ECVP/ESVP Summer School in Veterinary Pathology

Summer School 2015 – Histology

Case 5
DOG
HD: Kidney.

100% of mid to deep renal cortex is characterized by coagulative necrosis/infarction, linear widespread haemorrhages and multifocal vasculitis with thrombosis.
Throughout the section the mid to deep renal cortex is intensely eosinophilic with loss of tubular detail, diffuse globar glomerular tuft necrosis and interstitial locally extensive to diffuse haemorrhages (renal infarct).
At the margins of the necrotic cortex, linear haemorrhages and accumulation of degenerated (karyorrhexis) neutrophils are evident
GLOMERULI: in the infarcted areas panglomerular, globar coagulative necrosis and hemorrhages is evident.
In some tufts, small numbers of degenerated neutrophils and karyorrhectic cellular debris are present (acute leukocytoclastic glomerular tuft vasculitis).
Bowman's spaces are expanded and completely occluded by deposition of abundant, intensely eosinophilic fibrillary to amorphous material, fibrin admixed with kariolytic neutrophils in association with variable numbers of erythrocytes (thrombi). Some glomeruli are almost completely substituted by fibrin.
TUBULI: In the infarcted areas epithelial cells of convoluted tubules and Henle's loops are severely swollen, with coarsely granular cytoplasm, have intensely eosinophilic homogeneous cytoplasm with loss of nuclear detail or swollen lightly basophilic nuclei (tubular coagulative necrosis, 0,5) and cells are variably detached and sloughed into the lumen. Tubular intercellular or luminal erythrocytes are evident (haemorrhages).
In the more viable areas, tubules are characterized by clear cytoplasmic vacuoles (hydropic degeneration) and granular cytoplasm (tubular degeneration).
Tubular basement membranes are multifocally intensely basophilic and angulated (basement membrane mineralization) and tubular lumens contain amorphous, granular, dark blue-purple material in association with necrotic debris (dystrophic mineralization).
INTERSTITIUM: the cortical interstitium is expanded by extensive haemorrhages and degenerated karyorrhectic neutrophils. Large vessels (arteries) are characterized by mural oedema, occasional accumulation of intensely eosinophilic, granular to amorphous material (fibrinoid change). In some medium sized and small arteries karyorrhectic nuclear debris and degenerated neutrophils are present (leukocytoclastic vasculitis). Vessel of all calibres are characterized by endothelial cell necrosis and detachment with intraluminal occlusive fibrin thrombi (necrotizing vasculitis).
RENAL MEDULLA: Interstitial hyperaemia and edema are evident. Collecting ducts are multifocally characterized by intraluminal granular or protein casts (either change)
RENAL CAPSULE: Diffuse renal capsular detachment is present.

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MD: Kidney: severe acute/hyperacute diffuse renal infarction with glomerular and interstitial vascular necrotizing leukocytoclastic fibrinoid vasculitis and thrombosis.
Severe, hyperacute diffuse fibrinonecrotizing and hemorrhagic nephritis with vasculitis.

