Case Report

Alpha Fetoprotein producing Gastric Hepatoid Adenocarcinoma
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Abstract
Gastric carcinoma generally presents as adenocarcinoma and rarely shows a hepatoid pattern, it may or not produce alpha-fetoprotein. The interpretation of the lesion may be difficult in a patient with a hepatic mass and raised alpha-fetoprotein level. A 51 year old man with hepatoid adenocarcinoma in stomach, producing alpha-fetoprotein is presented.

Introduction
Hepatoid adenocarcinoma (HAC) is a rare type of adenocarcinoma which looks like hepatocellular carcinoma (HCC) histopathologically, but develops in extrahepatic tissues. The stomach is the most common site of HAC. HAC also develops less frequently in lungs, pancreas, oesophagus, papilla vateri, colon, urinary bladder, ovary, uterus and the renal pelvis. Patients with HAC are older than those with primary HCC and the prognosis is usually poor. It spreads to the liver via haematogenous and/or lymphogenous vessels. Serum alpha-fetoprotein (AFP) level is usually increased but it may be normal in some cases. We report a case of gastric HAC metastasizing to liver with an extremely high level of serum AFP.

Case Report
A fifty-one year old man was admitted to the hospital with fatigue, pain in right upper quadrant of abdomen, decreased appetite and nausea without vomiting. These complaints were present for the last two months. He did not take alcohol but smoked one pack of cigarettes daily for 30 years. He had no history of surgery or blood transfusion or hepatitis before admission and there was no history of cancer in his family. On physical examination, Eastern Cooperative Oncology Group (ECOG) performance status was 2 and liver was palpable 5cm below the costal margin at the right mid-clavicular line. The examination of testes was normal. Liver enzymes were elevated as AST 277 IU/L, ALT 96 IU/L, GGT 177 IU/L, ALK 344 IU/L and LDH 1625 IU/L. Multiple nodular metastatic lesions were noted on sonographic examination of liver, but there was no evidence of chronic parenchymal liver disease. Tumor markers as Ca 19.9, Ca 72.4, carcinoembryonic antigen were normal, AFP was found to be 60500 ng/ml.

Computed tomography of abdomen also showed multiple, nodular metastatic lesions in the parenchyma of liver, perigastric lymphadenopathy of one cm in diameter, and thickness in the wall of stomach. A Vegetan, fragile mass 3 cm in diameter was noted in the fundus of the stomach on endoscopic examination. Multiple biopsies were taken from the lesion. The pathologic examination of endoscopic gastric biopsy revealed poorly differentiated adenocarcinoma of stomach. Tumor cells were large polygonal shaped with pleomorphic centrally placed nuclei, prominent nucleoli and relatively abundant eosinophilic or vacuolated cytoplasm. Because of high serum alpha-fetoprotein and normal Ca-19.9, Ca-72.4, and Carcinogenic Embryonic Antigen (CEA), fine needle aspiration from liver was performed with the suspicion of synchronous hepatocellular carcinoma. Air dried smears were stained with May-Grunwald-Giemsa stain. Cell block sections
prepared from fine needle aspiration biopsy of liver tumor displayed characteristically hepatoid features. Neoplastic cells of hepatoid tumor had hyperchromatic and centrally placed nuclei, prominent nucleoli, and abundant granular or clear cytoplasm resembling those of a gastric tumor. Immunohistochemical stain was performed on both gastric biopsy specimens and cell block of liver tumor by avidine-biotine-peroxidase technique using the antibodies to AFP, hepatocyte paraffin antibody 1 (Hep Par 1), polyclonal CEA, monoclonal CEA, TAG. 72, MOC-31, CD10, CD34, cytokeratin 7 (CK 7), cytokeratin 18 (CK 18), cytokeratin 19 (CK19), cytokeratin 20 (CK20). Similar results were obtained for both tumor. Tumor cells displayed strongly AFP (Figure 1a, 1b) and CK7, CK18, and CK19 positivity. Focal membranous and cytoplasmic immunstainings for monoclonal and polyclonal CEA, MOC-31 and CD10 were also observed in the tumor. No immunoreactivity was found for the other antibodies.

Hepatitis B surface antigen, anti body to hepatitis C (A-HCV) by ELISA were negative. HBV-DNA and HCV-RNA by PCR were also negative.

Chemotherapy with 5-flourouracil and cisplatin was started as palliative treatment. The patient did not return after the first cycle of chemotherapy. He expired four months later at home.

**Discussion**

HAC mimics hepatocellular carcinoma but occurs in extrahepatic tissues. AFP is frequently produced by hepato-cellular and germ cell tumors. In addition, gastrointestinal tract cancer, especially gastric tumors may produce AFP. Approximately six percent of all gastric cancers produce AFP. On the other hand, majority of gastric hepatoid adenocarcinomas produce AFP, but some of them do not. Ishikura et al described the first case of hepatoid adenocarcinoma in 1985. AFP producing gastric cancer is usually diagnosed in advanced stage, but early gastric cancer can also produce AFP. AFP level was moderately elevated in our case compared to reports of other authors. To exclude the possibility of concomitant malignancy which produces AFP as hepatocellular carcinoma or germ cell tumors, biopsies from two different lesions in the liver were done. Sonographic examination of testes was normal. Hep-Par-1 which is highly specific and sensitive marker for hepatoid adenocarcinoma to distinguish it from hepatocellular carcinoma was found negative in our case.

The prognosis of HAC producing AFP is usually poor, but the role of AFP is not clear in the pathogenesis of disease. Adachi et al reported AFP producing gastric cancers had a poorer outcome. The expression of vascular endothelial growth factor (VEGF) may occur in AFP-producing gastric cancers. But its contribution to the poor prognosis of AFP-producing gastric cancers is not clear. Nagai et al reported that AFP producing hepatoid adenocarcinoma form did not have a worse prognosis than AFP producing gastric adenocarcinoma. AFP levels may become normal after curative operation and so AFP can be helpful in the disease follow-up.

In patients with a gastric tumor and unexpected high level of serum AFP, the probability of AFP producing gastric adenocarcinoma or hepatoid adenocarcinoma which has a worse prognosis, must be kept in mind in the differential diagnosis.

**References**


