

CLINICAL PATHOLOGY AND PATHOMORPHOLOGICAL STUDIES OF DOGS WITH JAUNDICE RELATED TO PLASMA-LYMPHOCYtic INTERSTITIAL NEPHRITIS

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ABSTRACT

Dogs are considered maintenance and incidental hosts for some infectious diseases, and also are potential source of infection. This is a oclinical pathology and pathomorphological studies of four dogs with jaundice and kidney disorder. The clinical pathology examinations demonstrated that those dogs showed elevation values of mean cell haemoglobin concentration (MCHC), granulocytes, aspartate aminotransferase (AST), alanin transaminase (ALT), total bilirubin, blood urea nitrogen (BUN) and creatinine. All dogs were treated with antibiotic and symphomatic therapy, unfortunately it was not help. Histopatological evaluation found that, the kidneys of all dogs were characterized by inflammatory reactions. The inflammatory cells consisted of plasma-lymphocytic cells, and were frequently form multifocal composition in the interstitial spaces and accompanied by formation of interstitial fibrosis, degeneration and necroses of tubular epithelial cells. In addition, histopathological changes on liver were characterized by congestion and hemorrhages which considered relate to the AST and ALT values. These findings suggested that clinical pathology examinations were strongly associated with the occurrence of plasma-lymphocytic interstitial nephritis in dogs.

Key words dog, jaundice, interstitial nephritis

Jaundice is the commonest presentation of patients with liver and biliary disease and this condition occurs when bilirubin concentration above the normal value; bilirubin becomes visible within the sclera, skin, and mucous membranes. Investigations show an isolated unconjugated hyperbilirubinemia with normal liver enzyme activities and reticulocyte concentration (Beckingham and Ryder, 2001). Patient with obstructive jaundice, especially when exposed to the additional stress of an invasive diagnostic or therapeutic procedure, are prone to septic complications and renal dysfunction, contributing to high morbidity and mortality rates (Pain *et al.*, 1985).

Leptospirosis is a zoonotic disease with reservoirs in companion animals, livestock, and wild animals. More than 200 *Leptospira serovars* have been identified (Vinetz, 2001). The outbreaks occur by exposure to water contaminated with urine or tissue from infected animals (Faine *et al.*, 1999). Leptospirosis in dogs can result from infection with several different serogroups of *Leptospira*. Dogs are considered maintenance hosts for serovar canicola, incidental hosts for other serovars, and are a potential source of infection for pet owners (Bolin, 1996).

The present study was designed to carry out pathomorphological changes of four dogs from several organs and describe pathogenesis of the disease which suspected Leptospirosis.

MATERIAL AND METHODS

We retrospectively reviewed the relationship between hematological evaluation of four dogs with jaundice and kidney disorder. All cases were taken samples from sera for hematological examination of liver and kidney function.

Case 1

A one-year-old male dog, Labrador Retriever was presented to the Teaching Animal Hospital of IPB with history of weakness, jaundice, vomit, and body temperature was 39° C. The serum sample was taken and examined for hematological evaluation e.g. mean cell hemoglobin concentration (MCHC), granulocytes, aspartate aminotransferase (AST), alanin transaminase (ALT), total bilirubin, blood urea nitrogen (BUN) and creatinine. Additional sample was evaluated for *Leptospira* sp. by ELISA. The dog was immediately treated with antibiotic and symptomatic therapy. Unfortunately, he died after overnight treatment. The necropsy procedure was performed at the owner's request.

Case 2

The second case was a two-year-old female dog of Collie, presented to the 24-hours Sunter Clinic with two days history of weakness, vomit, jaundice, anuria and black diarrhea. The blood sample was immediately taken for hematological evaluation. The dog was treated with antibiotic, vitamin and gave infusion of ringer dextrose. But the condition dropped after one night, the euthanasia and necropsy were performed at the owner's request.

Case 3

The third dog was two-year-old female dog of Pincher, presented to the 24-hours Sunter Clinic with history of weakness, vomit and jaundice. Blood sample was taken for evaluation. The dog was treated with antibiotic, vitamins and ringer dextrose infusion. Nine hours after hospitably the dog was die and then necropsy procedure was performed.

Case 4

A 3-years-old female dog of Golden Retriever was presented to the Teaching Animal Hospital of IPB with history of weakness and vomitus. The veterinarian gave her with antibiotic and symptomatic therapy, and accompanied by hematological examinations. The dog still had vomitus for three-days before die.

The necropsy procedures were performed in four dogs, by gross and histopathological examination. Several organs were taken and fixed with 10% buffered-neutral formalin, routinely stained with Hematoxylin and Eosin (HE). Selective renal tissues were stained with Masson trichrome, Alcian Blue-Periodic Acid Schiff (AB-PAS), and Gram.

