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Pathology in Practice

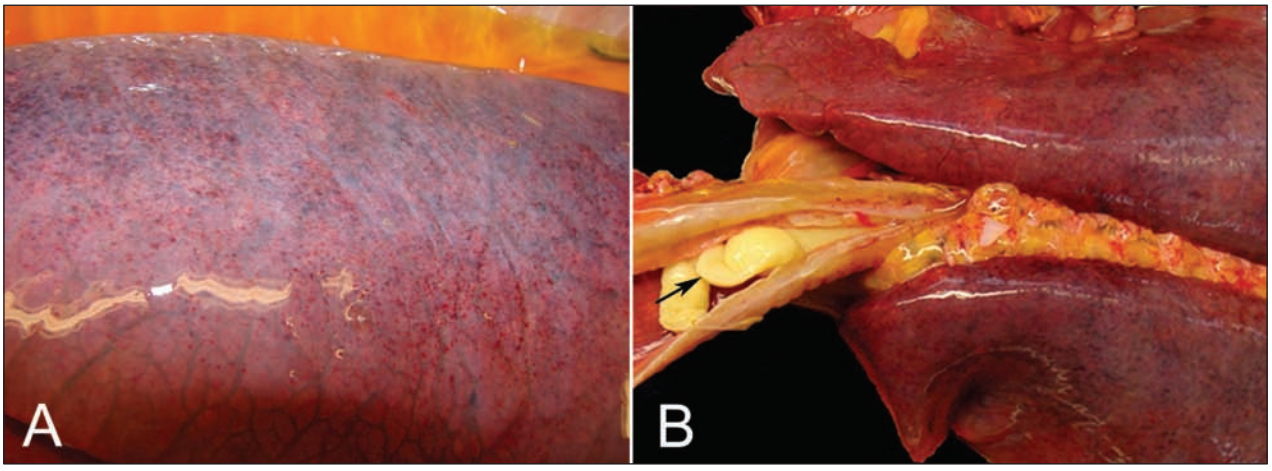

Figure 1—Photographs of the right caudal lung lobe (A) and tracheal lumen (B) of a male equine fetus that was aborted by its dam at a gestational age of approximately 8.5 months. Interlobular edema and diffuse petechiation of the visceral pleura are evident, and a moderate amount of straw-colored fluid is present in the thoracic cavity. A yellow-tan fibrinous cast (arrow) is visible within the tracheal lumen.

History

During its first pregnancy, a 9-year-old Pinto mare aborted a male fetus at a gestational age of approximately 8.5 months. The mare had contact with a gelding that had no clinical signs of disease. The vaccination status of each horse was current; the horses had received a tetanus toxoid vaccine and vaccines against rabies virus, West Nile virus, eastern and western equine encephalitis viruses, equine herpesviruses 1 and 4 (EHV-1 and EHV-4), and equine influenza virus.

Clinical and Gross Findings

Prior to abortion, the mare had a rectal temperature of 34.7°C (94.5°F) and was pawing at the ground. Auscultation revealed slow gastrointestinal tract motility, but the horse was able to defecate and had a normal appetite. No udder development was observed prior to abortion of the fetus. The aborted fetus, placenta, and a serum sample from the mare were submitted to the New York State Animal Health Diagnostic Center for evaluation.

On examination, the aborted fetus was in good body condition with minimal autolysis. The most prominent external gross finding was the presence of a small amount of meconium in the hair of the mane. The pleural cavity contained 2 L of transparent yellow-orange fluid. The caudal lung lobes were expanded, as denoted by rib impressions on the surface of the lungs; interlobular septae were edematous, and there were widespread petechial hemorrhages on the visceral pleura (**Figure 1**). A soft yellow-tan fibrinous cast was present in the distal portion of the trachea and extended distally into the bronchi. No gross changes were observed in the placenta.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

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Histopathologic Findings

Samples of the brain, heart, lungs, thymus, bronchial lymph nodes, liver, spleen, kidneys, adrenal glands, gastrointestinal tract, and placenta were routinely processed for histologic examination; lesions were identified in the lungs, thymus, and adrenal glands. In the lungs, small amounts of fibrin and numerous squamous and sloughed respiratory epithelial cells were evident within the lumen of the trachea, bronchi, and proximal bronchioles. Scattered bronchiolar epithelial cells contained nuclei that had marginated chromatin and small pale eosinophilic viral inclusion bodies (**Figure 2**). Alveoli contained protein-rich fluid and a moderate number of alveolar macrophages that had foamy cytoplasm. The tunicae adventitia of small to medium-sized arteries, interlobular septae, and visceral pleura were edematous. Small, irregularly scattered foci of necrosis were present in the adrenal glands near the corticomedullary junction with rare eosinophilic intranuclear viral inclusions identified in adrenocortical cells surrounding the necrotic foci. Small numbers of eosinophilic intranuclear inclusions were also present in thymic epithelial cells; however, there was no associated tissue damage as detected in the lungs and adrenal glands.

