Primary hepatic choriocarcinoma in a 49-year-old man: Report of a case

Ryosuke Sekine, Masanobu Hyodo, Masayuki Kojima, Yoshiyuki Meguro, Akifumi Suzuki, Taku Yokoyama, Alan T Lefor, Norio Hirota

We report a case of hepatic choriocarcinoma in a man diagnosed at autopsy after a rapid downhill clinical course. The patient was a 49-year-old man who presented with acute right-sided abdominal pain. There were no masses palpable on physical examination. Radiographic findings showed large multi-nodular tumors mainly in the right lobe of the liver. Fludeoxyglucose-positron emission tomography scan showed uptake only in the liver, and no uptake in the testes. We initially planned to perform a liver resection for the presumed diagnosis of intra-hepatic cholangiocarcinoma. However, the tumors grew rapidly and ruptured. Multiple lung metastases rapidly developed resulting in respiratory failure, preventing liver resection or even biopsy. He died 60 d after initial presentation with no pathological diagnosis. Postmortem studies included histopathological and immunohistological examinations which diagnosed a primary choriocarcinoma of the liver. Primary hepatic choriocarcinoma is very rare but should be considered in the differential diagnosis of a liver tumor in a middle aged man. Establishing this diagnosis may enable treatment of the choriocarcinoma. Liver biopsy and evaluation of serum human chorionic gonadotropin are recommended in these patients.

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Key words: Hepatic choriocarcinoma; Male; Human chorionic gonadotropin; Liver biopsy; Fludeoxyglucose-positron emission tomography

Core tip: Evaluation of serum human chorionic gonadotropin levels in addition to other liver tumor markers should be performed in middle-aged men with undiagnosed hepatic tumors, to rule-out the possibility of primary hepatic choriocarcinoma. Liver biopsy is important to diagnose this rare and highly malignant tumor.

INTRODUCTION

Choriocarcinoma is a rare, aggressive, malignant germ-cell neoplasm of trophoblastic cells, which are among the first cells to differentiate from the fertilized egg to enable...
implantation. Choriocarcinoma is prone to rapid hemato-
genous metastases, and the first clinical manifestation
is often metastatic lesions\[6\]. The characteristic laboratory
finding in patients with choriocarcinoma is an elevated
serum human chorionic gonadotropin (hCG) level. Cho-
riocarcinoma is less common in men than women, and
comprises only 1% of all germ-cell tumors, most often
with the primary lesion in the testes\[3\]. There are only
seven patients previously reported in the English litera-
ture with primary choriocarcinoma of the liver\[3,5,8\]. These
patients have been reported from Asia, including Japan
and China. We report here a 49-year-old Japanese male
with primary choriocarcinoma of the liver diagnosed at
autopsy, who presented initially with acute abdominal
symptoms and a rapid downhill clinical course. Establish-
ing the diagnosis early may enable treatment of choio-
carcinoma. Consideration of this lesion in a patient with
an undiagnosed liver mass is essential, necessitating eval-
uation of serum hCG level and urgent liver biopsy.

CASE REPORT

A 49-year-old male presented to the emergency room
with acute right-sided abdominal pain and fever. He had
a previous history of diabetes mellitus and hepatitis C.
Physical examination was positive for abdominal tenderness.
Contrast-enhanced computed tomography (CT) and magnetic
resonance imaging (MRI) scans revealed a multi-nodular
hepatic tumor more than 10 cm in diameter in the right
lobe (Figure 1A). Laboratory data showed white blood count
(WBC) and liver function tests within normal limits but an
elevated C-reactive protein to 8.75 mg/L. Serum carcinoembrionic antigen (CEA)
was elevated to 18.5 ng/mL but α-fetoprotein (AFP)
and CA19-9 were within normal limits. We suspected a
metastatic liver tumor or intra-hepatic cholangiocarci-
oma. Endoscopy found no primary lesion in the gastro-
testinal tract and fludeoxyglucose-positron emission
tomography (FDG-PET) scan showed abnormal uptake
only in the liver (Figure 1B). We planned to perform liver
resection with a presumptive diagnosis of intra-hepatic
cholangiocarcinoma but avoided performing a liver bi-
opsy due to the risk of dissemination. Before he could
undergo liver resection, the tumors grew rapidly and rupt-
ured (Figure 2A). Multiple lung metastases rapidly de-
veloped, accompanied by severe respiratory failure (Figure
2B). Due to pulmonary, biopsy or resection of the liver
were not possible and the patient died 60 d after initial
presentation.

