Fibrolamellar hepatocellular carcinoma: A Case Report

Introduction

Fibrolamellar hepatocellular carcinoma (FLHC) occurs in non-cirrhotic livers, most frequently in adolescents or young adults with no gender predominance, with a more favorable prognosis than the usual hepatocellular carcinoma (HCC). It is a relatively rare condition accounting for less than 1% of primary liver cancers. Therefore, studies especially on the clinical course and epidemiology of FLHC are either individual case reports or small case series, mostly from western countries. Studies from eastern Asian countries are restricted to some case reports. Reviewing the literature, we could not find any similar report of FLHC from our region.

Herein, we report an Iranian young patient with definite diagnosis of FLHC.

Case Report

An 18-year-old boy with history of right upper quadrant abdominal pain 2.5 years ago, which had been relieved spontaneously in 2 days and then relapsed 3 months later, was presented with a probable diagnosis of renal problems. Lab studies, which included serum aminotransferases, alkaline phosphatase, bilirubin (total and direct), BUN and creatinine were all in the normal range. Ultrasonography reported a huge ill-defined mixed echogenicity, heterogeneous structure in the posterior aspect of the right lobe of liver extending from sub-diaphragmatic region to the upper pole of the right kidney measuring about 135 x 124 mm. The lesion seemed to be hepatic in origin. The rest of liver parenchyma was normal in echogenicity pattern. Intra- and extrahepatic biliary ducts and the portal vein were normal in diameter. The gallbladder showed normal wall thickness without stone, sludge or space-occupying lesions. Kidneys, ureters, and the bladder were normal in ultrasonography.

He was treated with the diagnosis of hepatic abscess, and the pain was tempo
rarily relieved. One month later, the pain relapsed and he was admitted in our hospital. He had nocturnal sweating, weight loss of about 10 kg within last 4 months. He mentioned no pruritus, frequency, urgency, melena, hematochesia or hematemesis. He had no history of discoloration of feces, or changes in urine color. Vital signs were stable except for an oral temperature of 39.5 °C. In physical examination, the conjunctiva was not pale, sclera was not icteric, and lymphadenopathy was detectable in axillary and inguinal regions. Lungs were clear; there was no abnormal heart sounds on auscultation. The abdomen was soft with no tenderness, rebound tenderness or guarding—no palpable mass was detected. Extremities were normal.

On CT scan, there was a 10cm diameter mass that showed heterogeneous enhancement in the arterial and portal phases. Incomplete obliteration of the IVC was also visible (Figure 1A). Both kidneys were of mildly prominent size—measuring about 123 × 47 mm (right) and 122 × 56 mm (left) — with normal parenchymal echogenicity and cortical thickness. There was no evidence of stone or hydronephrosis. Spleen was 132 mm in diagonal diameter (mildly prominent) with homogenous parenchyma.

Ultrasoundography-guided liver biopsy was performed. Biopsy reported large pleomorphic polygonal neoplastic cells with eosinophilic cytoplasm and hyperchromic nuclei with mild to moderate mitotic activity that has been separated with lamellar hyalized connective tissue. It was compatible with fibrolamellar hepatocellular carcinoma (Figure 2).

Due to the large tumor size and non-sufficient normal liver tissue, the patient was considered inoperable.

Intraarterial chemotherapy was done for the patient when the diagnosis was confirmed, then tumor embolization was performed for 5 times at different phases. For this purpose, after preparing the patient using the sterile setting, femoral puncture with super selective catheterization of the proper hepatic artery was done. Under fine fluoroscopy, controlled infusion of lipiodole suspension was done (10cc lipiodole + 50mg adriablastine). Post-embolization angiography showed complete cessation of blood flow through the proper hepatic artery and its branches (Figures 3A and 3B). After first embolization, control CT scan showed droplets of lipiodole in the tumor and previous enhancement did not appear coincided the significant reduction of blood flow through the tumor.
bulk (successful embolization criteria) (Figure 1B).

The last CT scan which was taken 3 months ago and after the last episode of embolization, revealed a considerable tumor size reduction.

At the time of this report, after 26 months of the diagnosis, the patient had none of the previous symptoms and his weight loss was reversed. Now, he was a candidate for surgical operation.

