

COLLISION TUMOUR: A CASE REPORT OF MIXED HEPATOCELLULAR AND CHOLANGIOCARCINOMA

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ABSTRACT

Introduction: Combined hepatocellular-cholangiocarcinoma (cHCC-CC), also known as mixed HCC-CC, is a rare form of primary liver cancer, showing histopathological features of both hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC). Combined hepatocellular-cholangiocarcinoma (cHCC-CC) is a rare variant of primary hepatic cancer, with the reported incidence of this tumor varying between 0.4 and 4.7%. The purpose of this case report is to document this rare case in the literature so as to increase the awareness of this entity in our locality and beyond.

The Case: We present a case of a 40 year old black male patient who presented with a seven month history of malaise, three month history of epigastric pain, jaundice, and weight loss. He had history of significant alcohol intake and cigarette smoking. Liver function test was deranged. Serology showed positivity of hepatitis B surface and core antigens. Also hepatitis C antigen and antibody were positive. Ultrasound revealed an enlarged liver with at least two well defined irregular hypo echoic masses. Histology reported a mixed hepatocellular and cholangiocarcinoma. He was managed conservatively and died after about a month on admission in hospital.

Conclusion: Mixed hepatocellular and cholangiocarcinoma is a rare tumour with bad prognosis. A multidisciplinary approach and prompt treatment is required in the management of patients with this malignancy.

Key words: Hepatocellular carcinoma, Cholangiocarcinoma, Collision, Mixed tumour.

Introduction

A hybrid, mixed or collision tumour is a clinical condition where two or more histologically distinct tumour types occur at the same time in a particular anatomical location. It could also be defined as occurrence of two or more distinct synchronous primary tumors, benign or malignant, appearing in the same anatomic region. ⁽¹⁾ Combined hepatocellular-cholangiocarcinoma (cHCC-CC), also known as mixed HCC-CC, is a rare form of primary liver cancer, showing histopathological features of both hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC). ⁽²⁾ Combined hepatocellular-cholangiocarcinoma (cHCC-CC) is a rare variant of primary hepatic cancer, with the

reported incidence of this tumor varying between 0.4 and 4.7%. ^{1,2,3,4} However, as histopathological confirmation is not necessary to diagnose HCCs. ⁽³⁾ WHO now recognizes cHCC-CC as a distinct subtype of hepatic malignancy, the diagnosis, prognosis and treatment of the neoplasm remains ill defined. ⁽⁴⁾ The purpose of this case report is to document this rare case in the literature so as to increase the awareness of this entity.

The Case

We present a case of a 40 year old Negroid male patient who presented with a seven month history of general body weakness, three month history of epigastric pain, yellowish discoloration of eyes and,

progressive weight loss. Patient has a history of significant alcohol intake: about six bottles per day for fifteen years. Patient also smokes cigarettes: one pack daily for fifteen years. On physical examination, patient was jaundiced, with type IV finger clubbing and skin hyperpigmentation was observed; an enlarged liver, about eight centimetres below the costal margin with some tenderness observed.

Investigations done showed bilirubin positivity on urinalysis, deranged liver function test with elevated levels of total and conjugated bilirubin (314.1 umol/L and 260umol/L respectively); Alkaline phosphate at 462 IU/L. Routine haematological profile was unremarkable. Serology showed positivity of hepatitis B surface and core antigens. Also hepatitis C antigen and antibody were positive. Retroviral screening was negative. Ultrasound examination revealed an enlarged liver harbouring at least two well defined irregular hypo echoic masses in the left lobe, the largest measures 2.8 x 2.3 cm; dilated intrahepatic duct were also noted.

Medical management included IV fluids, antibiotics, lactulose, lanolin, cholestyramine and diuretics. The working diagnosis was primary liver cell carcinoma secondary to hepatitis B and C infection

Intra-op findings revealed a shrunken gall bladder, a cirrhotic liver with umbilicated peripheral nodules; normal looking pancreas with no masses. Liver nodule was biopsied. On gross examination of the biopsied liver tissue was a wedged shaped yellow to greenish dark brown tissue with a rough to irregular surface.

Sections were taken for histological examination, where the diagnosis of Combined Hepatocellular carcinoma and cholangiocarcinoma was made. Patient was managed conservatively and later developed convulsion, lapsed into unconsciousness, and died after about a month on admission in hospital.

Pathomorphology

Macroscopically, specimen consisted of a wedged shape partially encapsulated greyish-white tissue measuring 1.5cm by 1.0cm by 0.5cm. Cut surface was solid, and greyish-white with tinge of green. It was wholly processed as four blocks.

Microscopic sections show polygonal cells disposed in trabecular and pseudoglandular pattern, exhibiting

pleomorphism, high nucleocytoplasmic ratio, and prominent nucleolus, with foci of bile pigments. These cells are interwoven, invested, and abutting, multiple foci of variously sized/shaped acini lined by atypical cells with intracellular mucin. Figure 1 and 2.

