

Hepatocellular Carcinoma in dog

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ABSTRACT

This report presents clinical, ultrasonographical and pathological findings in a 13-year-old dog with hepatocellular carcinoma (HCC). Ultrasound Sonography (USG) examination of liver revealed anechoic areas with irregular borders. Gross examination of liver and spleen revealed multifocal firm nodules of various sizes. Cut section of liver was greasy. Upon gross examination of lungs, haemorrhagic nodule and pale appearance were noticed. Upon cytological examination, hepatocytes showed multiple nuclei and nuclear atypia along with vacuolated cytoplasm and few naked nuclei. Cytology of spleen revealed multinucleated cells and few hepatocytes which might indicate metastasis. On histopathological analysis, pleomorphic hepatocytes with vacuoles, multinucleated cells and mitotic figures were noticed. These results supported the possibility of hepatocellular carcinoma (HCC). With Masson's Trichrome staining, collagen fibers stained blue colour around the portal triad indicating periportal cirrhosis. Histopathology of spleen revealed islands of fibrous tissue around vasculature which was also confirmed by Masson's Trichrome staining. Immunohistochemical analysis of liver revealed intense immunopositivity for Proliferating Cell Nuclear Antigen (PCNA) and cytokeratin 18 in neoplastic hepatocytes.

Keywords: Cytokeratin, hepatocellular carcinoma, nuclear atypia

INTRODUCTION

Dogs seldom develop primary liver tumours, which account for 0.6% to 1.3% of all canine neoplasms. The most frequent malignant liver tumour is hepatocellular carcinoma (HCC), although others include bile duct carcinoma, carcinoids, sarcomas, lymphomas, and systemic mastocytosis¹. Hepatocellular carcinomas have been reported in a variety of domestic animal species, including cattle, sheep, pigs, cats, dogs, and horses; however, dogs may be more amenable to HCC than the majority of other animals. HCC is the sixth most prevalent type of cancer in people across the globe which is frequently attributed to chronic liver diseases like cirrhosis, non-alcoholic steroid hepatitis, and hepatitis B and C infection. In domestic animals, factors including persistent infections from parasites, viruses, and bacteria, hereditary factors, or ingestion of chemicals like aflatoxins, pyrrolizidines, and nitrosamines may play a pivotal role in developing HCC². It frequently manifests in dogs with more than 10 years of age and male dogs are more susceptible. Certain dog breeds, including miniature schnauzers, shih tzus, Welsh Corgis, beagles and Scottish terriers with vacuolar hepatopathy have significant risks of acquiring HCC³.

HCCs can manifest in three different ways: massive form, nodular form and diffuse form. Massive HCC is usually a single neoplasm which often only affects one or two contiguous liver lobes. Nodular HCCs develop scattered nodules, frequently throughout multiple liver lobes. They range in size from tiny, spherical, distinct lesions with a few centimeters in diameter to enormous, diffuse masses with a diameter of more than 10 cm. Minute, hazy masses that are dispersed throughout the liver parenchyma affecting various lobes are the hallmarks of diffuse HCCs. Tumours may vary from well diffuse to highly anaplastic at the microscopic level². Solid, pseudoglandular, cirrhous, clear cell type and trabecular are the histological subtypes of HCC⁴. Others include peritheliomatous, peliod, and cobblestone⁵. The primary

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objective of this study is to evaluate clinical, ultrasonographical, gross, cytological, histopathological and immunohistological findings of HCC in dog.

Case Description

A 13-year-old female dog was brought to the Veterinary Clinical Complex, College of Veterinary Science in Rajendranagar, Hyderabad, with a history of lethargy and anorexia for the previous 10 days. The animal was in recumbent position. Clinical findings included pit edema, ascites, and melena. On USG examination, anechoic areas with irregular borders and moth eaten appearance of the liver were revealed (Fig. 1A). X-ray of thoracic region revealed opacity in lungs (Fig. 1B).

The animal passed away during treatment and was presented to Department of Veterinary Pathology, Rajendranagar for necropsy examination.

