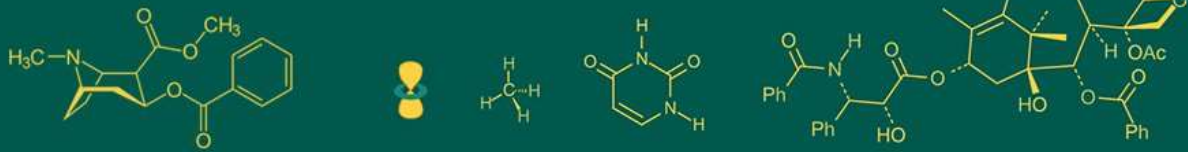


International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
 ISSN Online: 2617-4707
 IJABR 2024; SP-8(7): 80-82
www.biochemjournal.com
 Received: 02-04-2024
 Accepted: 06-05-2024

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Metastatic cholangiocellular carcinoma in turkey: A rare case report

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DOI: <https://doi.org/10.33545/26174693.2024.v8.i7Sb.1445>

Abstract

Hepatic and biliary neoplasms are common among domestic animals in comparison to wildlife. Neoplasms of liver can be primary or secondary in origin. Hepatocellular carcinoma and cholangiocellular carcinoma are some frequently occurring neoplasms of birds and among them cholangiocellular carcinoma is the most commonly reported neoplasm. The incidence and mortality of this cancer are rising in the world. Cholangiocellular carcinoma is characterised by proliferation of bile duct epithelial cells and can extend upto capsular region leading to its serosal dissemination and metastasis to other visceral organs. The present report describes a rare case of cholangiocellular carcinoma in turkey with metastatic foci in lungs and kidneys. Necropsy revealed the enlargement of liver along with presence of yellowish-white coloured multifocal and slightly raised nodules of variable sizes (ranging from 0.5-2.5 cm in diameter). Microscopically, it showed the presence of cuboidal to low columnar epithelial cells arranged in duct and solid island formation along with pleomorphism and 2-3 mitotic figures/high power field. Infiltration of inflammatory cells, mainly heterophils was evident. In conclusion, gross and histopathological alterations are suggestive of cholangiocellular carcinoma and its metastasis to other organs. While it should be differentiated from hepatotoxin-induced bile duct proliferation, immunohistochemistry against cytokeratin can be used for confirmation.

Keywords: Cholangiocellular carcinoma, bile duct, metastasis, nodules, turkey

Introduction

Neoplasms of liver and biliary system are generally common in domestic animals whereas infrequent in wildlife ^[1]. Liver neoplasms in birds can be either primary in origin or can occur from metastasis from other visceral organs ^[2]. Primary liver carcinomas are classified as hepatocellular carcinoma and cholangiocarcinoma ^[3]. Hepatocellular carcinoma (HCC) and cholangiocellular carcinoma (CCC) are frequently occurring neoplasms of birds. CCC is the most frequently reported tumour of liver among captive as well as free-ranging birds ^[2]. CCC originates from the epithelial cells of bile duct causing bile duct obstruction ^[2]. It can extend to the liver capsule leading to extensive serosal dissemination, and also metastasizes to the lymphatic system and lungs ^[1, 4]. Macaws, parrots, conures are some of the most commonly affected birds⁵. However, occurrence of CCC is documented in various captive birds such as flamingo, Amazon parrot, Florida sandhill crane and psittacine *Amazona aestival* ^[1]. The neoplasm can occur either in the form of a single nodule or there could be multiple neoplastic nodules ^[4]. Clinical signs are infrequent, although emaciation and weakness can occur in affected ones. Gross examination can reveal variable sized, white to yellow-coloured nodules and expansion can occur in one or multiple lobes of liver ^[5]. The present study describes the gross and histopathologic characteristics of cholangiocellular carcinoma in turkey.

Materials and Methods

An adult male turkey of approximately 4-5 years age was presented to the Department of Veterinary Pathology, College of Veterinary Sciences of the Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar for necropsy. After detailed post mortem examination of the bird, gross lesions were recorded. Representative tissue samples of liver showing gross changes were collected in 10% neutral buffered formalin. After proper fixation, tissues were processed by paraffin embedding technique and sections were cut into of 4 µm thick sections using semi-automatic rotary microtome (Yorco YSI 060 semi-automatic rotary microtome).

Staining of sections were done with haematoxylin and eosin (H&E) stain as described elsewhere [6].