At autopsy, the liver weighed 4080 g with numerous
hemorrhagic satellite nodules in the right lobe. There
were multiple hemorrhagic lung nodules up to 3 cm in
diameter, and microscopic metastases were identified in
other viscera, including a para-aortic lymph node, the
right adrenal gland, peritoneum, right renal capsule, and
spleen. There was no malignant change or scar in the tes-
tes. Histological findings of the hepatic tumors showed
choriocarcinoma with a biphasic pattern of mononuclear
cytotrophoblasts and giant multi-nucleated syncytiotro-
phoblast cells (Figure 3A).

Immunohistochemistry was positive for an antibody
to hCG subunits α (Figure 3B) and β (Figure 3C). Control
tissue slices of placental chorionic villi stained with the
same antibody showed staining limited to the syncy-
tiotrophoblast layer. The syncytiotrophoblast cells in the
liver were strongly positive for hCG, as were those in the
other organs involved. Serum hCG was evaluated post-
mortem, significantly elevated at 53000 IU/mL.

DISCUSSION

Choriocarcinoma is an uncommon, aggressive tropho-
blastic malignant neoplasm that is prone to early hema-
託genous metastases. It typically presents as a primary
tumor of the uterus or genital tract in gestational females.
In males the primary lesion is usually in the testes, but
represents only 1% of all testicular tumors\[5\]. Extra-
genital choriocarcinomas are less common, and often
exist with other carcinomas, tending to occur in mid-line
organs\[8\]. Pure extra-genital non-midline choriocarci-

mas are the least common type. Only seven previous
male patients with choriocarcinoma of the liver have
been reported in the English language literature (Table
1\[3,5\]). Hepatic choriocarcinoma has been recognized as
a primary malignant tumor of the liver since 1992 when
first reported by Fernández Alonso et al\[3\]. The other pa-
tients were reported from Asia (China and Japan), with
a majority from China\[5,5\].

The patient in this report presented with acute ab-
dominal symptoms and a multi-nodular tumor in the
right lobe of the liver. Based on radiographic appearance,
an elevated serum CEA and the absence of a lesion in the
gastrointestinal tract, the leading diagnosis was intra-
hepatic cholangiocarcinoma. FDG-PET scan showed no
other lesions, including the testes. Based on these find-
ings, a liver resection was planned in this patient. FDG-
PET scan has been reported previously in the diagnosis of
choriocarcinoma\[6,7\]. Furthermore, FDG-PET scan is
also useful to evaluate the efficacy of treatment of liver
lesions such as surgery or chemotherapy\[8\].

In the differential diagnosis of malignant liver tu-
mors in a patient presenting with an acute abdomen,
sarcomatous changes from hepatocellular carcinoma or
cholangiocarcinoma must be considered. Both of these
tumors can have a rapid clinical course and generally have
poor outcomes. Sarcomatous change in primary liver
tumors has been reported from Asian countries as well
as choriocarcinoma\[9-12\]. Sarcomatous changes are seen
in about 2%-4% of patients with resected hepatocellular
carcinoma. Patients with sarcomatous changes have a
worse prognosis than that in patients with typical hepatic
lesions. More than half of the patients with sarcomatous
cancers died within a year of resection\[9\].

The characteristic laboratory finding in choriocar-
cinoma is an elevated hCG level in the blood or urine.
This patient had an elevated serum hCG level in a post-
mortem blood sample. In male patients, there are few reasons to evaluate serum hCG levels except in patients with testicular tumors\textsuperscript{[11-13]}. When we evaluate a middle aged patient with an aggressive liver tumor, we recommend checking serum hCG as tumor marker in addition to AFP, CEA and CA19-9.

