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Case # 6

Slide # N1008307

**Signalment:** Premature newborn foal.

**History:** The colt was 11 days premature. The foaling was normal, but the colt was rather weak and could only stand without assistance. He did not latch on to nurse until 6 hours of age and never nursed well. He was administered mare's milk several times with a tube. The neonate became weaker and depressed, the suckle reflex disappeared. Then he became apneic and died one day after parturition. The mare was vaccinated against EHV-1 and EHV-4 at 4, 5, 7, and 9 months of gestation. She was also vaccinated against tetanus, encephalitides and *Neorickettsia risticii* at 10 months of gestation.

**Gross findings:** There were petechiae on lung, small intestine and diaphragm. The cranoventral lung lobes were red and gelatinous with prominent interlobular septa and the dorsal lung had subpleural emphysema and edema. A pulmonary bulla measuring 8cm x 5cm x 3m involved the caudoventral aspect of the right lung lobe. No other gross abnormalities were observed.
Slide description

Lung: Bronchi, bronchioles, and to a lesser extent alveoli, are lined by attenuated and necrotic epithelium, with intraluminal sloughed cells, admixed with small to moderate numbers of necrotic and viable neutrophils, small number of lymphocytes and macrophages, and numerous short bacillary bacteria. Frequently, bronchioles and bronchi are lined by syncytial cells. Occasionally epithelial cells and syncytial cells contain a single, round, 3-5 um in diameter, eosinophilic, intranuclear inclusion surrounded by a clear halo and marginating chromatin. Diffusely, the alveolar septa and bronchiolar interstitium are moderately expanded by hyperemic vessels, and few previously described inflammatory cells. The subpleural and interlobular connective tissue is moderately expanded by increased clear space with ectatic lymphatics (edema), hemorrhage, fibrin, congested vessels, and few lymphocytes and neutrophils.

Morphologic diagnosis

Lung: severe, multifocal to coalescing, acute, bronchointerstitial pneumonia with severe bronchiolar necrosis, intranuclear inclusion bodies, syncytia, and bacteria.

Indirect Immunohistochemistry

Lungs: abundant EHV-1 antigen within bronchiolar epithelium (including syncytia), pneumocytes, endothelium and leukocytes.

Other findings

Spleen: severe lymphoid follicle necrosis
Spleen: rare cells containing EHV-1 antigen.
Liver: one small cluster of necrotic hepatocytes containing EHV-1 antigen.
Adrenal gland: one small cluster of cortical epithelial cells containing EHV-1 antigen.

Cause

Equine herpes virus 1 (associated with *Escherichia coli*)

Discussion

Equine herpesvirus 1 (EHV-1) causes acute respiratory disease in foals and yearlings, and is the most important viral cause of equine abortion. Some EHV-1 isolates also cause myeloencephalopathy, which may precede or accompany abortion epizootics. The economic impact of EHV-1 can be devastating. Other equine herpesviruses include EHV-2, EHV-3, EHV-4, and EHV-5. EHV-6-7-8 are asinine viruses. Equids are primary hosts of EHV-9 which can infect gazelles, giraffes and other species. The role of the pathologist in the post mortem diagnosis of these infections is paramount. The large majority of EHV-1 induced abortions occur in the last third of pregnancy. The increased susceptibility of the late pregnant mare to abortigenic infection is, perhaps, generally
related to anatomical and endocrine changes in the placental barrier, which may facilitate microcotyledonary infarction as pregnancy proceeds. It is also possible that the areas of Arcadian hematophagic trophoblasts, located at the base of the villi and maturing late in pregnancy, play a role in the transmission of the virus, as observed in equine arterivirus infection. Prostaglandin release may also give a substantial contribution. The incubation period for EHV-1 abortion is variable and premonitory clinical signs are rare in the mare. A mare that aborts does not become immune to other EHV-1 infections, but abortions in successive pregnancies are rare. Rapid diagnosis and isolation of the aborting mare are paramount to minimize the spread of the infection. The aborted fetus is generally fresh and enclosed within the fetal membranes. The following pathological changes, suggestive of EHV-1 abortion, may be seen but fetuses with no gross lesions are often observed: mucosal petechiae, meconium staining, yellowish-orange fluid within the body cavities, splenomegaly, perirenal edema, pulmonary edema, friable thymus. Pathognomonic changes are gray foci of hepatic necrosis within the liver, but they are present just in a small percentage of cases. Histological examination allows identification of coagulative necrosis in liver, lung, thymus, spleen and other lymphoid organs, lung, and small intestine. The necrotic foci are generally associated with peripheral intranuclear viral eosinophilic inclusions with margination of nuclear chromatin, which are always identified if the organs mentioned above are examined. If fetal infection occurs close to pregnancy term, the infected foal may be born weak and die shortly after because of severe necrotizing bronchointerstitial pneumonia and multifocal visceral necrosis. Pulmonary lesions are predominant in these foals and the lung should always carefully examined. Syncytia formation in EHV-1 infection, as seen in this case, is rarely described. Previous reports include a Wednesday Slide Conference AFIP (2007 conference 2 case # 4) case, a report of syncytia in the lungs of aborted fetuses from a study and in experimental neurologic disease. There are some reports linking EHV-1 glycoprotein K and glycoprotein B to the ability to form syncytial cells in cell culture. One report describes formation of syncytial cells in cell culture inoculated with attenuated virus. These findings may suggest that EHV-1 strains forming syncytia in field cases are less aggressive, but this needs to be established. The Escherichia coli infection identified in this case seems most likely associated with inhalation of ingesta. The neutrophilic infiltrate is considered the inflammatory response toward this bacterial infection. Neutrophils are not generally associated with EHV-bronchiolar necrosis. The abundant, diffuse EHV-1 pulmonary distribution detected via IHC is unusual, but was previously observed by us. In addition, is not unusual to observe infected newborn foals mainly affected by pulmonary lesions such as necrotizing bronchiolitis or sporadically bronchointerstitial pneumonia, and minimal to mild lesions with little virus in other organs. The infected foals are clinically indistinguishable from foals with sepsis/septicemia and are dangerous shedders of EHV-1. These foals can be indentified via EHV-1 isolation and/or PCR in vivo.
References