

INTRA-HEPATIC INVASIVE BILE DUCT CARCINOMA IN A SHE-CAMEL (*Camelus dromedarius*)

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ABSTRACT

An intra-hepatic bile duct carcinoma was incidentally detected in the liver of an adult she camel during a routine meat inspection in the local abattoir at Al-Ahsa province, Kingdom of Saudi Arabia. Examination of the carcass revealed a grossly enlarged liver with numerous distorted grayish-white nodules of variable sizes. A large amount of ascitic abdominal fluid was also recovered during dissection and evisceration. The case was tentatively and primarily diagnosed as a terminal stage of chronic granulomatous liver disease. However, the microscopic examination for the hepatic nodulations revealed few complicated hyperplastic as well as excess of neoplastic proliferations of biliary epithelium in the form of ill-developed bile ductules separated with fibrous tissue stroma. Numerous mitotic figures, lymphocytic infiltration and blood pigments were also detected.

Key words: Bile duct, cholangiocarcinoma, granulomatous liver disease, histopathology, liver, she-camel

Cholangiocarcinoma, a malignant tumour arising from bile duct epithelium, is a fairly common type of primary liver cancer in human beings (Goodman, 2007, Wakasa *et al*, 2007). The tumour is apparently rare in domestic animals with a few cases being reported in dogs and cats (Popp, 1990). However, some lesions of chronic cholangiohepatitis with variable degrees of inflammation, biliary hyperplasia, and an oval cell hyperplasia have also been described in ferrets (García *et al*, 2002). These lesions were suggested to be representing a continuum of precancerous stages of hepato-biliary disease with a potential for malignant transformation. Multiple firm nodules with histological evidence of bile ductule carcinoma were incidentally found on exploratory laparotomy and liver biopsy in a cow (Warner *et al*, 1985). A transitional type of combined hepatocellular and cholangiocellular carcinoma was also reported in a male dog (Shiga *et al*, 2001). A joint occurrence of hepato-cellular and cholangiocellular tumours has also been described in a mare (Kato *et al*, 1997). In addition, a typical case of cholangiocarcinoma was recently reported in an 18-year-old male camel (Birincioglu *et al*, 2008).

There are many reported risk factors for the development of cholangiocarcinoma. These factors include long standing inflammation, parasitic infestations (trematodes as liver flukes) and chronic injury of the biliary epithelium (Chapman, 1999;

Parsonnet, 1999). Metaplasia of hepato-cellular carcinoma to intra-hepatic cholangiocarcinoma was suggested to be one of the pathogenic pathways of combined hepatocellular and cholangiocarcinoma (Wakasa *et al*, 2007). In some cases cholangiocarcinoma were reported to be associated with inflammatory disorders as well as malformations of the ducts, but most of these cases were cited to be of unknown etiology (Goodman, 2007). It was known that the incidence of cholangiocarcinoma increases with age and most cases occur in animals above 10 years of age; neither a breed nor sex prevalence has been reported in animals (Popp, 1999). The present communication described one of the invasive intra-hepatic cholangiocarcinoma in a slaughtered adult she camel.

Materials and Methods

The material of this report was collected from a slaughtered she-camel in a local abattoir at Al-Ahsa province, Kingdom of Saudi Arabia. The liver was considerably enlarged with multiple grayish-white nodules. Tissue specimens were collected from the nodules and other affected areas of the liver for histopathological studies in the Department of Pathology, Faculty of Veterinary and Animal Resources, King Faisal University at Saudi Arabia. Specimens were fixed in 10% neutral buffered formalin solution, processed through the paraffin

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embedding technique, then sectioned and routinely stained with haematoxylin and eosin (Culling *et al*, 1985) for the light microscopy.