The strategy for choriocarcinoma of the liver is not established because of its rarity and highly malignant behavior. We believe that urgent liver resection before manifestation of distant metastases and chemotherapy may be the best course for prolongation of survival. In a patient with gastric choriocarcinoma and multiple liver metastases, Waseda \textit{et al}\textsuperscript{[14]} reported pathological complete response using etoposide and cisplatinum, with a two year disease-free survival after surgical resection. Methotrexate and actinomycin D may also be important agents in the treatment of choriocarcinoma. The use of cyclophosphamide, etoposide and vincristine have also been reported. Cisplatinum and 5-FU were used in other reports. Shi \textit{et al}\textsuperscript{[5]} reported five patients with hepatic choriocarcinoma. Two of the five patients underwent liver resection with adjuvant chemotherapy, and three of the five patients
Table 1  Previous reports of men with primary hepatic choriocarcinoma

| Ref.          | Year | Age, yr | Time to death |
|---------------|------|---------|---------------|
| Fernández Alonso et al[1] | 1992 | 62      | 1 yr          |
| Arai et al[2]  | 2001 | 65      | 45 d          |
| Shi et al[3]  | 2010 | 39      | 6 mo          |
| Shi et al[3]  | 2010 | 45      | 2 mo          |
| Shi et al[3]  | 2010 | 48      | 3 mo          |
| Shi et al[3]  | 2010 | 36      | 5 mo          |
| Shi et al[3]  | 2010 | 40      | 8 mo          |
| Present case  | 2011 | 49      | 2 mo          |

Pathological diagnosis
Liver biopsy with immunohistochemistry is recommended.

Treatment
Urgent surgical resection and chemotherapy is recommended.

Term explanation
Hepatic choriocarcinoma in a middle-aged male is the least common.

Experiences and lessons
In a middle-aged male with an aggressive liver tumor, evaluation of serum hCG levels and liver biopsy should be performed.

Peer review
The study reported a case of a patient suffering primary hepatic choriocarcinoma, which is a kind of very rare, especially in men, and malignant trophoblastic cancer. The description of this case is very interesting for the detection and differentiation of this type of aggressive tumor among other primary liver cancers and the conclusions are enlightening for the clinical management of these patients.

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COMMENTS
Case characteristics
Acute abdominal pain and fever in a 49-year-old man.

Clinical diagnosis
Primary hepatic choriocarcinoma.

Differential diagnosis
Hepatic choriocarcinoma.

Laboratory diagnosis
Elevated hCG in blood or urine is definitive.

Imaging diagnosis
Multi-nodular liver tumor with uptake by FDG-PET.

with distant metastases were treated with chemotherapy after needle biopsy. The two patients who underwent resection survived only six and eight months respectively, despite having received adjuvant chemotherapy. Of the three other patients reported, two were diagnosed with undifferentiated carcinoma and one with metastatic choriocarcinoma by needle biopsy. These patients underwent chemotherapy including 5-FU and platinum, but all died within five months.

Liver biopsy was not performed in the present patient because the diagnosis of intra-hepatic cholangiocarcinoma was suspected, and biopsy could result in an increased risk of tumor dissemination. His condition rapidly deteriorated due to respiratory failure, which precluded the safe conduct of any invasive procedures. The diagnostic accuracy of needle or aspiration biopsy is not adequate, and may lead to an incorrect diagnosis of poorly differentiated carcinoma because of the similarity to cytrophoblasts. The accuracy of liver biopsy is still controversial in establishing the diagnosis of choriocarcinoma. However, in order to enable rapid treatment of such an aggressive tumor, liver biopsy should be performed without hesitation.

In a middle-aged male with an aggressive liver tumor, evaluation of serum hCG levels in addition to other liver tumor markers should be performed. Liver biopsy is important, especially in Chinese and Japanese patients, to detect this rare and highly malignant tumor.
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