A pooled sample composed of tissue specimens from the lungs, bronchial lymph nodes, thymus, spleen, adrenal glands, and placenta was submitted for fluorescent antibody (FA) testing for EHV-1 and viral isolation. The FA test for EHV-1 yielded a positive result, and EHV-1 was recovered from viral cultures. The serum sample from the mare had an anti–EHV-1 antibody titer of 1:512.

Morphologic Diagnosis

Mild, acute, diffuse, fibrinous, necrotizing tracheitis, bronchitis, and bronchiolitis with rare intraepithelial intranuclear herpetic inclusion bodies; mild, pleural, interlobular, and alveolar edema with moderate alveolar histiocytosis; and mild, acute, multifocal, necrotizing adrenalitis with intranuclear eosinophilic herpetic inclusion bodies.

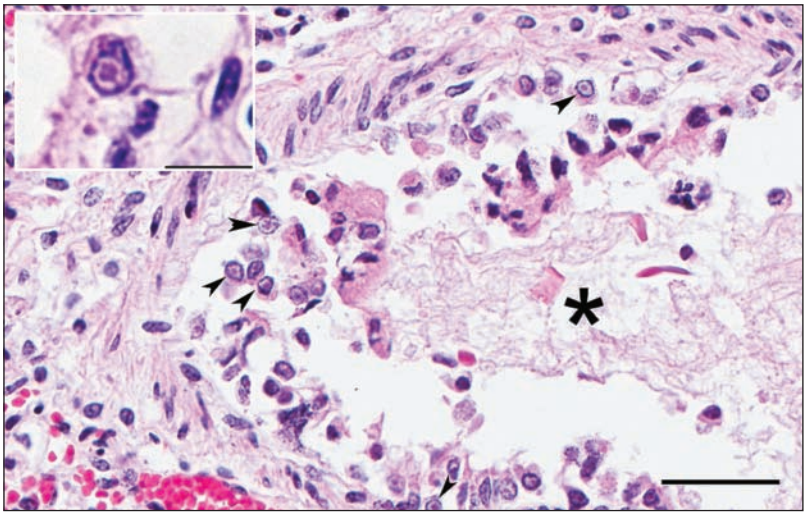

Figure 2—Photomicrograph of a bronchiole in a section of lung from the fetus in Figure 1. The bronchiole lumen contains fibrin (asterisk) and multiple sloughed epithelial cells with marginated nuclear chromatin and eosinophilic intranuclear viral inclusion bodies (arrowheads). H&E stain; bar = 100 µm. Inset—Higher-magnification view of an epithelial cell with an intranuclear viral inclusion. H&E stain; bar = 20 µm.

Comments

In fetuses aborted by mares as a result of EHV-1 infection, typical gross findings include pulmonary edema characterized by expanded, abnormally heavy lungs that can have prominent rib impressions on the pleural surface and widened interlobular septae; pinpoint white foci on the surface of the lungs and liver representing foci of necrosis; and widespread petechial hemorrhage. Fibrin casts within the trachea and bronchi develop less commonly, but when present, they support the gross diagnosis of EHV-1 infection.[1]

Histologically, the respiratory epithelium in an equine fetus aborted as a result of EHV-1 infection is variably necrotic and the cells contain eosinophilic intranuclear inclusion bodies that are characteristic for herpesvirus infection. Pulmonary edema is characterized by expansion of the vascular tunica adventitia, expansion of the interlobular septae and pleura, and presence of eosinophilic fluid in the alveolar spaces. Less common histopathologic findings include foci of necrosis throughout the liver, in the adrenal glands, and in lymphoid organs.[1] Although not all of the classic changes were identified in the aborted foal of this report (ie, there was a lack of hepatic and lymphoid organ necrosis), the identified gross and microscopic lesions were considered to be characteristic of equine herpesvirus-related abortion. Despite the lack of lymphoid organ necrosis in this fetus, the presence of intranuclear viral inclusion bodies in the thymic cells indicated that infection of the lymphoid organs had occurred. Although EHV-4 infection can cause abortion in pregnant mares, it is far less common than EHV-1–induced abortion. Infection with EHV-1 was confirmed in this case by results of FA testing and virus isolation. Although the mare was seropositive for EHV-1, the importance of this fact is inconclusive because a subsequent convalescent sample was not collected for analysis; ideally a convalescent sample should be collected for analysis 2 weeks after collection of the initial sample. The presence of anti–EHV-1 antibodies in serum may be a result of vaccination.

