpesvirus, specifically equine herpesvirus-5 (EHV-5).

Name of the Condition: Equine multinodular pulmonary fibrosis (EMPF).

Discussion: In this case, clinical signs are attributed to progressive pulmonary disease consistent with the diagnosis of EMPF. Bronchoalveolar lavage fluid and lung biopsy samples submitted for polymerase chain reaction (PCR) during the horse's initial presentation confirmed infection with EHV-5. Grossly, the lung had numerous firm, pale tan nodules, with the right pulmonary lobes being more severely affected, which was consistent with pulmonary nodules seen on previous diagnostic imaging test. Histologically, the pulmonary interstitium had evidence of fibrosis which affected up to 80% of a section and formed discrete nodules. The nodules were sharply demarcated from the surrounding normal pulmonary parenchyma and intranuclear viral inclusion bodies were identified in macrophages.

EMPF is a chronic, progressive, fibrosing interstitial pulmonary disease that has been associated with infection with the EHV-5 and has a very poor prognosis (1). Horses initially present non-specifically with a history of weight loss, fever, lethargy, and respiratory signs such as cough, increased respiratory effort, and respiratory distress. These are non-specific signs that can be related to viral, bacterial, or toxic causes, though chronic interstitial pneumonia with nodule formation is suggestive of EHV-5 infection developing into EMPF (2). Typical lesions of EMPF seen via thoracic radiographs show a nodular interstitial pattern and a general roughening of the pleura with nodular lesions also apparent via ultrasound (3). In the post-mortem examination, these lesions can be visualized grossly with the presence of fibrotic nodules throughout the lung. Characteristic histologic findings that support the diagnosis of EMPF are marked interstitial fibrosis with fibrotic nodule formation and a mixed inflammatory infiltrate of the lung (1). To date, all reported cases of EMPF have been associated with EHV-5 infection, but the exact mechanism behind this has yet to be determined (2).

References:

1. Easton-Jones C. Recent advancements in our understanding of equid gammaherpesvirus infections. *Equine vet j* 2022;54:11-23.
2. Marenzoni ML, Passamonti F, Lepri E, Cercone M, Capomaccio S, Cappelli K, Felicetti M, Coppola G, Colletti M, Thiry E. Quantification of Equid herpesvirus 5 DNA in clinical and necropsy specimens collected from a horse with equine multinodular pulmonary fibrosis. *J Vet Diagn* 2011;23:802-806.
3. Schwarz B, Klang A, Bezdekova B, Sárdi S, Kutasi O, Hoven R. Equine multinodular pulmonary fibrosis (EMPF): five case reports. *Acta Vet Hung* 2013;61:319-32.

*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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