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Pathological and immunohistochemical study of multinodular hepatic cirrhosis in a dog

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Abstract

Multinodular liver cirrhosis is a common end stage pathological condition in humans and dogs, mostly results from chronic hepatitis. A carcass of 9 year, male, and Labrador retriever dog was presented for necropsy to the Department of Veterinary Pathology, Madras Veterinary College, TANUVAS, and Chennai. Grossly, the liver was shrunken and showed presence of diffuse, scattered, multiple, variable size yellowish tawny colour nodular growth. The tissue pieces along with mass was collected, fixed and processed routinely by paraffin embedding technique and sections were stained by H&E and Masson's trichrome stain. Microscopically, tissue section revealed presence of multiple, variable sized islands of hepatocyte separated by bundles of collagen fibers which was infiltrated with lymphocytes, plasma cells and few macrophages. Proliferation of bile ducts were evident in the periportal areas. The collagen fibers was demonstrated by Masson's trichrome stains. The tissue sections showed positive signals to cytokeratin, vimentin and Ki-67. Based on the gross, microscopical changes and immunohistochemistry, the case was diagnosed as multinodular liver cirrhosis.

Keywords: Cirrhosis, dog, histopathology, immunohistochemistry, liver, multinodular

1. Introduction

The liver which accounts approximately 3-8% of the total body weight in carnivores and plays a central role in diverse metabolic activities (Nottidge *et al.*, 2003) [9]. The liver is having high degree of differentiation and also retains high capacity to regenerate (Roger, 1993) [10]. So, it is able to maintain normal metabolic activities for a long period. Multinodular liver cirrhosis is a common end stage pathological condition in humans and dogs mostly results from chronic hepatitis (Favier, 2009) [4]. Among domestic animals, liver cirrhosis has been reported mostly in adult dogs (William, 1991) [13]. Chronic hepatitis which may result from microbial infections, metabolic diseases, hepatotoxins, breed-related inherited progressive liver diseases and autoimmunity which gradually progress to irreversible cirrhosis characterized by bridging fibrosis, inflammation, and nodular regeneration (Watson, 2004) [12].

2. Case history

A 9 year, male, Labrador Retriever dog carcass was presented to the Department of Veterinary Pathology, Madras Veterinary College, TANUVAS, Chennai-600007. The history showed that the animal was depressed and anorectic for 5 days before death.

3. Materials and Method

Systematic necropsy was carried out. Grossly, the liver was shrunken and surface was irregular. The surface of liver revealed diffuse, scattered multiple, variable sized nodules. The nodules were embedded in liver parenchyma and were measuring from 2 millimetres to 1 cm diameter (Fig. 1). Most of the nodules were raised above the surface of liver, few were extruded from parenchyma and connected with their capsular material. The gall bladder was slightly distended. No other lesions were observed in any other visceral organs. Tissue pieces were collected in 10% formalin for histopathological examination. The fixed tissue was processed by standard paraffin embedding technique and sections were stained with H&E (Haematoxylin & Eosin) and Masson's trichrome stain (Bancroft & Gamble, 2008) [2]. The immunohistochemical (IHC) studies were also performed in tissue sections for the markers on Vimentin, Cytokeratin and Ki-67 as per manufactures protocol (Bancroft & Gamble, 2008) [2].

4. Results

Histopathological examination of liver tissue revealed presence of multiple, variable size islands of hepatocyte separated by bundles of fibrous tissue and collagen (Fig. 2). Central veins were dilated and filled with inflammatory cells composed of lymphocytes, erythrocytes and scanty eosinophilic fluid. Marked areas of degenerative changes of hepatocytes were observed around the pericentral vein region (Fig. 3). Periportal fibrosis was marked and characterized by marked fibrous tissue proliferation and collagen deposition in subcapsular regions and interlobular regions (Fig. 4). Infiltration of lymphocytes, plasma cells and few macrophages were observed in between the collagen bundles (Fig. 5). Proliferation of bile ducts were marked in the periportal areas (Fig. 6). Collagen bundles in the interlobular regions and subcapsular regions were positive to Masson's trichrome stains (Fig. 7). The tissue sections under IHC showed positive signals to cytokeratin (Fig. 8) and fibrous tissue showed mild to moderate positivity to vimentin (Fig. 9). The mild expression of Ki-67 marker was observed in the proliferative cells (Fig. 10).