Equine herpesvirus 1 is ubiquitous and a highly contagious pathogen that causes respiratory tract infections, late-term abortions, and myeloencephalopathy in horses and has a major economic impact on the horse industry.[2–5] Infection in juveniles and adults generally develops through inhalation of the virus and infection of the respiratory mucosal epithelium. Direct damage to the respiratory epithelium can result in clinical signs of respiratory tract disease. Virus from infected respiratory epithelial cells can spread to regional lymph nodes and the tonsils. A subsequent cell-associated viremia develops, and the infected circulating leukocytes can transfer the virus

to endothelial cells, particularly in the superficial microcaruncular crypts of the endometrium and, to a lesser extent, the CNS. Infection of the endothelium in these areas results in vasculitis, ischemia, and rarely infarction.[4,5] Equine herpesvirus 1 infection of the endothelium in the microcaruncular crypts allows passage of the virus from the uterus to the placenta and fetus.[4] Similar to findings in adult horses, the virus has tropism for respiratory tract epithelium, vascular endothelium, and lymphoid tissue in fetuses. Other tissues such as adrenocortical cells, hepatocytes, and thymic reticular cells can also be affected. Although no gross or histologic changes attributable to EHV-1 infection were identified in the placenta of the fetus of this report, the placenta can have a high viral burden and be useful for diagnostic testing.[4,6,7] Following an EHV-1–induced abortion, it is not uncommon for the placenta to be the only organ submitted for evaluation. Results of diagnostic testing of placental samples generally provide evidence of the cause of abortion[7]; however, other tissues from an EHV-1–aborted fetus should be tested to aid in obtaining a definitive diagnosis. These tissues include samples of lungs, tracheobronchial lymph nodes, other lymph nodes, tonsils, and adrenal glands.

Herpesviral infections can become inactive within lymphoid tissues and the trigeminal nerve, forming latent infections that can be reactivated at any time during the course of the animal's life. Reactivation of latent infections generally occurs during periods of stress, such as pregnancy, or following administration of glucocorticosteroids.[4,5] The potential latency and reactivation of herpesvirus infections has made control of the spread of the virus difficult. Vaccination has proven useful in decreasing infection of respiratory tract epithelium, viral shedding, and development of viremia in association with newly acquired infections. However, reactivation of latent infections can result in viremia and viral shedding without development of any clinical signs. This is particularly important in vaccinated mares with latent infections that have successfully foaled because, once maternal immunity has waned, they can pass the virus to their foals.[2–4] Transfer of EHV-1 or EHV-4 from vaccinated mares to foals as young as 22 days old has been reported,[3] suggesting that maternal immunity may not be entirely sufficient to prevent development of herpesvirus infections. Data regarding the efficacy of current vaccines to control cell-associated viremia, abortion, and neurologic disease attributable to EHV-1 are not consistent; some reports[3–5] indicate that vaccination can prevent development or reduce the severity of these effects, whereas others indicate vaccine administration imparts no significant effect.

Because of the highly contagious nature of EHV-1, abortion may be the only clinical sign of disease on a particular horse farm. Recognition of gross lesions attributable to EHV-1 infection can lead a veterinarian to implement a number of precautionary measures to limit the spread of virus to other horses on the premises. Some of the precautionary measures that may be used include isolation of pregnant mares from other horses, vaccination and quarantine of unaffected horses, handling affected mares last when multiple horses need to be handled, installation of disinfectant footbaths at the entrance of the barn and at the entrances of the stalls of affected animals, and elimination of indirect contact (through common-use objects such as water or feed buckets and tack supplies) among horses.[4,5]

References

1. Schlafer DH, Miller RB. Equine herpesvirus-1. In: Maxie MG, ed. *Jubb, Kennedy, and Palmer's pathology of domestic animals*. 5th ed. 2007;532–534.
2. Brown JA, Mapes S, Ball BA, et al. Prevalence of equine herpesvirus-1 infection among Thoroughbreds residing on a farm on which the virus was endemic. *J Am Vet Med Assoc* 2007;231:577–580.
3. Foote CE, Love DN, Gilkerson JR, et al. EHV-1 and EHV-4 infection in vaccinated mares and their foals. *Vet Immunol Immunopathol* 2006;111:41–46.
4. Lunn DP, Davis-Poynter N, Flaminio MJBF, et al. Equine herpesvirus-1 consensus statement. *J Vet Intern Med* 2009;23:450–461.
5. Reed SM, Toribido RE. Equine herpesvirus 1 and 4. *Vet Clin Equine* 2004;20:631–642.
6. Irwin VL, Traub-Dargatz JL, Newton JR, et al. Investigation and management of an outbreak of abortion related to equine herpesvirus type 1 in unvaccinated ponies. *Vet Rec* 2007;160:378–380.
7. Smith KC, Whitwell KE, Blunden AS, et al. Equine herpesvirus-1 abortion: atypical cases with lesions largely or wholly restricted to the placenta. *Equine Vet J* 2004;36:79–82.