Results

On dissection and evisceration of the carcass, an excess outflow of a large amount of abdominal fluids was seen. Gross examination of the enlarged liver revealed presence of numerous pale to grayish or white nodular formations of variable sizes. Most of the smaller nodules tended to coalesce to form other larger masses of distorted irregular shape (Figs 1 and 2). The cut section of the nodular masses was extremely firm, and sometimes exhibited fleshy to compact texture with no evidence of exudation, calcification or cyst formation. The remaining parts of the liver parenchyma appeared

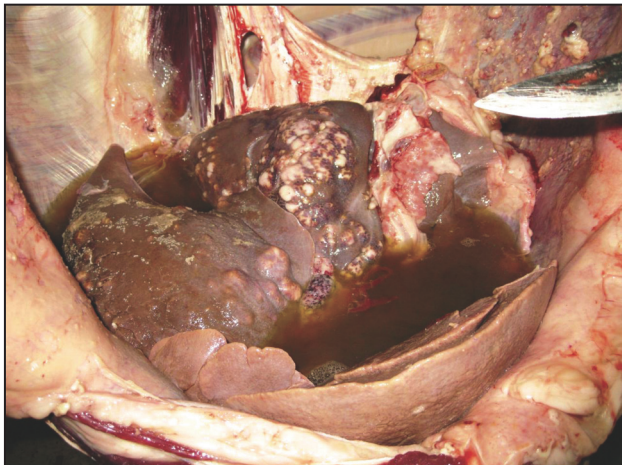


Fig 1. Opened abdomen of slaughtered she-camel. Ascites with variable sized nodular formations in the liver.

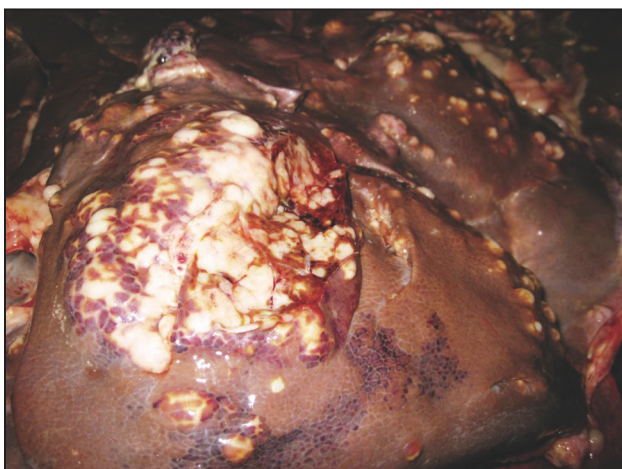


Fig 2. Liver of slaughtered she-camel. Multiple of variable sized nodular growths with large area of coalesced nodules.

with some discolourations of yellow to deep brown. Inspection of the whole carcasses, however, did not reveal significant lesions in all other visceral organs, except of those icteric yellowish discolourations.

The microscopic examination for the nodular new growths revealed scattered clusters of numerous newly formed ill-developed neoplastic ductules with some other few differentiated ductules. The excess of the neoplastic proliferations appeared to be invasive to most of all the hepatic tissue and were mostly associated with an excess of the fibrous tissue stroma. The hepatic cells at the affected areas appeared several degenerative changes mainly fatty changes. The differentiated ductules acquired the papillary form of the complicated hyperplasia (Fig 3). On an

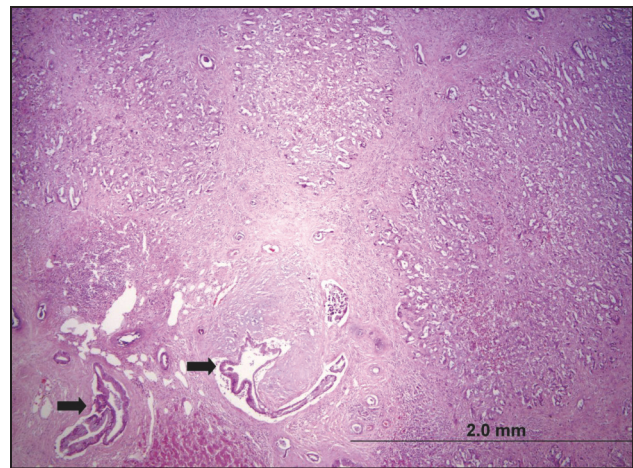


Fig 3. Cholangiocarcinoma in the liver of slaughtered she-camel. Clusters of small ill-developed neoplastic ductules and others differentiated ductules took the papillary form (arrows) separated with an excess of fibrous stroma. H&E, Bar = 2.0 mm.