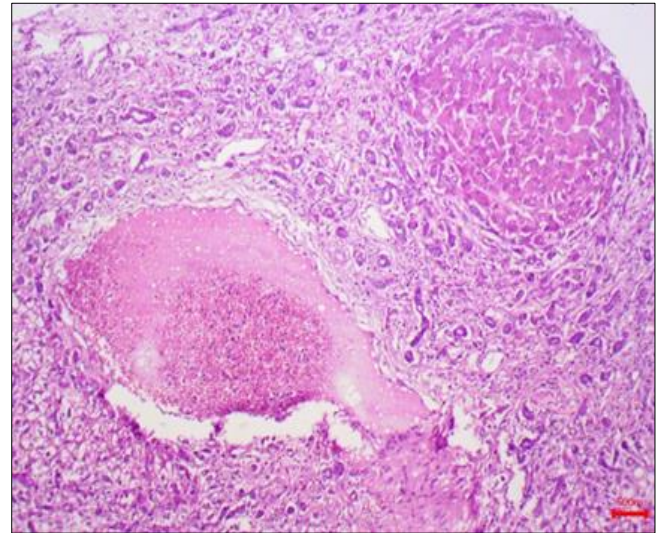


Fig 3: Liver: Dilatation of central vein, filled with inflammatory cells mainly lymphocytes, RBCs and some eosinophilic fluid and degenerative changes with vacuolations of hepatocytes, H&E, bar= 50µm



Fig 1: Liver: Scattered, multiple, variable size measuring around few millimetres to 1 cm diameter, yellowish tawny colour nodular growths

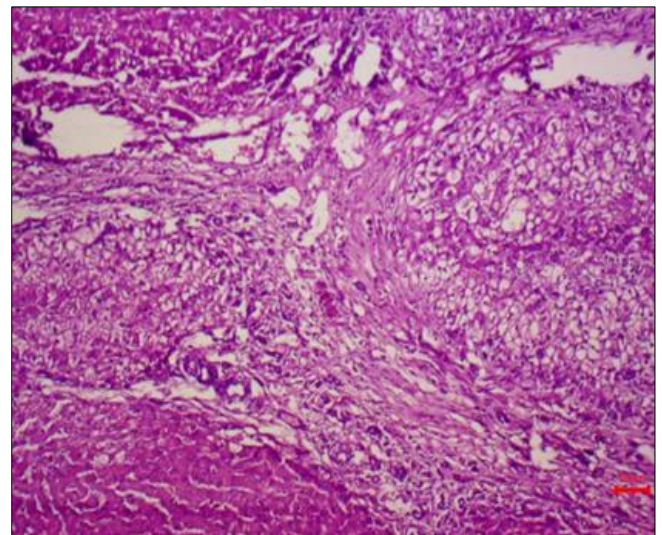


Fig 4: Liver: Deposition of collagen fibers in subcapsular regions and interlobular regions referred to as periportal fibrosis, H&E, bar= 50µm

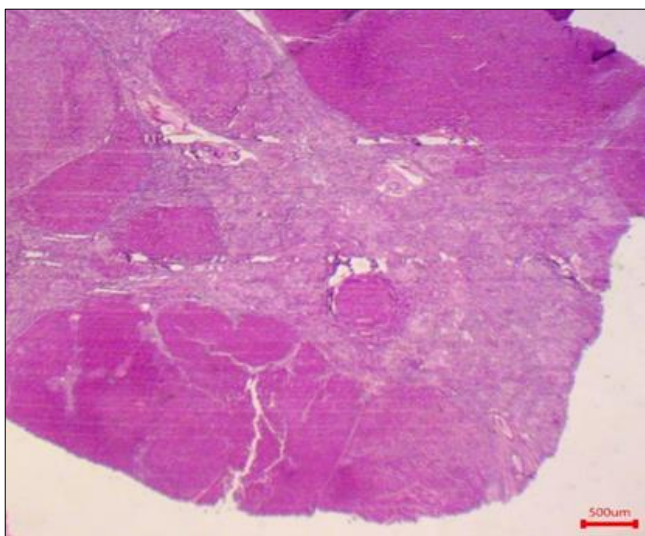


Fig 2: Liver: Multiple variable size islands of hepatocytes separated by strips of fibrous and collagen cells, H&E, bar= 500µm