Histologic Description	***Points***
Style	1
100% (0,5) of mid-deep renal cortex (0,5) is characterized by coagulative necrosis/infarction (1), linear widespread haemorrhage and multifocally vasculitis (0.5) with thrombosis (0.5)	3
Mid Cortex	
The mid deep renal cortex is diffusely hypereosinophilic	0,5
Delimited by linear hemorrhages	0,5
Delimited by linear accumulation of degenerated (karyorrhectic) neutrophils	0,5
Glomeruli	
Panglomerular	0,5
Globar	0,5
degenerated neutrophils/ karyorrhectic cellular debris	0,5
glomerular tuft necrosis	0,5
Bowman's spaces expanded (0,5) and occluded (0,5) by abundant, deeply eosinophilic fibrillary to amorphous material (fibrin thrombi) 0,5	1,5
Cortical tubules	
intensely eosinophilic homogeneous cytoplasm with loss of nuclear detail or swollen lightly basophilic nuclei (tubular coagulative necrosis)	0,5
Granular or vacuolar cytoplasm (tubular degeneration).	0,5
tubular basement membranes expanded, basophilic and angulated (mineralization)	0,5
tubular lumens with amorphous, granular, dark blue-purple material (dystrophic mineralization)	0,5
Interstitium	
Hemorrhages	1
Vascular wall accumulation of intensely eosinophilic, granular to amorphous material (fibrinoid change)	0,5
vascular karyorrhectic nuclear debris and degenerated neutrophils	0,5
endothelial cell necrosis	0,5
intraluminal occlusive fibrin thrombi	0,5
Interpretation as fibrinoid leukocytoclastic (0.5) and necrotizing vasculitis (0.5)	1
Renal medulla	
Interstitial hyperaemia and edema Collecting ducts intraluminal granular or protein casts. (One of these changes will get 0,5)	0,5
Diffuse renal capsular detachment	0,5

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MD/MDs: Severe (0,5) acute/hyperacute (0,5) diffuse renal necrosis/infarction (1) with glomerular and interstitial necrotizing leukocytoclastic and fibrinoid vasculitis (1) with thrombosis ALSO Severe, hyperacute diffuse fibrinonecrotizing and haemorrhagic nephritis with acute vasculitis	*3*
E/Es *Leptospira interrogans* serovar *icterohaemorrhagiae*	1
	20

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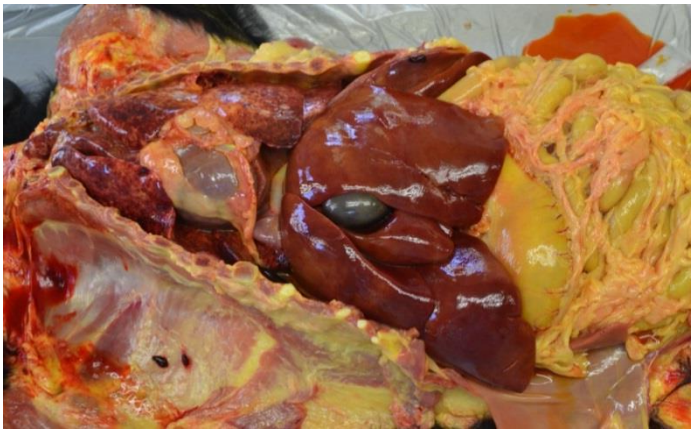
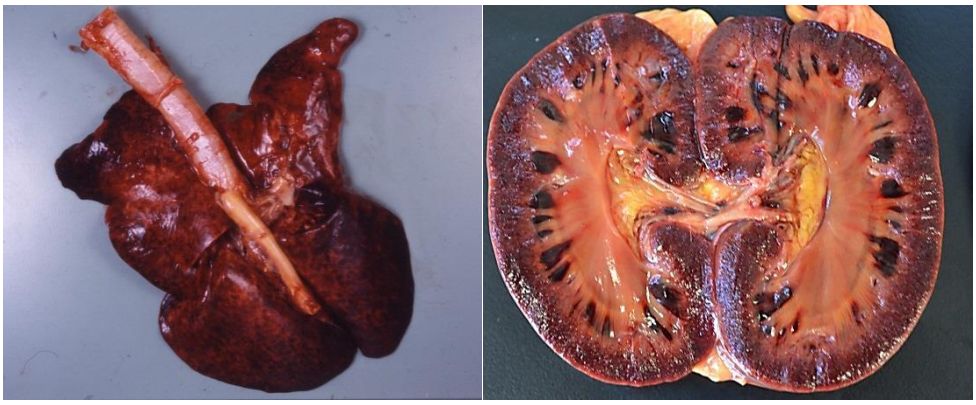
Gross images of the case.