Figure 1

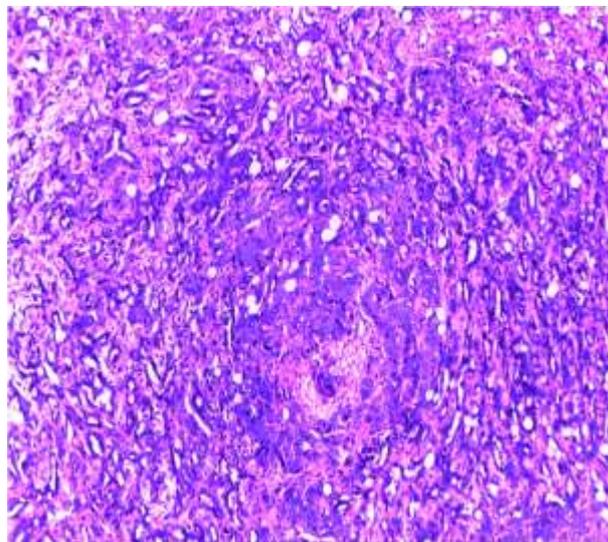
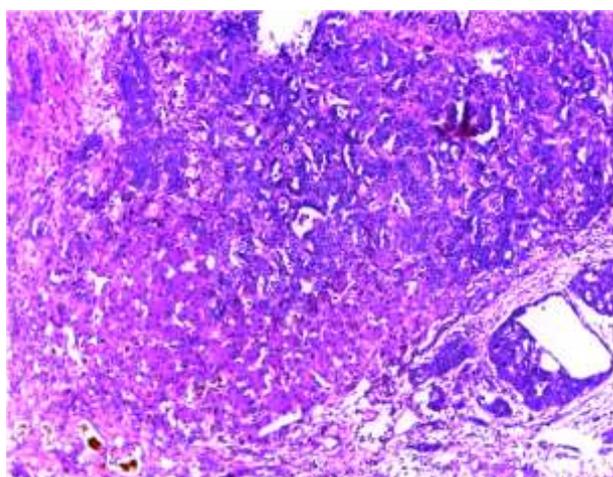


Figure 2



Discussion

Combined Hepatocellular carcinoma and cholangiocarcinoma is a rare form of primary liver cancer presenting as "mixed tumors", with histopathological evidence of hepatocellular and biliary epithelial differentiation closely mixed within the same tumor.^(5,6) This neoplasm was first described in 1949, and not much is understood with regard to its histopathogenesis, biological behaviour, clinical features, and prognosis, in comparison to Hepatocellular carcinoma or Cholangiocarcinoma⁽⁷⁾.

Classically Allen and Lisa separated combined hepatocellular carcinoma and cholangiocarcinoma into three subtypes: (A) separate tumors, each with single histopathology, (B) contiguous tumors with separate histopathologies, and (C) mixed histopathologies in individual tumors⁽⁸⁾. This case falls into Allen and Lisa class C, as the two entities are microscopically entangled. Goodman et al also classified this neoplasm into three groups: Type I “collision tumors,” which had both components but no areas of transition, Type II “transitional tumors” with areas of intermediate differentiation and identifiable transition between 2 components, and Type III “fibrolamellar tumors,” which had features of both the fibrolamellar variant of hepatocellular and cholangiocellular differentiation throughout without separate areas of one or the other⁽⁹⁾. Goodman's type I tumor corresponds to Allen and Lisa's type A and type B. Type III tumor, however, is not comparable to Allen and Lisa's type C but represents a special variant of fibrolamellar HCC.

The clinical and laboratory findings in this patient (average age, male/female ratio, hepatitis viral positivity, serum AFP level, and the presence of cirrhosis) is similar for hepatocellular and cholangiocarcinomas as separate entities. Looking at some of the similarity in the clinicopathology of these two diseases, some investigators have ventured that the cholangiocarcinoma components in the combined tumors were those transformed from part of the hepatocellular carcinoma tumors.⁽¹⁰⁾

Other reports highlight the similarity in the clinical backgrounds of the combined tumor patients seems to indicate that this combined tumor represents a variant of ordinary hepatocellular carcinoma that exhibits cholangiocellular metaplasia, rather than a true intermediate disease entity between hepatocellular carcinoma and cholangiocarcinoma^(9,10).

Imai et al showed the same p53 gene mutational pattern in both hepatocellular and cholangiocarcinoma components and the same Rb-1 locus replication error pattern in both components in some patients with combined tumor, thus providing genetic evidence that both components had the same origin.⁽¹¹⁾ This, coupled with genetic studies on allelic status of chromosome arm in both components of combined hepatocellular-cholangiocarcinoma have provided evidence to suggest that a proportion of these tumors are derived from a single clone because, both components within the same tumor share identical allelic losses.^(4,11)

Although chemotherapy is a treatment option for CHCC-CC, Surgery has been shown to be much of value.¹² But even with treatment, the survival outcome of patients is bad.¹² As the index patient was not clinically stable for treatment, this adds up to the background poor prognosis of the disease, culminating in patient's dead.

Conclusion

Mixed hepatocellular and cholangiocarcinoma is a rare tumour with bad prognosis. A multidisciplinary approach and prompt treatment is required in the management of patients with this malignancy.

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