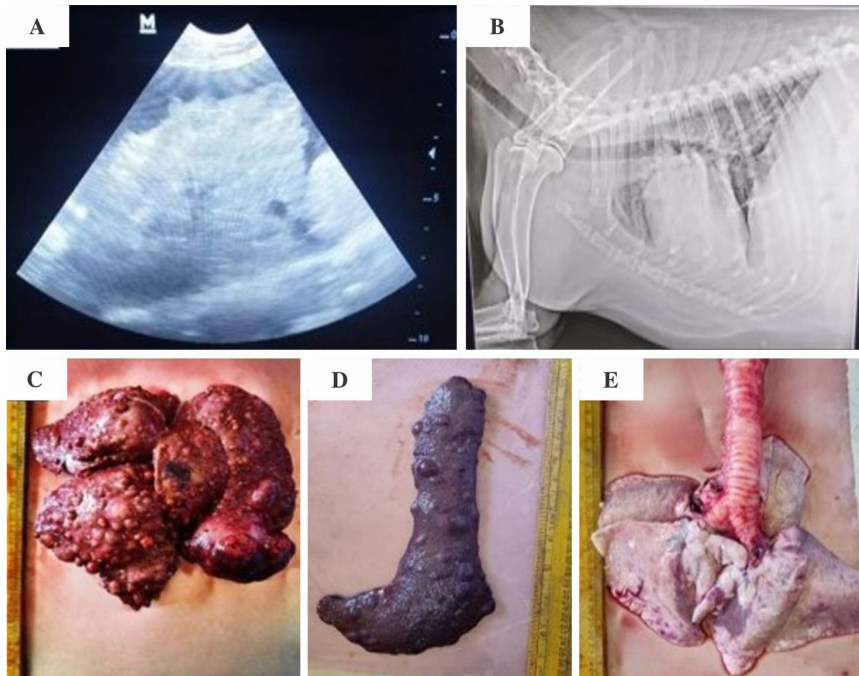


Fig 1. A. USG examination of liver revealed anechoic spaces with irregular borders. B. Radiograph of thoracic region revealed opacity in lungs C. Multiple random nodules of various sizes which are hard in consistency and haemorrhagic noticed on liver D. Multiple random nodules of various sizes which are hard in consistency and haemorrhagic observed on spleen E. Gross examination of lung showing haemorrhagic nodule and appears pale.

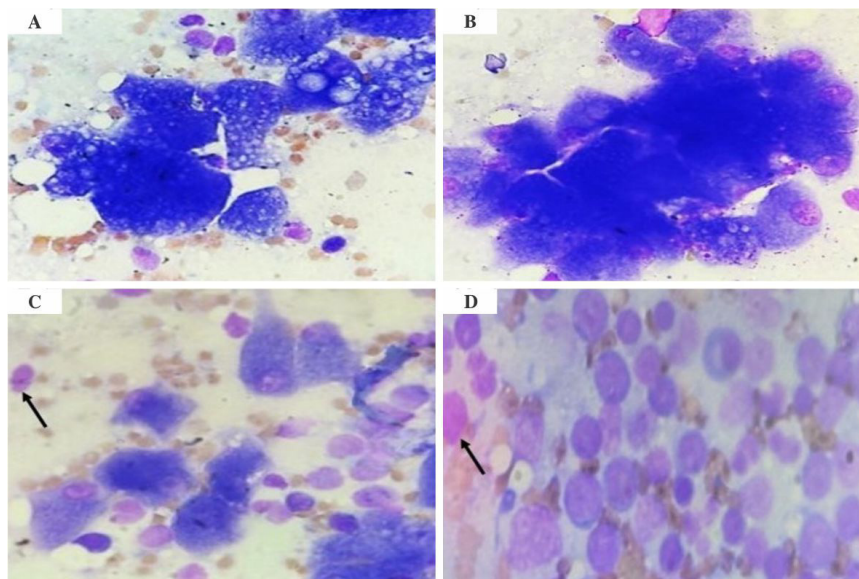


Fig 2. A. Impression smear of liver nodule showing pleomorphic hepatocytes with atypical naked nuclei and vacuolated cytoplasm (Giemsa x1000). B. Impression smear of liver nodule showing sheet of neoplastic hepatocytes and few giant cells (Giemsa x1000). C. Impression smear of liver nodule showing atypical naked nuclei of hepatocytes. Arrow- naked nuclei (Giemsa x1000). D. Impression smear of nodules on spleen showing atypical nuclei of hepatocyte (Arrow) (Giemsa x1000).

