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Acquired hepatic encephalopathy due to leptospirosis in dog: A case report

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Abstract
A carcass of four year old male dachshund presented to the Department of Veterinary Pathology, College of Veterinary and Animal Sciences, Mannuthy, formed the material for the study. The dog had a history of nervous symptoms. In necropsy, jaundice, fatty liver, petechial hemorrhages on the kidney, splenic necrosis, catarrhal enteritis, and severe congestion in the brain were observed. Impression smear from hippocampus subjected to the direct fluorescent antibody technique to rule out the possibility of rabies. On histopathological examination, liver revealed fatty change. In kidney, desquamation of tubular epithelium with cast formation was observed. In intestines, infiltration of inflammatory cells in the mucosal layer with a proliferation of goblet cells. In brain, cerebral edema, gliosis, satellitosis, vacuolation were observed. Alzheimer's type II cells could also be observed. Liver and kidney tissue samples were subjected to molecular examination and found positive for leptospirosis. Hence the condition was concluded as a case of acquired hepatic encephalopathy due to leptospirosis.

Keywords: hepatic encephalitis; leptospirosis; cerebral oedema; alzheimer's type ii astrocytes

1. Introduction
Hepatic encephalopathy is a complex neurological abnormality that occurs along with liver and kidney diseases. Hepatic encephalopathy can occur as a result of congenital portal vena cava shunt or acquired liver or kidney disease in species including dogs, cats [1]. In dogs, it can occur as a result of either congenital or acquired liver diseases. Liver dysfunction aggravate the accumulation of toxic metabolite which leads to the altered neurotransmission and finally manifested as hepatic encephalopathy [2]. Pathogenesis of hepatic encephalopathy is complex and incompletely understood, however increased ammonia concentration in the blood contributes to its pathogenesis [3]. In human, changes like Spongiosis or micro aviation, neuronal necrosis, gliosis and Alzheimer type I1 astrocytes have been the pathogical features of hepatic encephalitis in brain [4].

2. Materials and Methods
A four year old male dachshund dog which was under treatment for sudden epilepsy, convulsions and tremors was presented to the Department of Pathology, College of Veterinary and Animal Sciences, Mannuthy following its death for postmortem examination. A detailed necropsy was conducted. Gross lesions in all organs were recorded. For detailed histopathological examinations, tissue samples were collected in 10% Neutral Buffered Formalin. After fixation, tissue sections were processed through different gradients of alcohols and xylene. Then paraffin blocks were made. Tissue sections of 5 micron thickness were cut using microtome, finally stained by Hematoxylin and Eosin (H&E) standard protocol (Luna. 1968). Samples of kidney and liver were collected for molecular diagnosis. Tissue sections of liver and kidney was subjected to DNA extraction using the commercial available kit followed by genus specific Polymerase Chain Reaction for Leptospira species. A primer pair specific to *Lip 32* gene was employed for this study [5]. Impression smears from hippocampus were taken for the direct fluorescent antibody test (FAT) to detect rabies.
On detailed postmortem examination yellowish discoloration was observed in the mucous membrane of eye and mouth, friable fatty liver, pin point hemorrhages on the kidney surface, necrosis on the spleen, severe catarrhal enteritis, cerebral congestion with oedema was observed.

3. Results

On direct fluorescent antibody testing using fluoroscen isothicyanate conjugated antibody directed against the nucleo capsid of rabies virus. The result was negative with the absence of apple green fluorescence.

Detailed histopathological examination revealed a severe fatty change of entire liver parenchyma with loss of normal architecture. Numerous small vacuoles were seen within the individual hepatocytes (micro vesicular) around the nucleus, while in other hepatocytes, very large coalescing vacuole displacing the nuclei to periphery giving a characteristic signet ring (macro vesicular) appearance. (Fig: 1). The section of the kidney showed desquamation of tubular epithelium with cast formation in the lumen. Infiltration of inflammatory cells was also observed in the interstitium of the kidney (Fig: 2). In the intestines, severe infiltration of inflammatory cells in the mucosal layer with the proliferation of goblet cells. Congestion and hemorrhage were also evident in the intestinal mucosa. In the brain, peri-neuronal edema with neuronal degeneration was prominent. Degenerated neurons were seen, and they are surrounded by glial cells (Satellitosis) (Fig: 3). Congestion and hemorrhage were also observed. Alzheimer's type II astrocytes characterized by swollen vesicular nuclei could be detected in the brain section (Fig: 4). Severe vacuolation and spongiosis were also observed.

In Polymerase Chain Reaction assay, amplicon of size 767 bp corresponding to *Lip 32* gene was documented in agarose gel electrophoresis.

5. Discussion

Hepatic encephalopathy is a serious complicated neuropathological condition seen in acute and chronic liver failure[6]. Acute and chronic liver failure may be due to congenital or infectious causes. Lipidosis can be seen in both conditions. In chronic liver lipidosis, hepatocytes lose their ability to remove by-products mainly ammonia from circulation which remains in systemic circulation and eventually crosses blood brain barrier to reach CNS leading to metabolic, circulatory and nervous disturbances. The adverse effects are frequently manifested as neurological signs and are together called hepatic encephalopathy. Same pathogenesis can also see in kidney failure condition also. Leptospirosis is one of the common infectious diseases that affect dog, cats and humans causing chronic liver and kidney failure [7]. In this case, leptospira infection caused hepatic injury with severe lipidosis along with renal failure leading to hyper-ammonemia. The metabolite which crossed the blood brain barrier resulted in characteristic changes in mental status to stupor and aggressive convulsions. Neuropathological studies by earlier workers had revealed that the main cause of death in hepatic encephalopathy in humans was due to cerebral herniation with brain edema as a result of astrocyte swelling [8]. The clinical signs and histopathology of brain sections in this case also confirmed with the above findings. Moreover, interstitial nephritis and renal tubular degeneration induced by leptospira organisms resulted in the formation of cast inside the tubule and these results are also compatible with previous works [9, 10]. In acute liver failure condition in transgenic mice, ammonia level in the body increased and produced effect as astrocyte swelling, brain edema, vacuolation and spongiosis [11]. The same lesions were observed in this case also. Hepatic encephalopathy in humans with congenital hyperammonemia, that resulting from the inherited defects of urea cycle enzymes caused neuropathological damage and formation of Alzheimer's type II astrocytes [12]. The present study also revealed same neuropathological abnormalities as a result of hyperammonemia due to liver and kidney damage caused by leptospira infection. Histopathological sections of brain also revealed astrocytes with swollen and vesicular nuclei similar to Alzheimer's type II cells. In this case, the clinical signs, gross and histopathological lesions point to hepatic encephalopathy due to an acquired infectious cause.