In this case Leptospirosis was confirmed by PCR. The dog had not been vaccinated. Leptospirosis in dogs may present, clinically and pathologically, as either an acute to peracute infection (L. interrogans serovars *icterohemmorrhagiae*) with hemorrhage, hepatic dysfunction and jaundice or as a subacute nephritis (L. interrogans serovars *canicola)*. The peracute disease is characterized by fever, hemorrhages, bloody diarrhea, vomiting, icterus and rapidly fatal outcome. Some dogs and human beings have been reported to die with ARDS. Acute-Peracute lesions are evident in dogs (generally non vaccinated) dying during the septicemic stage. In the liver there is hepatic dissociation with hepatocellular shrinkage. Foci of necrosis may be seen. Kuppfer cells contain hemosiderin and hyperhaemia is frequent. Renal lesions are reported to be rare and not so acute. More than 200 different serovars have been identified in the *Leptospira interrogans* complex.(3) Prior to 1960, serovars *icterohemmorrhagiae* and *canicola* were believed to be responsible for most clinical cases of canine leptospirosis. They invade many organs, including the kidneys, liver, spleen, central nervous system, eyes and genital tract. Signs of hepatic and renal dysfunction and

of coagulation defects usually predominate in dogs with leptospirosis. The peracute form is characterized by massive leptospiremia, causing shock and often death with few premonitory signs. The liver is another major organ damaged during leptospirosis. The degree of icterus in both canine and human leptospirosis usually corresponds to the severity of hepatic necrosis. In contrast, the icterus, hemoglobinemia and hemoglobinuria which develop in cattle with leptospirosis result from a specific hemolytic toxin produced by serovar pomona.
Tissue edema and disseminated intravascular coagulation may occur rapidly and result in acute endothelial injury and hemorrhagic manifestations. *Leptospira* lipopolysaccharides stimulate neutrophil adherence and platelet activation, which may be involved in inflammatory and coagulatory abnormalities. Although the virulence factors associated with leptospires have not been fully elucidated, it appears that their toxic components are associated with outer membrane proteins rather than the secretion of specific toxins. Attachment to the host cell is likely mediated by fibronectin-binding protein on the bacterial surface that binds to host extracellular matrix proteins. Infection of the host cell is via receptor-mediated endocytosis. Pathogenic species of *Leptospira* contain sphingomyelinases and other hemolysins, which may play roles in erythrocyte and endothelial cell membrane damage that results in hemolytic anemia, jaundice, hemoglobinuria and hemorrhage observed in acute leptospirosis. Once in the bloodstream, leptospires evade phagocytosis; the mechanism for this is thought to be induction of macrophage apoptosis. Leptospires are cytochemically gram negative bacteria; however, they differ from other gram negative organisms in several ways, including the following: The LPS of leptospires is not as endotoxic as other gram-negative bacteria; and leptospires, unlike other gram negative organisms, activate the host immune response through TLR-2 rather than TLR-4 pathway.
Laboratory abnormalities usually include leukocytosis, thrombocytopenia, increased serum urea and creatinine, electrolyte disturbances, bilirubinemia and increased serum hepatic enzyme activities. Coagulation parameters may be altered in severely affected animals. Urinalysis abnormalities include bilirubinuria, sometimes glucosuria, proteinuria and increased numbers of granular casts, leukocytes and erythrocytes in the sediment.

Serovar	Maintenance host	Incidental host	Clinical conditions
Bratislava	Pigs, hedgehogs, horses	Dogs	Reproductive failure, abortions, stillbirths
Canicola	Dogs	Pigs, cattle	Acute nephritis in pups. Chronic renal disease in adult animals
Grippotyphosa	Rodents	Cattle, pigs, horses, dogs	Septicemic disease in young animals; abortion
Hardjo	Cattle, sheep, deer	Humans	Influenza-like illness; occasionally liver or kidney

			disease
Icterohaemorrhagiae	Rats	Domestic animals, humans	Acute septicemic disease in calves, piglets and lambs; abortions
Pomona	Pigs, cattle	Sheep, horses, dogs	Acute haemolytic disease in calves and lambs; abortions