On Gross examination of liver, hepatomegaly with greasy appearance along with multifocal haemorrhagic, diffuse firm nodules were noticed (Fig. 1C). On the cut surface, caseous necrosis was noticed at centre of the nodules. Firm nodules of varying sizes were visible upon gross examination of the spleen (Fig. 1D). Gross examination of lungs revealed focal haemorrhagic nodule and appeared pale (Fig. 1E). Fine needle aspirates of liver mass revealed cluster of hepatocytes with few multinucleated hepatocytes, nuclear atypia with anisokaryosis, naked nuclei (Fig. 2C) in some areas and vacuolated cytoplasm (Fig. 2A). Cytology of impression smears of spleen nodules revealed multinucleated cells and few hepatocytes (Fig. 2D) which indicate metastasis. The resected liver and spleen tissues were fixed in 10% neutral buffered formalin, processed routinely and then embedded in paraffin. Paraffin sections of 5 μ m thickness were cut and stained with Haematoxylin and Eosin (H&E) and Masson's Trichrome stain (MTS).

Histopathology of liver showed neoplastic hepatocytes with vesicular to vacuolated cytoplasm, hyperchromatic nuclei, pleomorphic and multinucleated cells along with mitotic figures (Fig. 3A). With Masson's Trichrome stain, incremental fibrosis with collagen fibers that stained blue colour were noticed in between the hepatic cords and around the portal triad (Fig. 4A) which indicate periportal cirrhosis. Infiltration of inflammatory cells was also observed. Histopathological examination of spleen revealed islands of fibrous tissue along with fibrous thickenings around the vasculature (Fig. 3C). With Masson's Trichrome staining, collagen fibers which stained blue colour were observed around the splenic vessels (Fig. 4B). Depletion of lymphocytes, prominent trabeculae, haemorrhage, congestion and thickening of splenic vessels were also noticed. Immunohistochemical examination of

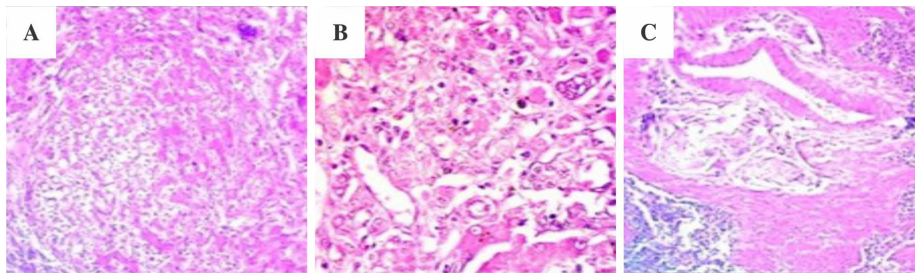


Fig. 3. A. Photomicrograph of liver showing neoplastic hepatocytes with vacuolation and atypical mitotic figures (H&E x100); B. acinar pattern forming neoplastic cells and hepatocytes with foamy cytoplasm (H&E x400); C. Photomicrograph of spleen showing Islands of fibrous tissue and fibrous thickenings around vasculature with depletion of lymphocytes (H&E x100).