Results

Gross examination revealed the marked liver enlargement with the presence of multifocal to coalescing, variable sized (ranging from 0.5-2.5 cm in diameter), yellowish-white coloured, raised nodules (Fig. 1). Multifocal small sized nodules were evident in the other visceral organs viz., lung and kidneys. Microscopically, there were marked alteration in the architecture of liver due to fibrosis and extensive infiltration of neoplastic tissue in the form of islands. Pleomorphic population of cuboidal to low columnar epithelial cells with granular cytoplasm infiltrated the area which were arranged in the form of irregular ductules and solid islands (Fig. 2). 2-3 mitotic figures per high power field (hpf) were evident (Fig. 3). Ductules were present with or without lumen which were separated from each other by thin connective tissue septa (Fig. 2 & 3). Inflammatory cells infiltration chiefly heterophils and a few lymphocytes were evident along with bile retention. Apart from the presence of neoplastic cells in the liver, other visceral organs such as kidneys and lungs also revealed the presence of foci of neoplastic cells. Kidneys revealed focal interstitial nephritis characterized by interstitial hemorrhages, degenerative changes and necrosis of epithelium. Metastatic foci of biliary epithelial cells were evident at a few places (fig. 4). Sections of lung also revealed the islands of neoplastic cells at few places along with vascular changes and sever fibrosis (Fig. 5). Spleen revealed capsular thickening, hemorrhages, infiltration of inflammatory cells mainly heterophils and depletion of lymphocytes in the white pulp area.



Fig 1: Photograph of enlarged liver with rounded borders showing presence of multifocal to coalescing, variable sized, yellowish-white, slightly raised nodules (arrow heads)

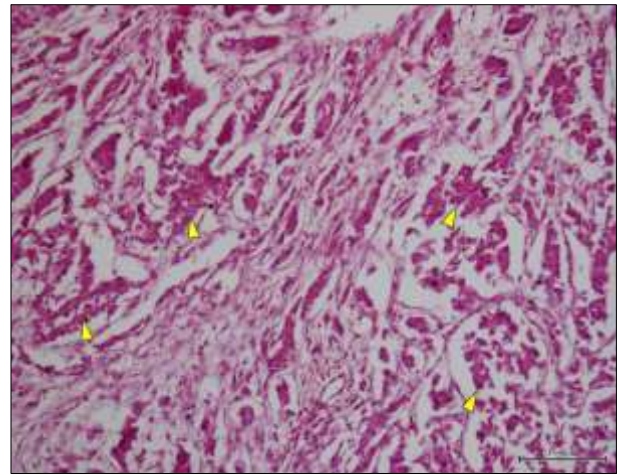


Fig 2: Cholangiocellular carcinoma: section of liver showing islands of neoplastic biliary epithelial cells (arrow heads) with prominent nucleoli and mild pleomorphism, separated by thin connective tissue septa. H&E×200

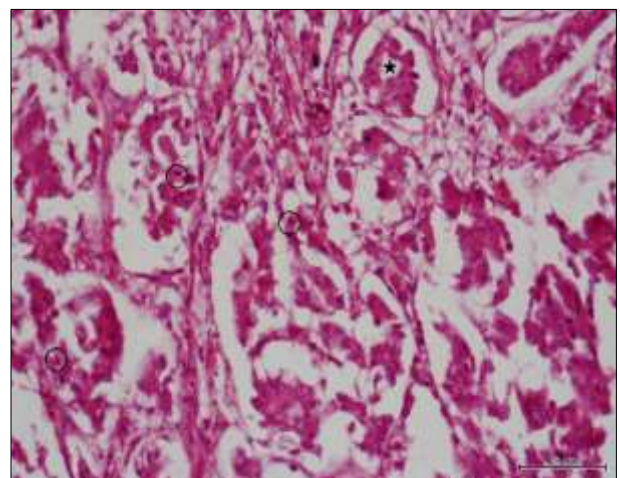


Fig 3: Cholangiocellular carcinoma: section of liver showing neoplastic cells with some arranged in duct pattern (star) along with presence of multiple mitotic figures (encircled). H&E×400

