



Diagnostic Exercise

From the CL Davis/ Foundation

Case #:146 Month: May Year 2020

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Clinical History: A 20-day-old female Holstein calf from a dairy farm at which four calves presented respiratory difficulty. The animal was euthanized and a necropsy was performed.

Necropsy Findings: The carcass was in fair to poor nutritional condition, with very small amount of fat reserves, and severely dehydrated. The right lung had a well demarcated, focally extensive area of consolidation of the caudal portion of the cranial lobe and the middle lobe. Approximately 10 % of the total pulmonary parenchyma was affected.

Microscopic Images:

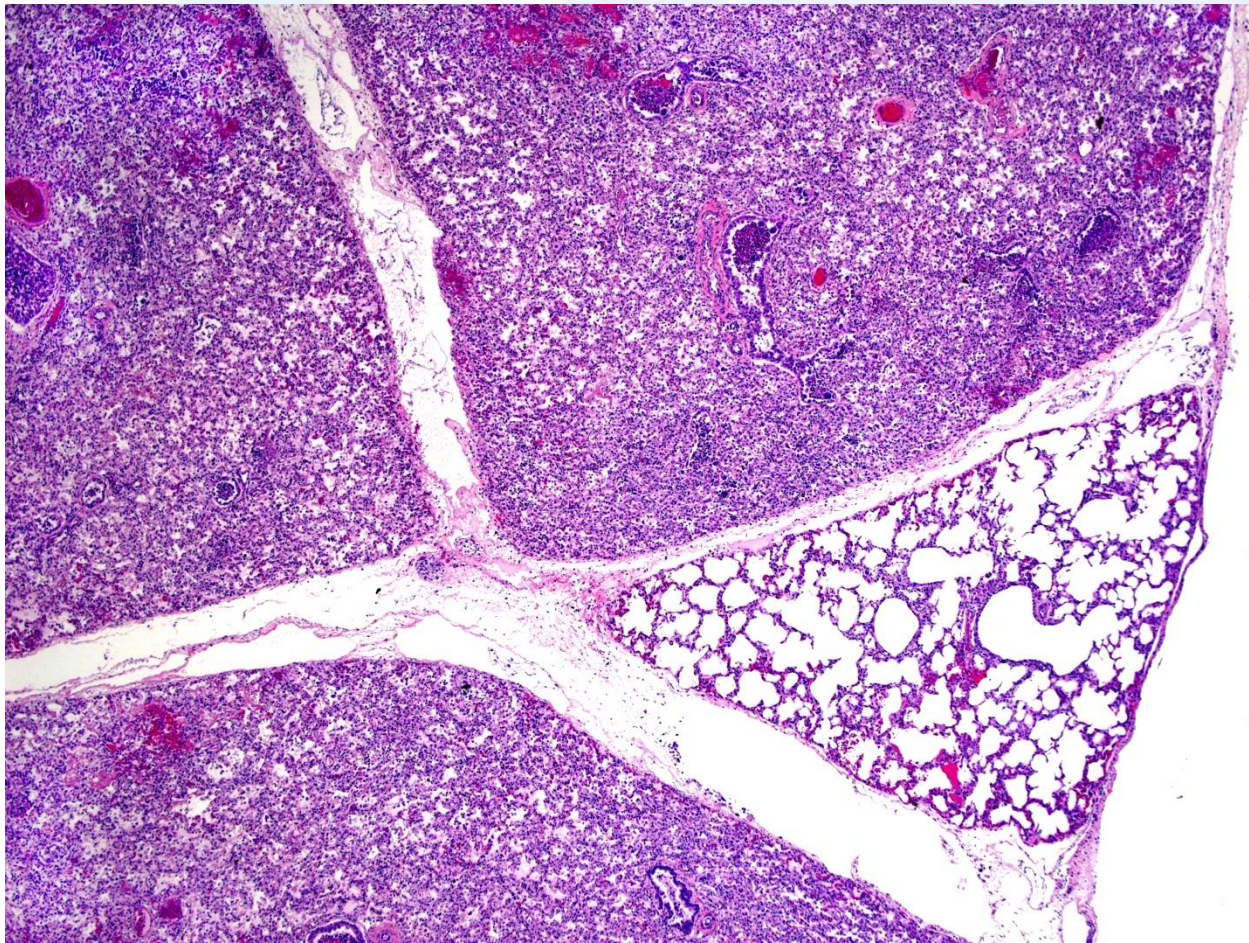


Figure 1. H&E

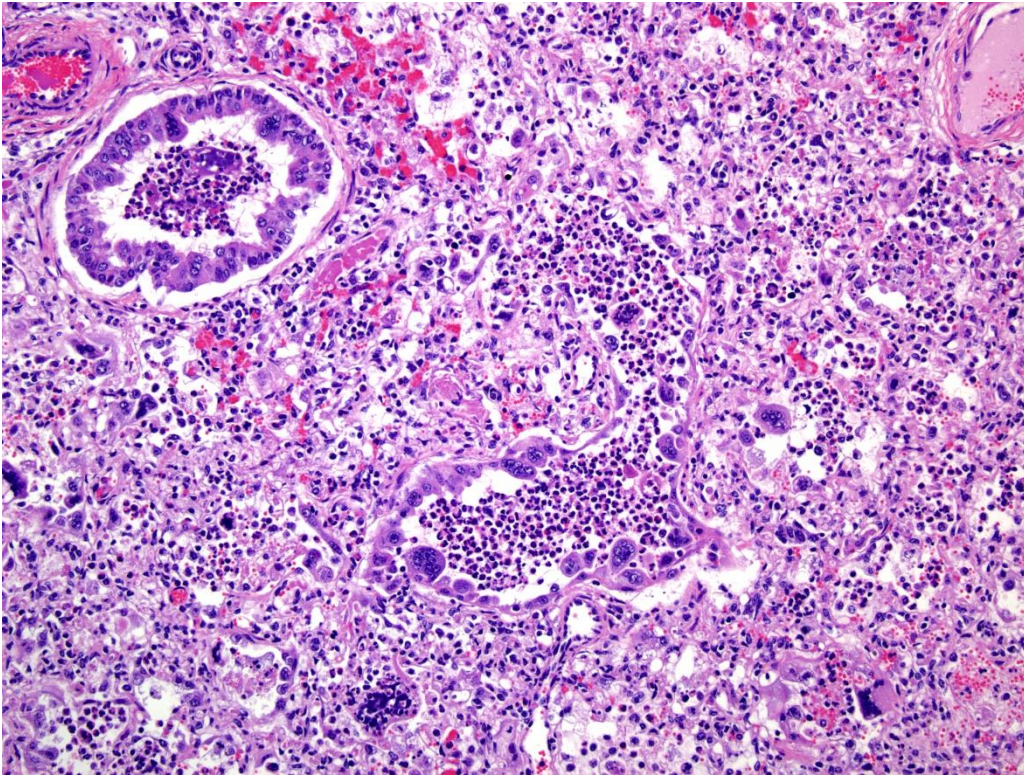


Figure 2. H&E

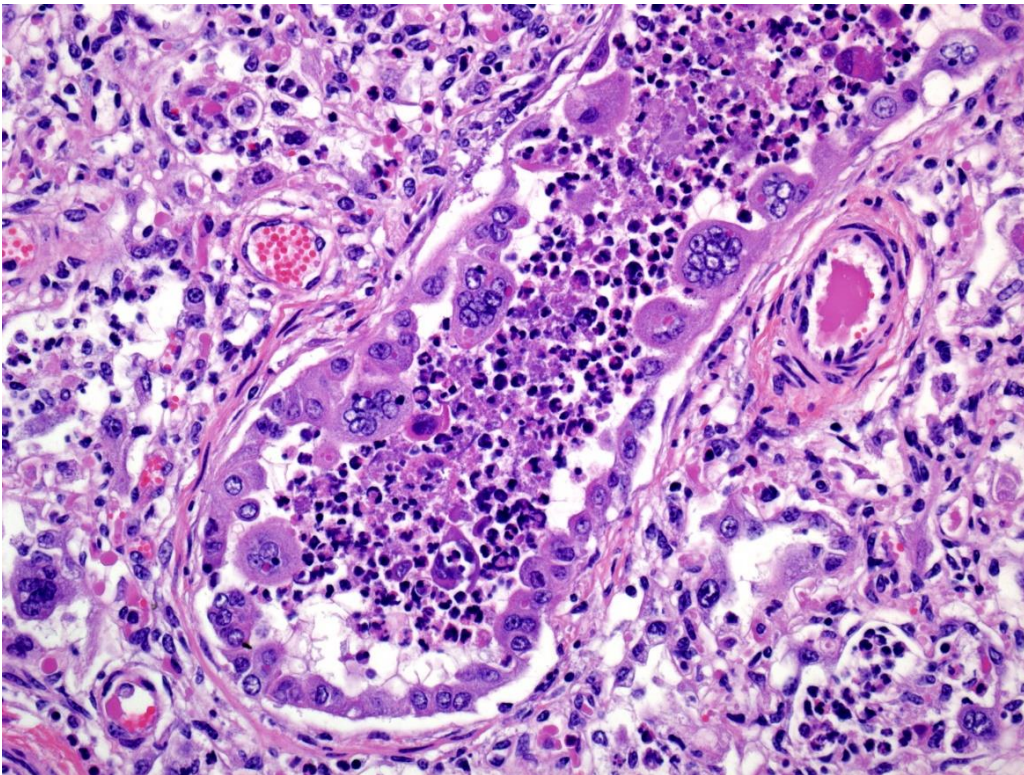


Figure 3 H&E

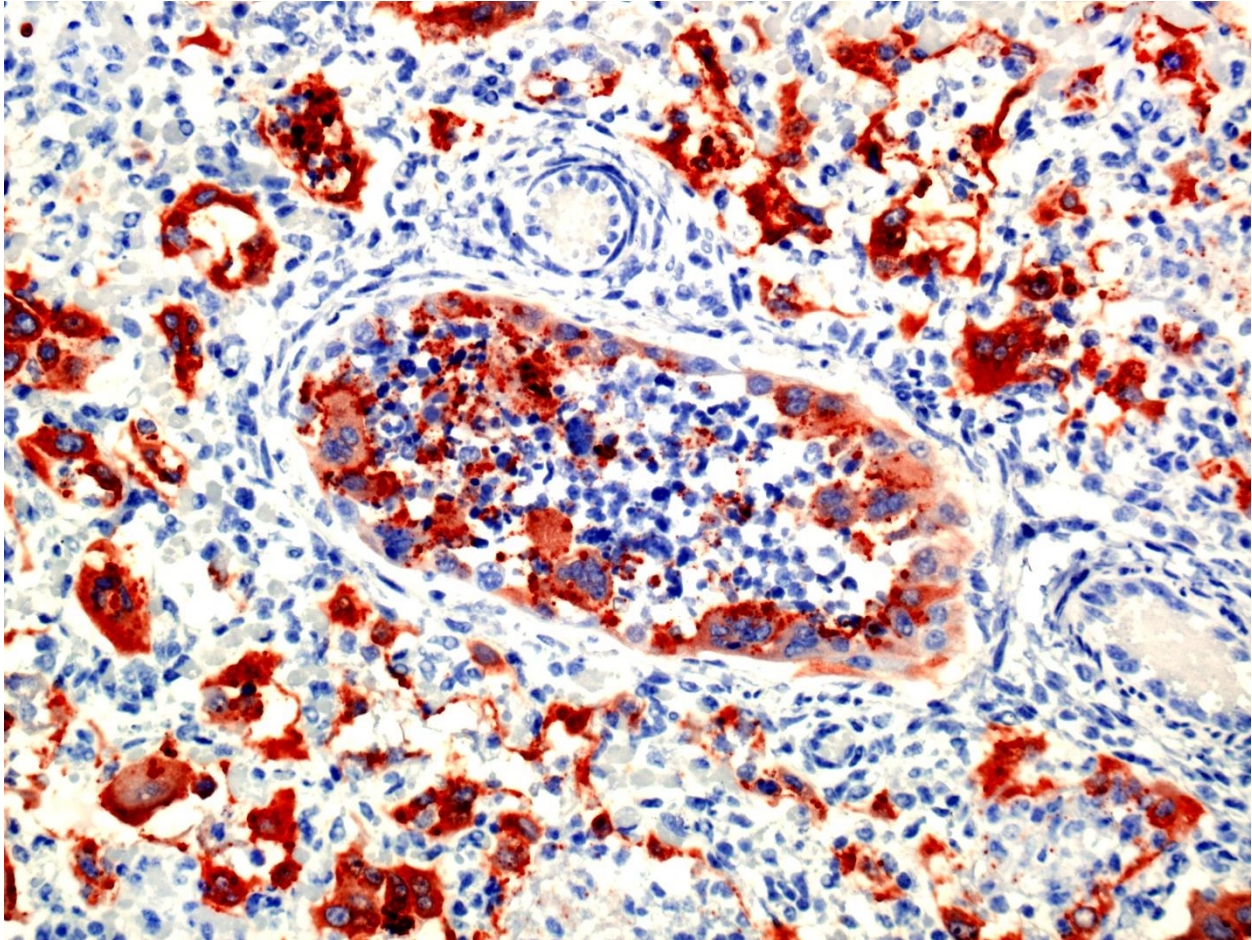


Figure 4. IHC for BRSV

Follow up questions:

1- Microscopic description:

Lung: Alveolar and bronchiolar lumina are variably filled with neutrophils, macrophages, fibrin, edema, haemorrhage, cell debris and sloughed epithelial cells (Figs. 1, 2 and 3). Type II pneumocyte hyperplasia (epithelization) is prominent (Figs. 2 and 3). Multifocally, the bronchiolar epithelium is flattened or necrotic. Multifocally in the bronchial epithelium, free in the bronchial lumen and less frequently in the alveolar lumen, are numerous multinucleated cells with abundant cytoplasm and centrally located nuclei (syncytial cells) (Figs. 2 and 3). In the cytoplasm of bronchial epithelial cells and syncytial cells, there are variably sized, eosinophilic inclusion bodies (Fig. 3). Interlobular septa are moderately expanded by clear spaces and dilated lymphatics (edema) and are infiltrated by few lymphocytes, plasma cells and macrophages. Occasionally, small foci of coagulative necrosis are seen in the lung parenchyma (Fig. 1). Immunohistochemistry for bovine respiratory syncytial virus (BRSV) is strongly positive in the cytoplasm of syncytial, bronchiolar and alveolar epithelial cells and macrophages (Fig. 4).

2- Morphologic diagnosis:

Broncho-interstitial pneumonia, fibrino-suppurative, focally extensive, with necrotizing bronchiolitis, bronchiolar/alveolar epithelial syncytial cells and eosinophilic intracytoplasmic inclusion bodies.

3- Two possible causes:

- i) Bovine respiratory syncytial virus (BRSV); with secondary bacterial infection (*Mannheimia haemolytica*, *Histophilus somni*, *Pasteurella multocida*, *Bibersteinia trehalosi*, *Mycoplasma bovis*).
- ii) Bovine parainfluenza virus 3 (BPIV-3) with secondary bacterial infection (*Mannheimia haemolytica*, *Histophilus somni*, *Pasteurella multocida*, *Bibersteinia trehalosi*, *Mycoplasma bovis*).

Comments:

This case was a co-infection of BRSV and *Bibersteinia trehalosi*. BRSV was confirmed by fluorescent antibody test (FAT) and immunohistochemistry (Fig. 4), and *B. trehalosi* was confirmed by lung culture. BPIV-3, bovine herpesvirus 1 (BoHV-1), bovine viral diarrhea virus (BVDV) and bovine coronavirus (BCoV) were ruled out by FAT on lung tissue.

BRSV is an enveloped, single negative-stranded RNA virus belonging to the *Pneumoviridae* family.⁴ This virus plays a predominant role in the bovine respiratory disease complex (BRDC), which has a direct impact on animal welfare and the cattle industry worldwide. BRSV infection is endemic in most countries; morbidity can be as high as 60-80% and mortality can reach up to 20%, particularly in young calves.⁵ The incubation period is 2-5 days.⁵ BRSV infects preferably epithelial cells of the respiratory tract, causing epithelial damage and immune cell chemotaxis, leading to inflammation and alteration of the immune system. These changes are usually complicated by secondary bacterial and/or mycoplasma infections.³

Gross lesions of BRSV infection have usually a cranioventral distribution in the lung and are characterized by atelectatic, well delineated, deep red areas of consolidation.^{1, 2} Occasionally, however, other parts of the lung can be affected and the lesion may also be diffuse.¹ Because most BRSV infections are complicated by secondary bacterial and/or mycoplasma infections, most cases present a fibrino-suppurative exudate restricted to the cranioventral pulmonary lobes.²

Microscopically, typical lesions of BRSV infections are bronchointerstitial pneumonia with necrotizing bronchiolitis, bronchiolar and alveolar epithelial syncytia and eosinophilic intracytoplasmic viral inclusions in syncytial cells and bronchiolar epithelium.^{2, 3} When secondary bacterial infections occur, like in this case, fibrino-suppurative inflammation is observed.²

BPIV-3 can produce similar lesions and should be considered a differential diagnosis. Confirmation of the etiology in cases of BRSV infection should be based on FAT, IHC, virus isolation and/or PCR.⁴

References and Recommended literature:

1- Caswell, J.L.; Hewson, J.; Slavić, D.; Delay, J.; Bateman, K. 2012. Laboratory and postmortem diagnosis of bovine respiratory disease. *Vet Clin North Am Food Anim Pract.* 28 (3), 419-441.

2- Caswell JL, Williams KJ. 2016. Respiratory Sistem. In: Jubb Kennedy and Palmer's Pathology of Domestic Animals. 6th ed. Saunders Elsevier, Philadelphia, USA, Ed Maxie MG. Vol 2, 465-590.

3- Sacco RE, McGill JL, Pillatzki AE, Palmer MV, Ackermann MR. 2014. Respiratory syncytial virus infection in cattle. *Vet Pathol.* 51 (2), 427-36.

4- Sarmiento-Silva RE, et al. Epidemiology, molecular epidemiology and evolution of bovine respiratory syncytial virus. *Viruses* 2012; 4: 3452-3467.

5- Valarcher JF, et al. Bovine respiratory syncytial virus infection. *Vet Res* 2007; 38:153-80.

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) Editorial Committee.

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