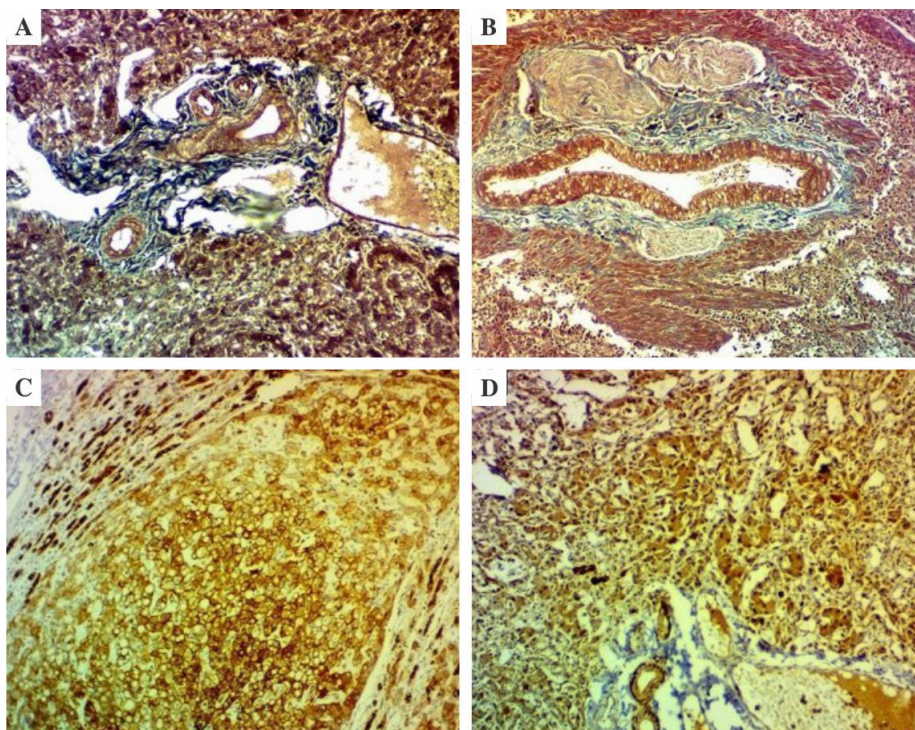


Fig.4. A. Photomicrograph of liver showing fibrous tissue proliferation around portal triad indicating cirrhosis (MTS x100); B. Photomicrograph of spleen showing extensive proliferation of fibrous tissue around dilated thickened vasculature (MTS staining x100); C. Photomicrograph of liver showing intense immunopositivity for PCNA in the nucleus of neoplastic hepatocytes (IHC-PCNA x100); D. Photomicrograph of liver showing intense immunopositivity for cytokeratin 18 in cytoplasm of neoplastic hepatocytes (IHC x100).

liver revealed intense immunopositivity for PCNA in the nucleus of neoplastic hepatocytes (Fig. 4C) and also showed intense immunopositivity for cytokeratin 18 in cytoplasm of neoplastic hepatocytes (Fig. 4D).

DISCUSSION

The most typical primary liver tumour in dogs is hepatocellular carcinoma which accounts for 50% of all hepatic tumours³. This study investigates clinical characteristics, USG findings and pathological findings associated with HCC in dog. In the current study, HCC is seen in 13 years old dog indicating age is the risk factor for HCC which was supported by previous studies that reported there will be an increased risk of HCC in dogs greater than 10 years old⁶. USG examination

of liver revealed anechoic spaces and irregular borders with moth eaten appearance. X-ray of thoracic region revealed opacity in lungs which represent nodule. Gross examination of liver showed multiple random nodules of various sizes which are hard in consistency and areas of haemorrhages. On cut section, the nodule exhibits a central area of dry, yellowish-white, cheese-like material indicative of caseous necrosis, with a well-demarcated margin separating it from the surrounding tissue. These findings were corroborated by previous studies². The nodular and diffuse forms tend to metastasize more frequently than the massive form⁷. Gross examination of spleen revealed multiple nodules of various sizes which implicated the spleen as metastatic site as reported by previous literature⁸. Upon gross examination, haemorrhagic nodule and pale appearance of lungs were noticed. These findings were supported by previous studies reporting lungs as the frequent metastatic site of HCC⁸.

Cytological analysis of liver nodules revealed palisading arrangement of hepatocytes, anisocytosis, anisokaryosis, multinuclearity, vacuolated cytoplasm and naked nuclei which are the most prominent cytological hallmarks of canine HCC⁹. Cytology of nodules on spleen revealed multinucleated cells and few hepatocytes which might indicate metastasis. These findings are similar to studies reported by previous studies¹⁰. Histopathology of liver showed pleomorphic, multinucleated cells and mitotic figures along with variably sized vacuoles in cytoplasm suggesting Hepatocellular carcinoma. Vacuolated cytoplasm may be

due to fat as gross examination of liver showed greasy appearance. With Masson's Trichrome staining, fibrosis is noticed with collagen fibers in between the hepatic cords and around the portal triad which indicates periportal cirrhosis suggesting cirrhosis as the pathological finding in canine HCC which was reported in previous literature¹⁰. Histologically, spleen revealed islands of fibrous tissue. With Masson's Trichrome stain, collagen fibers stained blue colour which are observed around the splenic vessels along with depletion of lymphocytes, prominent trabeculae, haemorrhage and thickening of splenic vessels were also noticed. Immunohistochemical analysis of liver showed intense immunopositivity for PCNA and cytokeratin 18 in neoplastic hepatocytes.

CONCLUSION

Based on USG examination, cytological, Histopathological and Immunohistochemical examination, moderately differentiated Hepatocellular carcinoma and metastasis to spleen was confirmed. Periportal cirrhosis was noticed. Histological patterns of Hepatocellular carcinoma should be emphasized more in detail. Diagnosis of tumour is difficult in early stages. To advance our understanding and combat Hepatocellular carcinoma as well as to improve therapeutic outcomes in the future, more thorough and in-depth study on histological patterns of Hepatocellular carcinoma and biomarkers is required.

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