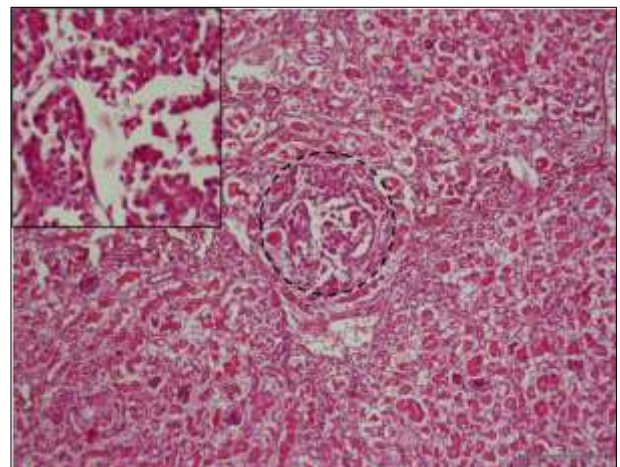


Fig 4: Section of kidney showing a foci of metastasized neoplastic cells (encircled); inset: higher magnification. H&E×100

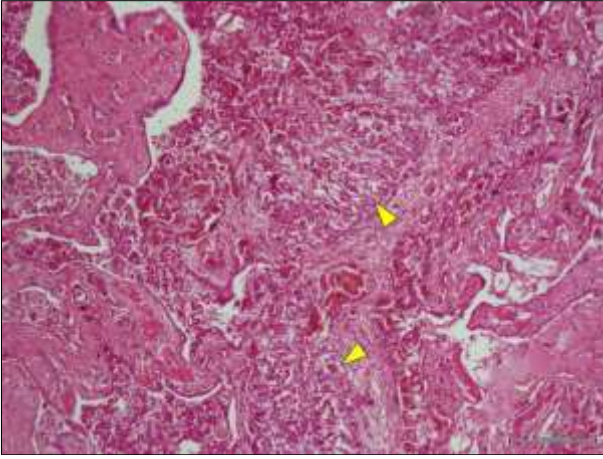


Fig 5: Section of lung showing islands of metastasized neoplastic biliary epithelial cells (arrow heads). H&E×100

Discussion

Neoplasms of liver are marked by abnormal, unchecked and progressive growth of hepatocytes or bile duct epithelium. Among these liver neoplasms, CCC is characterized by the proliferation of bile duct epithelial cells [1]. CCC is a common hepatic neoplasm in various species of birds. Apart from stem cell origin, chronic inflammation and biliary irritation are major risk factors for CCC. Aflatoxicosis, chemical poisoning, parasitic infection, hormonal disturbances or inadequate protein intake are some of the factors responsible for the CCC. Furthermore, development of the tumour can be triggered by hepatotoxins [4]. Grossly, liver surface showed the presence of white to yellow coloured, variable sized nodules, coalescing nodules along. Microscopically, liver parenchyma revealed the biliary epithelium characterised by cuboidal to low columnar epithelial cells arranged in duct formation. Neoplastic cells vary in their shape along with presence of 4-5 mitotic figures/hpf. Similar gross and histopathological features of CCC were reported by Noia [1] in adult male backyard chicken; Nouri *et al.* [7] in budgerigar (*Melopsittacus undulatus*). Ozmen [5], also documented more or less similar types of gross and histopathological changes in Ring-Necked Pheasant (*Phasianus colchicus*). In contrast to our findings, they did not report any mitotic figure in neoplastic cells and no metastasis of neoplastic cells in other visceral organs. Tafti *et al.* [4] also reported multicentric intrahepatic CCC in a 4 years male budgerigar (*Melopsittacus undulatus*) with grey to white coloured nodules in hepatic parenchyma. Microscopically, they observed neoplastic cells resembling biliary epithelium having 1-3 mitotic figures/hpf. Ilhan *et al.* [8] documented similar gross and microscopic changes in a 11 years old female cat. Apart from these, they also reported metastasis of neoplastic cells in other organs *viz.*, mesentery, lymph nodes, peritoneum, and lungs.

Conclusion

In conclusion, gross and histopathological findings are suggestive of cholangiocellular carcinoma. Cholangiocellular carcinomas should be differentiated from bile duct proliferation induced by chronic hepatotoxin which is generally accompanied by fibrosis and alteration in hepatic architecture. Furthermore, confirmatory diagnosis of cholangiocarcinoma in birds and other animals is done by the immunohistochemistry reaction against cytokeratin of the epithelial cells. Biliary duct neoplasms are common in

birds; however, this is a rare case report of cholangiocellular carcinoma in turkey.

Acknowledgement

The authors are grateful to the administration of LUVAS, Hisar and Head, Department of Veterinary Pathology, LUVAS, Hisar, for providing necessary facilities to carry out the investigation.

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