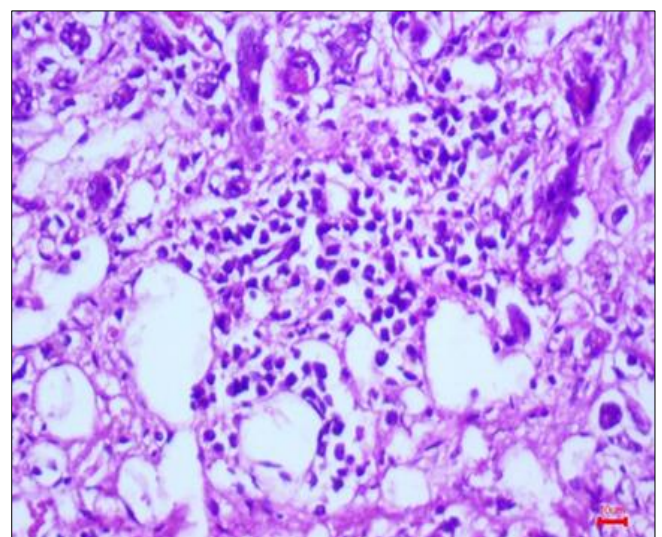


Fig 5: Liver: Infiltrations of lymphocytes, plasma cells and few macrophages in between the collagen fibers, H&E, bar= 10µm

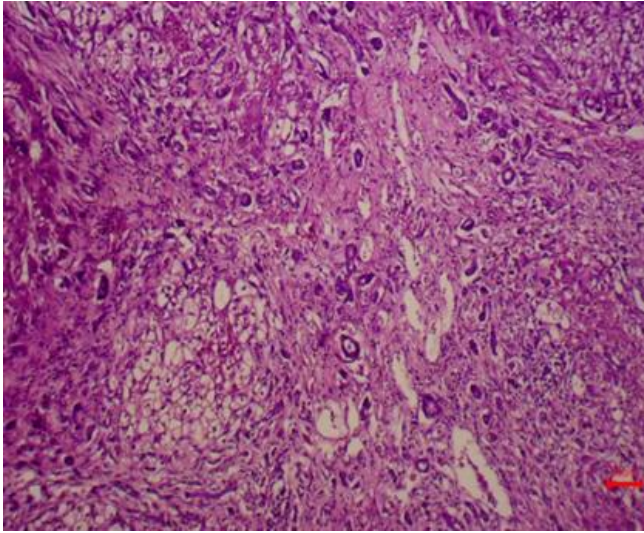


Fig 6: Liver: Bile ducts proliferation in periportal areas, H&E, bar= 50µm

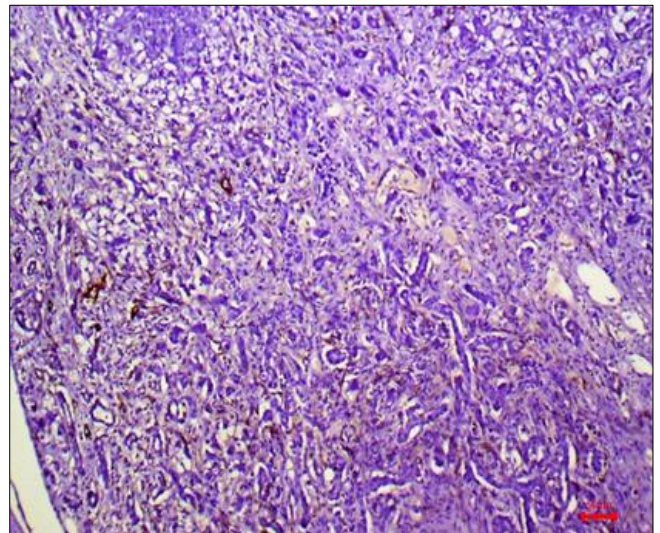


Fig 9: Liver: Mild cytoplasmic expression of vimentin in blood vessels and mesenchymal tissue, IHC, bar= 50µm

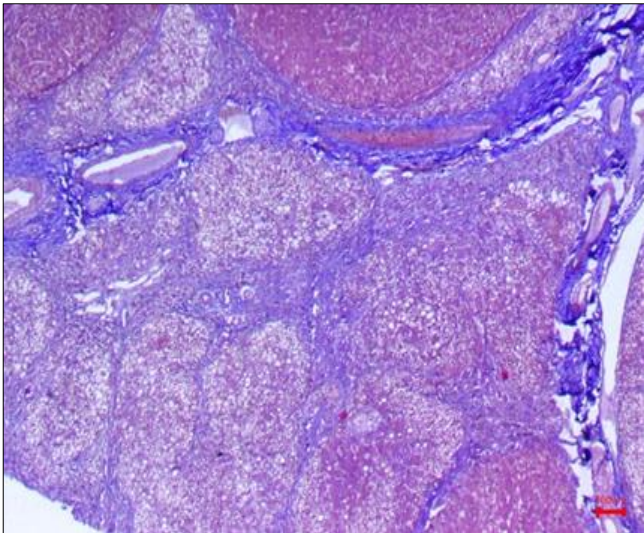


Fig 7: Liver: Proliferation of collagen fibers (blue colour) in the interlobular regions and subcapsular regions, Masson's trichrome stain, bar= 100µm