Discussion

Fibrolamellar hepatocellular carcinoma (FLHC) arises in non-cirrhotic livers of young individuals and has been considered to be less aggressive than hepatocellular carcinoma. It is believed to be a histological variant of hepatocellular carcinoma (HCC). Radiological evidence of cirrhosis, vascular invasion, or multi-focal disease—findings typical of hepatocellular carcinoma—is uncommon in fibrolamellar carcinoma—uncommon in fibrolamellar carcinoma.6

It is a relatively rare condition, accounting for less than 1% of primary liver cancers which is more common in western countries in comparison with Asian and African populations.2,3 The only reported population-based study of the epidemiology and prognosis of patients with fibrolamellar carcinoma (FLHC) is from USA.4

As our case, fibrolamellar carcinoma characteristically manifests as large hepatic mass in adolescents or young adults.6

The etiology of FLHC is unclear. It differs from hepatocellular carcinoma in demographics, condition of the affected liver, tumor markers, and prognosis. FLHC strongly resembles focal nodular hyperplasia (FNH), which is a benign liver lesion. Thus, FLHC may originate from FNH, because both occur in the liver with normal parenchyma. In addition, some reports describe areas of FNH adjacent to FLHC tumors; however, this finding likely represents a secondary reaction to local ischemic perfusion caused by the FLHC mass.2 FLHC is associated with cirrhosis in less than 10% of patients and typically arises in a background of normal liver function and normal histological architecture.2

The epidemiological features of FLHC in comparison with HCC are summarized in Table 1.

Our patient manifested with mild abdominal pain with no history of hepatic diseases or prominent physical finding. Patients usually have no symptoms, but if they have, it is abdominal pain and fullness. Symptoms may have existed since 10 days to 40 months.7

Patients usually have no sign, but if the tumor is large, a mass will be palpable in physical examination. Because FLHC will appear in a liver with no previous disorder, characteristics of cirrhosis will not be found in physical examination.2,5

Other less common manifestations are summarized in the Table 2.

In this case, liver enzymes and bilirubin were nor-
A Case of Fibrolamellar Hepatocellular Carcinoma

Table 1. Epidemiological features of fibrolamellar hepatocellular carcinoma versus hepatocellular carcinoma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HCC</th>
<th>FLHC</th>
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<tbody>
<tr>
<td>Associated with</td>
<td>Active inflammation, hepatitis B and C,</td>
<td>Unclear;</td>
</tr>
<tr>
<td></td>
<td>alcohol related cirrhosis and aflatoxin</td>
<td>Association with cirrhosis is less than 10%</td>
</tr>
<tr>
<td>Prevalence</td>
<td>The most common liver malignancy</td>
<td>Relatively rare</td>
</tr>
<tr>
<td>Frequency</td>
<td>Most common in Asia and Africa where</td>
<td>Most common in United States and Europe</td>
</tr>
<tr>
<td>prevalence of HCV</td>
<td>HBV is high</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male &gt; female</td>
<td>Male = female</td>
</tr>
<tr>
<td>Age</td>
<td>Fifth and sixth decades</td>
<td>Young adults (20-40 years) with no prior liver disease</td>
</tr>
</tbody>
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Table 2. Less common features of fibrolamellar hepatocellular carcinoma

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
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<tbody>
<tr>
<td>Weight loss</td>
<td>Migratory thrombophlebitis</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Hemobilia</td>
</tr>
<tr>
<td>Malaise</td>
<td>Obstructive jaundice</td>
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<tr>
<td>Fever</td>
<td>Gynecomastia</td>
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<tr>
<td>Chills</td>
<td></td>
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<tr>
<td>Abdominal distension</td>
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<td>Amenorrhea</td>
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most important factor), presence of a tumor capsule, and a lack of vascular invasion. In inoperable cases of fibrolamellar carcinoma, the patient may benefit from adjuvant chemotherapy (either systemic or intraarterial).

In this case the mass was not resectable, so intraarterial chemotherapy was performed.

A study revealed that age, gender and tumor size did not correlate with survival. Another study demonstrated that FLHC patients diagnosed before 23 years of age have worse prognosis than those diagnosed after age 23. Other factors associated with worse prognosis in this study are: lack of surgical treatment, presence of positive surgical margins, vascular invasion, and altered hepatic enzymes. Overall 5-year survival rate differs from 25 to 63% for both resectable and non-resectable tumors. Better survival rate exists for FLHC compared to typical HCC; this is largely due to the increased resectability rate and the lack of associated cirrhosis. Median patient survival is 50 months for patients with resectable FLHC versus 7 months for patients with non-cirrhotic resectable HCC.

At present, about 2.5 years have passed from the first presentation, and the patient is a candidate for surgery.

Fibrolamellar hepatocellular carcinoma should be kept in mind in young patients with hypervascular liver masses and no history of hepatic diseases.

References