

Latin Comparative Pathology Group

The Latin Subdivision of the CL Davis Foundation

Diagnostic Exercise

Case #: 49 Month: October Year: 2014

Answer Sheet

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Clinical History: Over last few years, a ranch has had sporadic cases of adults and young cattle going blind with high fever, convulsions, and ataxia. Some of the affected cattle died. The ranch has both sheep and cattle. No specific feed or field area seemed to be associated with cattle being affected.

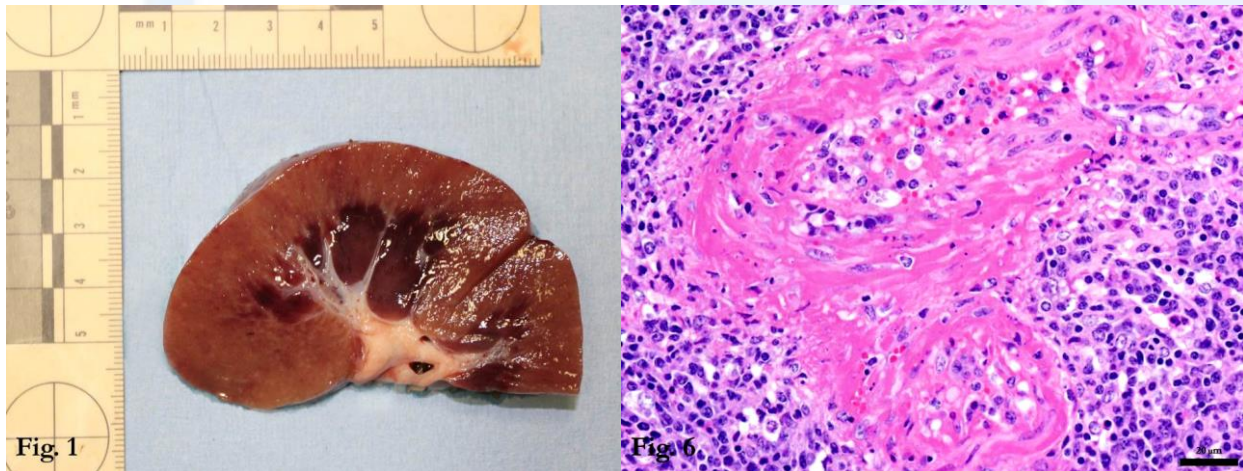


Fig.1 Gross image of one kidney fragment. **Fig.6** Same section of kidney with higher magnification, 40x (H/E).

Diagnoses:

- 1) The kidney has large numbers of poorly demarcated, white foci, up to 2 mm in diameter, distributed primarily in the cortex. The urine sample is red tinged and has multiple small, blood clots and fibrin flocculi.
- 2) In the three tissues shown, the arterioles have markedly **plump endothelium** and the walls are moderately to heavily infiltrated with **inflammatory infiltrates** that disrupt the fibers of the tunica media primarily, resulting in **vascular wall**

expansion (or thickening) and wall architecture disarrangement. Inflammatory cells include **lymphocytes** primarily with **fewer neutrophils** and **histiocytes**. There are also occasional segments of vascular wall **fibrinoid necrosis**. In addition to these common changes, in the **brain** the **Virchow-Robin space** of the arteriole seen is **expanded with hemorrhage** and **lymphocytes**. In the **lung**, the arteriolar wall has a segmental areas with **edema** and inflammatory cells, primarily **lymphocytes**, within the tunica media. The kidney is the most severely affected tissue where vascular wall **fibrinoid necrosis** is better evidenced. The vascular wall inflammatory infiltrates extend to the perivascular connective tissue, resulting in a **multifocal, interstitial, vasulocentric, lymphocytic, neutrophilic** and **histiocytic nephritis**. There is also **diffuse, tubular epithelium degeneration**, and occasional, **necrotic foci** containing **densely packed neutrophils**.