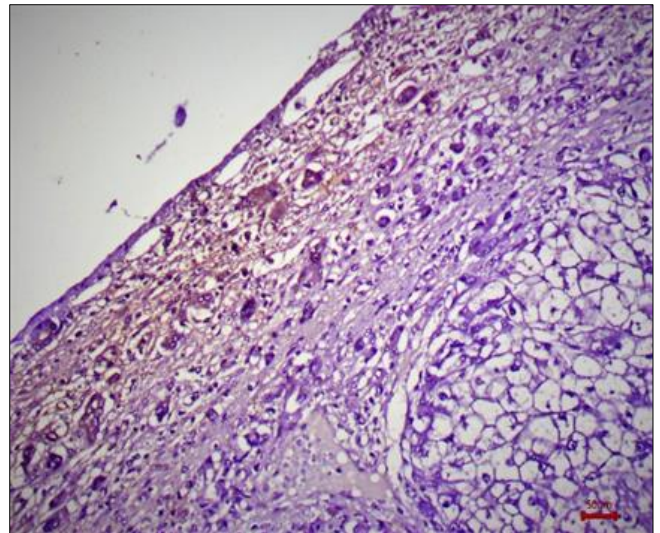


Fig 10: Liver: Mild nuclear expression of Ki-67 in proliferated cells, IHC, bar= 50µm

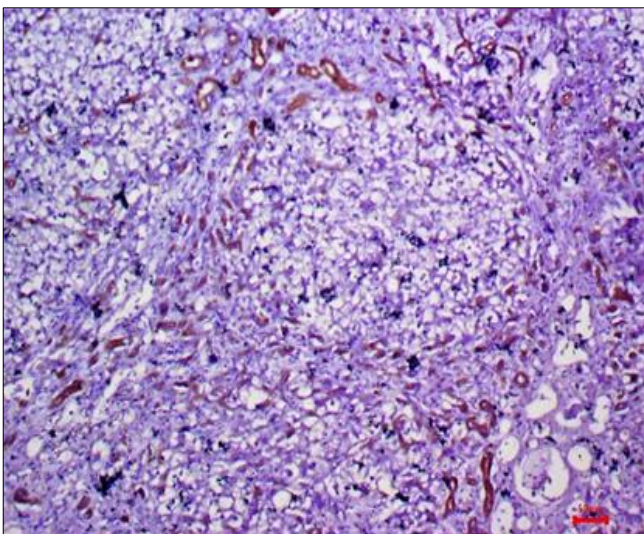


Fig 8: Liver: Moderate cytoplasmic expression of cytokeratin in epithelial cells, IHC, bar= 50µm

5. Discussion

Nodular cirrhosis is the final stage of chronic hepatitis which is considered to be irreversible and characterized by proliferative nodular lesions (Favier, 2009) ^[4]. Liver cirrhosis reportedly observe mainly in old dogs of both sexes (Herrtage, 1991) ^[6]. The breeds like Labrador Retrievers, American Cocker spaniels and Doberman pinschers were more susceptible to liver cirrhosis (Bexfield et al., 2012) ^[3]. The present case study was in accordance with the previous reports in a dog. The microscopical results showed various degrees of severity which extend from infiltration of mononuclear inflammatory cells to the fibrotic lesions in the interlobular regions and subcapsular regions of liver tissue. Similar results were also previously recorded (Fraquelli *et al.*, 2007) ^[5]. Other lesions such as marked areas of degenerative changes of hepatocyte particularly around the central vein region and infiltrations of plasma cells and macrophages in between collagen bundles were observed in this case were also in accordance with Mahdi and Ahmed (2021) ^[7]. The positive reaction of Masson's trichrome staining confirmed the presence of collagen within the liver parenchyma suggestive of chronic irritation (Abalaka *et al.*, 2020) ^[1]. The expression of cytokeratin and vimentin markers indicates

involvement of both epithelial and mesenchymal tissue in liver cirrhosis. The positive reaction of Ki-67 marker indicate the proliferation of cells (Vince *et al.*, 2014)^[11]. The structural and vascular distortions in the affected liver might have caused portal hypertension resulting which leads to the death of the affected dog (Moller & Bendtsen, 2018)^[8].

6. Conclusion

Multinodular liver cirrhosis is a common end stage pathological condition in humans and dogs, mostly results from chronic hepatitis. Based on the gross, microscopical changes and immunohistochemistry, the case was diagnosed as multinodular liver cirrhosis.

7. Acknowledgments

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