Guinea Pig Adenovirus

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Abstract
Necropsy pulmonary neumonias was diagnosed in one-month-old guinea pigs. Clinical signs ranged from decreased body condition, respiratory distress to sudden death. Gross necropy findings included dark red and heavy cranial lung lobes and multifocally similarly affected caudal lung lobes. Histopathologic findings included ectatic bronchi and bronchioles containing cellular and karyohytic debris, neutrophils, fibrin and sloughed necrotic respiratory epithelial cells. These epithelial cells often contained a single, large, 5–15 µm diameter, basophilic, intranuclear inclusion body. The intranuclear inclusion bodies were immunopositive for adenoviral antigen by immunohistochemistry. Lung and feces were positive for guinea pig adenovirus via PCR. DNA extracted and amplified from feces and formalin fixed lung yielded 99.9% homology with the hexon gene sequence of guinea pig adenovirus reference strain. Sloughed, necrotic bronchiolar epithelial cells contained nonenveloped viral particles, round to icosahedral, 70–90 nm diameter, variably electron dense viral particles consistent with adenovirus detected by electron microscopy. Adenovirus of guinea pigs, although inquently reported, remains a relevant cause of bronchopneumonia. Histopathompatibility, immunohistochemistry, PCR and electron microscopy are all useful modes of diagnosis.

Case Description
Intact male, one month-old, white Harleay guinea pigs (Cavia porcellus) were obtained at different dates from a commercial supplier and quarantined prior to use in a specific pathogen free facility. The guinea pigs were free of enteric parasites, endoparasites, Salmonella spp., Subclinical infections of Mycoplasma pneumoniae, hemolytic Streptococcus, Streptococcus pneumoniae, Pasteurella spp., Sendai virus (SENV), Reovirus 3 (REO3), Pneumonia virus of mice (PVM), Lymphocytic choriomeningitis virus (LCM), Simian virus 5 (SV5), and Cytomegalovirus (CMV).

Four guinea pigs demonstrated increased respiratory rate, dyspnea, weight loss and sudden death, either during quarantine or after being placed on study. The first guinea pigs demonstrating clinical signs died after showing respiratory symptoms. Subsequent guinea pigs were euthanized via CO2 inhalation when clinical signs were initially observed.

Histopathologic findings included bronchi, bronchioles and alveolar lumina containing numerous neutrophils, macrophages, lymphocytes, and fewer plasma cells and extravasated erythrocytes (Figure 2).

The lumina of the bronchi and bronchioles were often mildly to moderately ectatic, distended with abundant cellular and karyohytic debris, extravasated erythrocytes, fibrin and sloughed degenerate to necrotic respiratory epithelial cells. These epithelial cells often contained a single, large, 5–15 µm diameter basophilic, intranuclear inclusion body. The intranuclear inclusion bodies were immunopositive for guinea pig adenovirus by immunohistochemistry. Lung and feces from two guinea pigs tested positive for guinea pig adenovirus by quantitative real time polymerase chain reaction (qPCR) at a commercial testing facility. DNA was extracted and amplified from feces, fresh and formalin fixed lung samples and was sequenced (Figure 5). The adenovirus observed in this outbreak was described as 58–72 nm diameter viral particles in hexagonal crystalline array, forming large, basophilic, intranuclear inclusion bodies by light microscopy. Additional outbreaks of GpAV in guinea pigs were characterized as necrotizing bronchitis and bronchiolitis with similar prominent basophilic intranuclear inclusions in sloughed, necrotic epithelial cells. Inclusions contained typical adenoviral particles of 68–72 nm diameter, arranged individually or in crystalline arrays. GpAV infection was reproduced via intranasal inoculation of newborn guinea pigs and was found to be nonpathogenic in hamsters and rats. GpAV infection was first reported in guinea pigs, but the asymptomatic animals were found to have microscopic lesions of minimal bronchial epithelial necrosis with typical large basophilic intranuclear inclusions.

Guinea pig adenovirus was first reported in 1981, as the cause of necrotizing bronchitis and bronchiolitis with low morbidity and high mortality in guinea pigs from two commercial breeders and a closed colony. The adenovirus observed in this outbreak was described as 58–72 nm diameter viral particles in hexagonal crystalline array, forming large, basophilic, intranuclear inclusion bodies by light microscopy. Additional outbreaks of GpAV in guinea pigs were characterized as necrotizing bronchitis and bronchiolitis with similar prominent basophilic intranuclear inclusions in sloughed, necrotic epithelial cells. Inclusions contained typical adenoviral particles of 68–72 nm diameter, arranged individually or in crystalline arrays. GpAV infection was reproduced via intranasal inoculation of newborn guinea pigs and was found to be nonpathogenic in hamsters and rats. Subclinical infections were reported in guinea pigs, but the asymptomatic animals were found to have microscopic lesions of minimal bronchial epithelial necrosis with typical large basophilic intranuclear inclusions.

Adenoviruses are non-enveloped, linear double stranded DNA viruses with icosahedral symmetry that infect a wide variety of animals with clinical signs ranging from subclinical to anomic or respiratory manifestations. Guinea pig adenovirus (GpAV) is a distinct serotype within the genus Mastadenovirus and has the highest level of homology with other animal Mastadenoviruses (mammalian adenoviruses) and human subgroups A, C, E and F.1 Adenoviruses derived from birds (Aviadenovirus), frogs (Siadenovirus), fish (Ichthadenovirus) and some reptiles (Atadenovirus) are serologically distinct from Mastadenoviruses.

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Bronchopneumonia due to GpAV is typically of low morbidity with up to 100% mortality. Clinically affected animals are often young, but infections have been seen in adults guinea pigs in breeding colonies.1,2,3 Infected guinea pigs often show no or only brief clinical signs prior to death. On gross necropy the cranial lung lobes are usually considerably expanded, while the caudal lung lobes show multifocal consolidation. Histopathologic findings are characterized by a necrotizing bronchitis and bronchiolitis with sloughing of necrotic epithelial cells into the airways, often resulting in occlusion of the affected airways with necrotic epithelial cells admixed with cell debris, leukocytes and fibrin. The necrotic epithelial cells often exhibit karyomegaly with extremely large basophilic, round to 7–15 µm diameter, intranuclear inclusion bodies.4 Other differential diagnoses for pneumonia in guinea pigs include Paramyxovirus, Cytomegalovirus and bacteria such as Bordetella bronchiseptica, Streptococcus species, Staphylococcus species and Pseudomonas aeruginosa.5 Diagnosis of GpAV infection can be performed via immunohistochemistry, electron microscopy, serology or polymerase chain reaction.