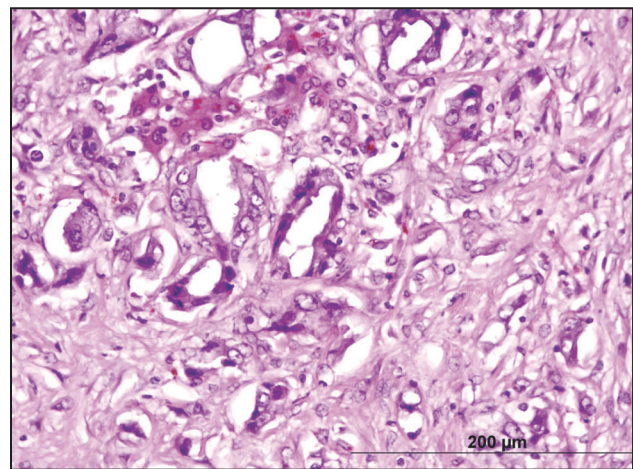


Fig 4. Cholangiocarcinoma in the liver of slaughtered she-camel. Several groups of incomplete neoplastic ductules formed of different pleomorphic cells with no basement membrane. H&E, Bar = 200 µm.

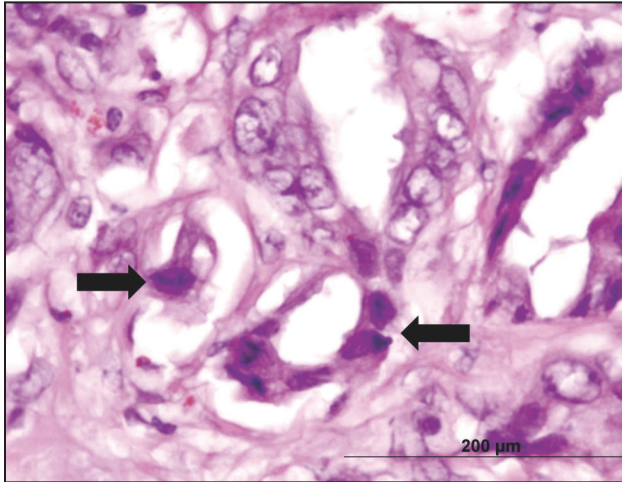


Fig 5. Neoplastic cells with excess of mitotic figures (arrows). H&E, Bar = 50.0 μm

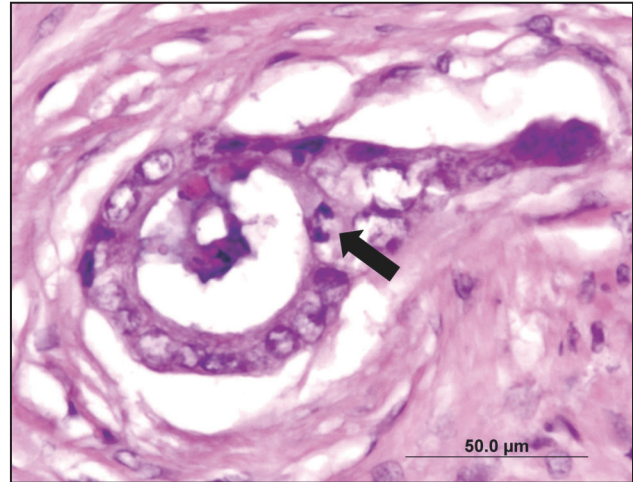


Fig 7. Neoplastic ductule appeared with pleomorphic neoplastic cells of vesicular nuclei as well as prominent mitotic figures (arrow). H&E, Bar = 50.0 μm .

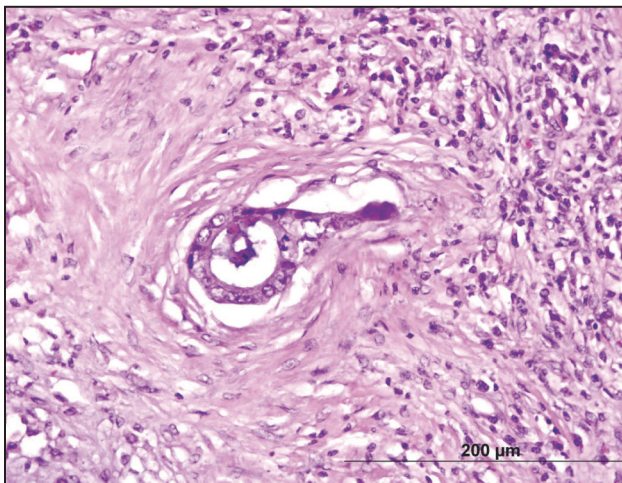


Fig 6. Cholangiocarcinoma in the liver of slaughtered she-camel. Neoplastic ductule embedded within the fibrous stroma and moderate numbers of lymphocytic infiltration. H&E, Bar = 200 μm .