- 3) All three organs: Vasculitis, lymphocytic, neutrophilic and histocytic, moderate to severe, with fibrinoid necrosis of the vascular wall. Additionally, brain, perivascular hemorrhage and lymphocytic cuffing (non-suppurative encephalitis), moderate to severe; kidney, multifocal, interstitial, vasulocentric, lymphocytic, neutrophilic and histiocytic nephritis; diffuse tubular epithelium degeneration, and multifocal necrotizing nephritis with neutrophilic infiltrates.
- 4) Malignant catarrhal fever (MCF), Ovine herpesvirus-2 (OHV-2).
- 5) Vasculitis in multiple tissues is the main lesion in this case and generally the main lesion in cattle with MCF, therefore other agents associated with vasculitis in cattle should be considered as differential diagnoses. Bovine Viral Diarrhea Virus (BVDV) (pestivirus) can cause vasculitis, chronic proliferative arterial lesions in the heart and lung arteries, but is typically associated with severe Peyer's patches necrosis and atrophy in the ileum and sometimes focal areas of lymphocytic myocarditis, neither of which were seen in this case. Orbiviruses, such as Bluetongue virus (BTV) and Epizootic hemorrhagic disease (EHD) can cause vasculitis in cattle, both diseases are rare in adult animals. Bacterial septicemia by *Salmonella* sp. or *Histophilus somni* can result in generalized thrombosis and vasculitis. Mycotic infections with vasculotropic fungi, such as *Aspergillus* sp. or Zygomycetes and drug induced hypersensitivity, should also be considered.

Typical Gross findings:

- Corneal edema (opacity), ocular mucopurulent discharge, occasional corneal ulceration, conjunctivitis and hypopyon.

- Extensive mucosal erosions along the whole gastrointestinal tract, with edema and hemorrhage.
- Mucopurulent nasal discharge, diffuse pulmonary edema, laryngeal and pharyngeal erosions covered with pseudomembranes.
- Multifocal, necrotizing nephritis with petechiae and ecchymoses.
- Ulceration and necrosis on the skin.

Typical microscopic findings:

- All tissues, vascular necrosis with perivascular and intramural lymphocytic infiltrates.
- Eye: Corneal edema with neovascularization, erosions and ulcers, and lymphocytic uveitis.
- Kidney: Small, up to 5 mm diameter infarcts and lymphocytic interstitial nephritis and pelvic mucosal hemorrhagic foci.
- Central nervous system: Perivascular edema, non-suppurative meningoencephalomyelitis.
- Gastrointestinal tract: Edema and congestion with mucosal erosions and abomasal ulcers.
- Oropharyngeal mucosa: Epithelial necrosis and lymphocytic pharyngitis.
- Skin: Lymphocytic dermatitis with edema and epidermal necrosis.

Discussion: Malignant catarrhal fever is a worldwide distributed disease that affects multiple organs and systems of domestic cattle and wild ruminants, including but not restricted to deer, buffalo, antelope and bison. The disease is caused by Gammaherpesviruses and is characterized by lymphocytic vasculitis with lymphoproliferation, erosive to ulcerative mucosal and cutaneous lesions, primarily affecting the respiratory and gastrointestinal systems. The corneal edema and lymphocytic uveitis are quite characteristic of this disease and might be helpful lesions to differentiate it from other erosive/ulcerative mucosal diseases. Affected cattle are supposed to be dead end hosts with no contagion between cattle. Contrarious to what expected with a herpesviral infection, this virus does not produce inclusion bodies or viral syncytial giant cells in affected cattle. Several Gammaherpesviruses can cause the disease in different species. In domestic cattle the disease can be caused by Ovine herpesvirus-2 (OHV-2) or Alcelaphine herpesvirus-1 (AHV-1). OHV-2 is sheep-associated MCF, it has a worldwide distribution. Sheep and goats do not develop clinical signs under natural exposure. The virus also infects bisons, water buffalos and deer species among other ruminants and has also been reported in domestic swine. Bisons are remarkably susceptible to OHV-2 MCF. AHV-1 is wildebeest-associated MCF and happens in Africa. Infected wildebeest remain infected for life and can transmit AHV-1

to their offsprings without occurrence of clinical signs. In this case presented here, OHV-2 was confirmed by PCR in kidney tissue.

Recommended literature:

1. Brown CC, Baker DC, Barker IK. Alimentary system. In: Maxie MG, ed. *Jubb, Kennedy and Palmer's Pathology of Domestic Animals*. Vol 2. 5th ed. Philadelphia, PA: Elsevier Saunders; 2007:152-158.
2. D. O'Toole and H. Li. The Pathology of Malignant Catarrhal Fever, With an Emphasis on Ovine Herpesvirus. *Vet Pathol* 2014, 51: 437-52.

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A final document containing this material with answers and a brief discussion will be posted on the C. L. Davis website by the end of the current month (http://www.cldavis.org/lcpg_english.html).