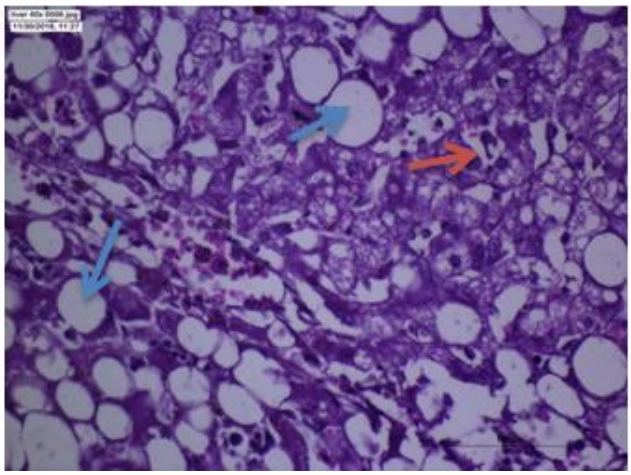

Fig 1: Liver- Sever lipidosis with macro vesicles (blue arrow) and micro vesicles (brown arrow).

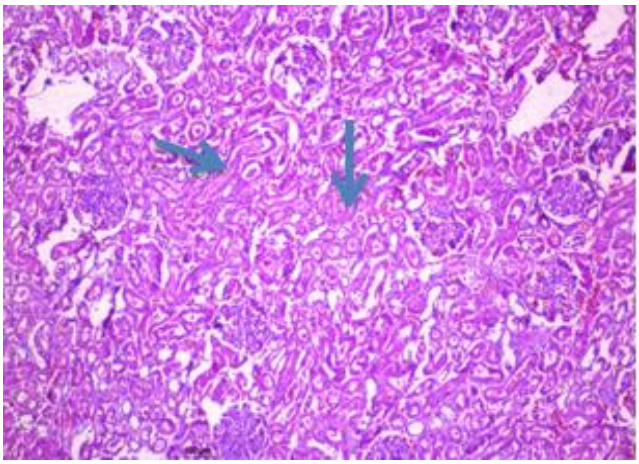

Fig 2: Kidney – Interstitial nephritis with cast formation inside the tubular lumen (arrow)

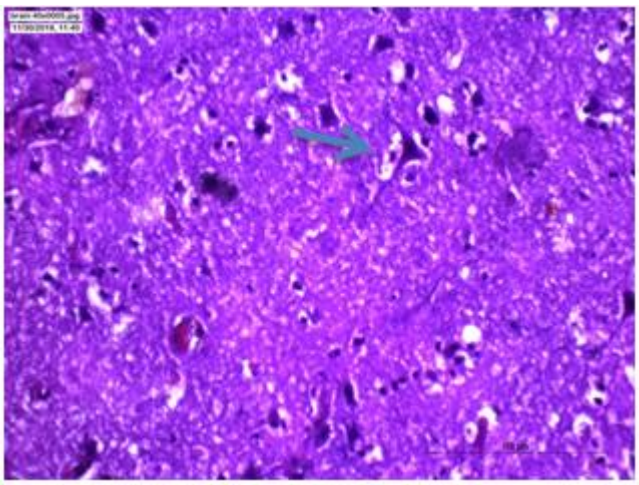

Fig 3: brain – Peri neuronal oedema, swollen neuron surrounded by cluster of glial cells (Satellitosis) (arrow)

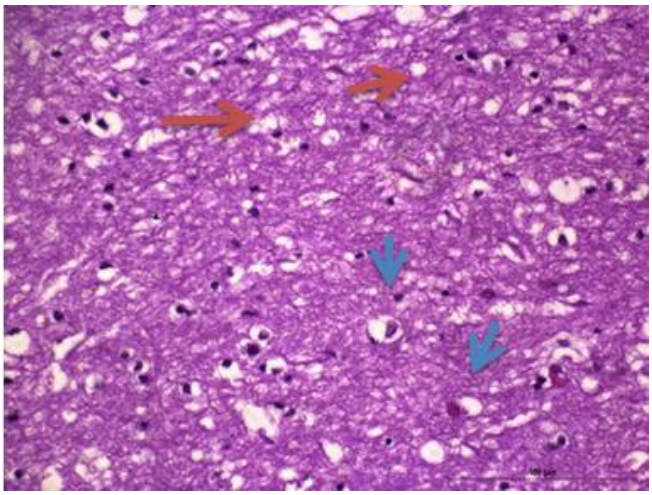

Fig 4: Brain – Severe vacuolation and edema (brown arrow) with astrocytes similar to Alzheimer's type II cells (blue arrow).

6. Conclusion

The present case report confirms, one of the reasons for acquired encephalitis in dogs could be leptospirosis because of liver and kidney damage. PCR based detection confirmed the root cause of the condition as leptospirosis.

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