RESULTS AND DISCUSSION

Serum samples from the all dogs were evaluated in a Laboratory of Clinical Pathology. The results of hematological examinations were presented in Table 1. In this table, the values of MCHC, Total WBC, Granulocytes, Lymphocytes and Neutrophil segment was increased. These results demonstrated that four dogs were suspected infect by infectious agents.

Table 1. Examination of clinical pathology

Examination	Case 1	Case 2	Case 3	Case 4
Hematology				
MCHC (g /dL)	NE	38.09*	43.5*	NE
Total WBC (10 ⁹ /L)	NE	18.9*	24.1*	NE
Granulocytes	NE	16.6*	20.3*	NE
Lymphocytes (%)	NE	5*	7*	NE
Neutrophyl segment (%)	NE	95*	92*	NE
Blood chemistry				
AST/SGOT (IU/L)	13.0*	164*	70*	341*
ALT/SGPT (IU/L)	154*	306*	69*	78*
ALP (S.U.)	NE	20	254*	NE
Total Bilirubin (mg/dL)	23*	10*	17.8*	NE
Ureum (mg/dL)	NE	256*	264*	44*
Creatinine (mg/dL)	1.4	9*	8.3*	12.1*
IgM for <i>Leptospira</i> sp. (ELISA)	positive	NE	NE	negative

NOTE : * = increased
NE = not examined

The clinical diagnosis of leptospirosis is inconclusive due to different clinical signs that can be attributed to other pathogenic agents (Vasconcellos, 1993). Adler *et al.* (1980) and Terpstra *et al.* (1980) reported on the use of the enzyme-linked immunosorbent assay (ELISA) as a diagnostic test for leptospirosis. In addition, patient which infected with *Leptospira interrogans* serovar hardjo, indicated that immunoglobulin M (IgM) was the predominant class of antileptospiral antibody produce in acute leptospirosis and that detection of specific IgM by ELISA appeared to be suitable as a diagnostic test. In case 1, the evaluation of IgM for *Leptospira* sp. was positive, but there was negative result was found in case 4.

Examination on blood chemistry of four dogs had similarities in results; revealed the elevation of AST, ALT and ALP and total bilirubin. In addition there were elevation on ureum and creatinin values. Table 2 indicates the presence of jaundice in three dogs (case 1, 2 and 3).

Table 2. Gross lesions

Organ	Case 1	Case 2	Case 3	Case 4
Mucosa	Jaundice (severe)	Jaundice (severe)	Jaundice (severe)	pale
Subcutaneous	Jaundice (severe)	Jaundice (severe)	Jaundice (severe)	pale
Lung	hemorrhage	hemorrhage	hemorrhage	hemorrhage
Heart	hypertrophy of left ventricle	petechiae on cardiac lipid, hypertrophy of left ventricle	hypertrophy of left ventricle	hypertrophy of left ventricle, endocarditis of left atrio-ventricular valve
Liver	swollen, hemorrhage	swollen, hemorrhage	swollen, hemorrhage	swollen, hemorrhage
Kidney	hemorrhage	interstitial nephritis (mild-moderate)	interstitial nephritis (mild-moderate)	Interstitial nephritis (severe)
Spleen	splenitis	splenitis	splenitis	pale
Gastric	NSL	hemorrhage gastritis	NSL	hemorrhage
Intestine	hemorrhage, enteritis	hemorrhage, enteritis	hemorrhage, enteritis	hemorrhage (mild)

NOTE : NSL = No significant lesion

Conjugated hyperbilirubinemia with variable dysarrangement of liver function is common in most cases of leptospirosis, whereas patterns of renal involvement include interstitial nephritis, acute renal failure, and tubular dysfunction (Sitprija *et al.*, 1980). Severe jaundice and oliguric renal failure are important prognostic markers which are associated with a high mortality (Heath *et al.*, 1965).

Leptospirosis is a zoonotic disease with reservoirs in companion animals, livestock, and wild animals. Acute phase or septicemic stage of leptospirosis in dogs are characterized by severe dehydration and jaundice, with many petechiae on the pleura, peritoneum, nasal and oral mucosae. Bile retention is indicated by plugging of bile canaliculi (Jones *et al.*, 1997). In our four cases the histopathological changes of livers are dominated with hemorrhages, Kupffer cells contains large amount of hemosiderin, and portal vessels are usually congested (Figure 1). Unfortunately the organisms are not seen clearly in sinusoids and within liver cells by routine HE stain.

The changes in the kidneys revealed visible hemorrhage, interstitial nephritis (Figure 2), fibrosis with minimal proliferation of collagen fibers. The glomeruli showed minimal changes, but convoluted tubules are usually severely altered. Affected tubules are surrounded by plasma cells and lymphocytes, which multifocally infiltrates. Degeneration and necroses of tubular epithelial cells were moderate to severely occurred.

According to the clinical signs, clinical pathology evaluation and pathomorphological examinations, we considered that the diagnosis of all four dogs suspected to leptospirosis.

These findings suggested that clinical pathology examinations were strongly associated with the occurrence of plasma-lymphocytic interstitial nephritis in dogs.