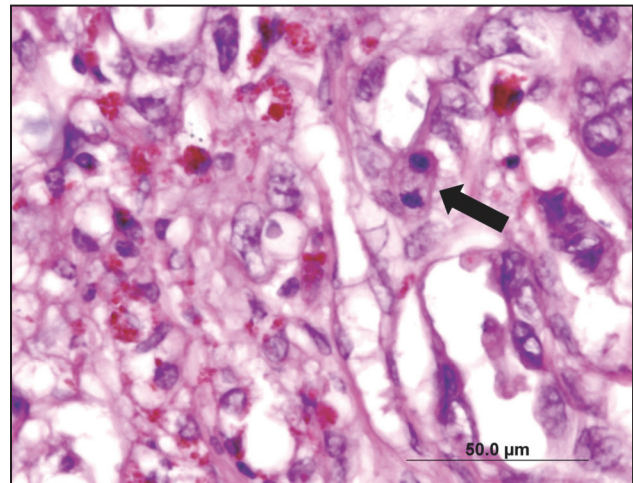


Fig 8. Cholangiocarcinoma in the liver of slaughtered she-camel. Excess of ill-developed neoplastic ductules appeared with clear mitotic figures (arrow) and golden brown blood pigments. H&E, Bar = 50.0 μm .

other hand, the incomplete or ill-developed neoplastic ductules appeared to be composed of pleomorphic cells with vesicular nuclei and did not seem to have a basement membrane (Fig 4). Some criteria of mitotic divisions could also be seen in some areas (Fig 5). The neoplastic ductules were associated with some inflammatory reactions in form of lymphocytic infiltrations, excessive fibrous stroma, and numerous mitotic figures (Figs 6 and 7). In some other areas the invasive neoplastic growths for the hepatic tissue was closely associated with extravasated erythrocytes and deposited blood pigments (Fig 8).

Discussion

Almost all primary liver carcinoma are broadly classified either as hepato-cellular carcinoma derived

from the hepatocytes, or cholangiocarcinoma arising from the intra-hepatic bile duct epithelium. The tumours arising from intra-hepatic bile ducts and gall bladder have been described in some animal species. In cattle, epithelial tumours of the intra-hepatic biliary duct and gall bladder have been reported as incidental findings in retrospective studies carried out in slaughter houses (Straffuss *et al*, 1973; Cullen and MacLachlan, 2001).

Cholangiocarcinoma is considered as one of the rare reported cases of primary carcinoma in the liver of camel. It was incidentally seen in one slaughtered she-camel in a local abattoir at Al-Ahsa province, Kingdom of Saudi Arabia. The detected findings of the ascites, as well as the icterus pigmentations can be attributed to the excess of hepatocytic degeneration

and necrosis and the damage in the biliary system that finally led to hepatic failure. On microscopic examination, the currently studied carcinoma was clearly composed of an excess of ill-developed small ductules of glandular structures with an excess of fibrous tissue stroma in addition to some other few hyperplastic differentiated ductules. The neoplastic cells which formed the ill developed ductules appeared with anisocytosis and pleomorphism. Their nuclei appeared round to oval and contained dense to vesicular chromatin. Features of the mitotic divisions were also seen in some areas.

The above mentioned and described features, for the present case of cholangiocarcinoma in the she-camel appeared nearly similar to those described features in the reported cases in male camel (Birincioglu *et al*, 2008), dogs and cats (Popp, 1990; Shiga *et al*, 2001; Garcya *et al*, 2002,) as well as in cows (Warner *et al*, 1985). Many varieties of cholangiocarcinomas, especially, in humans were diagnosed histo-pathologically (Goodman, 2007; Wakasa *et al*, 2007). These were papillary, tubular, mucinous, signet ring cell, adenosquamous, squamous, anaplastic, undifferentiated, miscellaneous, and unclassified forms. The present findings of dense sparsely and interstitial fibrous tissue stroma with rare prominent lymphocytic infiltration seems to be characteristic for the cholangiocarcinoma (Kim *et al*, 1999 and Tse-Ching *et al*, 2001) which is most rarely encountered primary carcinoma in the liver of the camel, especially in female.

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