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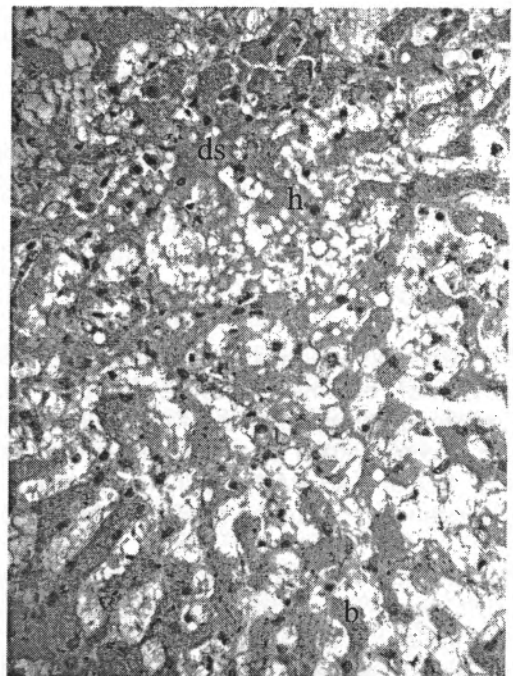
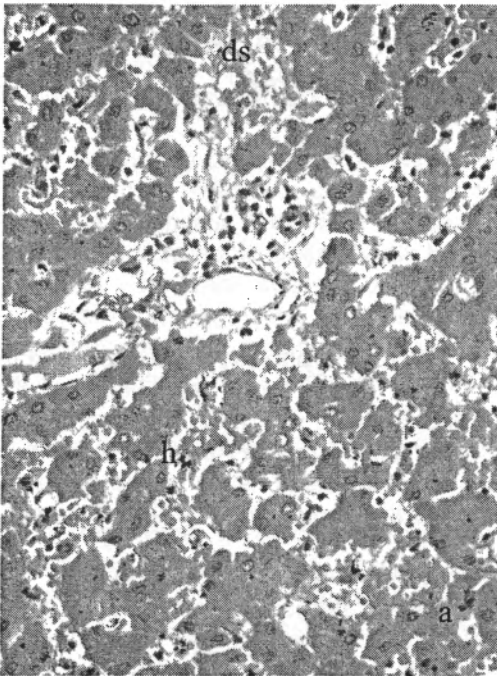


Figure 1. Liver of case 1 (a) and case 3 (b) demonstrated hemorrhage and dilation of sinusoids (ds). Some Kupffer cells contain hemosiderin (h). HE stain, (400 x).

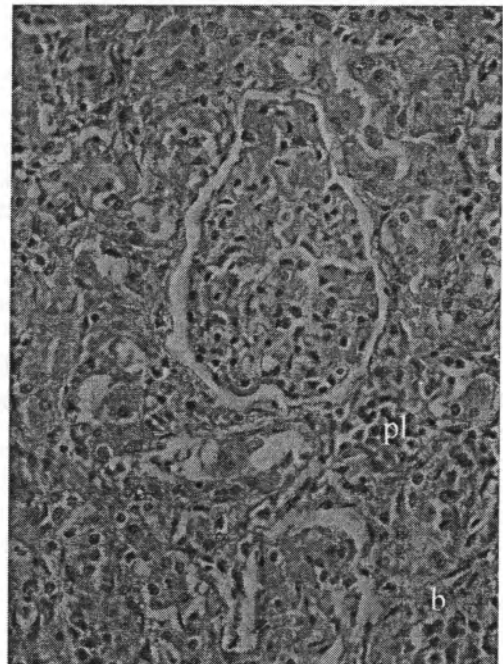
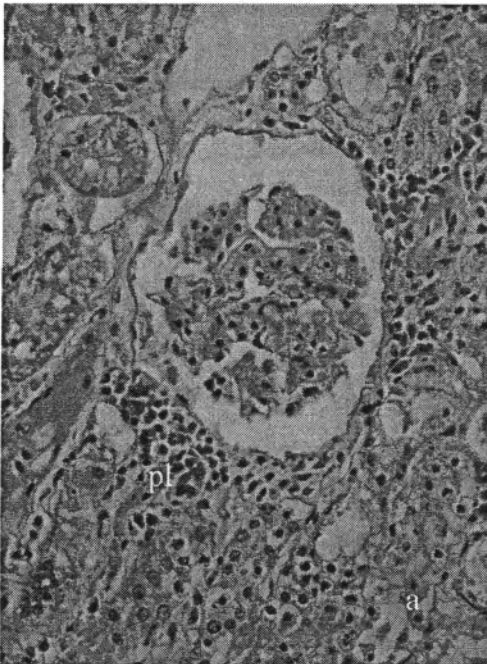


Figure 2. Kidney of case 2 (a) and case 3 (b) revealed infiltration of inflammatory cells consist of plasma-lymphocytic (pl) cells in the interstitium. HE stain, (400x)