Case Reports

Alpha-fetoprotein producing Gastric carcinoma : A rare entity

Alpha-fetoprotein (AFP) is a glycoprotein that is normally produced during gestation by the fetal liver and the yolk sac.[1] Elevation of serum AFP is considered pathological in adults. In clinical practice, the estimation of AFP in serum is used to screen high risk patients of chronic liver diseases for hepatocellular carcinoma. However, AFP levels may be elevated in patients of primary gastric carcinoma[2] as well as other malignancies.[3-9] (**Table 1**) AFP producing gastric cancer (AFPGC) constitutes only about 2.7% to 8% of all gastric cancers.[10] They have high metastatic potential and possibility of vascular invasion, liver and lymph nodal metastases resulting in poor prognosis.[2] In situations where associated liver mass is seen, it may be mistaken for coexistent hepatocellular carcinoma, like the index case.

We thus report this rare case of AFPGC, an entity which the treating physicians need to be familiar with.

Case Report

A 47 year-old male presented to the liver clinic of our hospital with dull aching pain in the upper abdomen for one and a half months. He had history of anorexia and weight loss. There was no history suggestive of chronic liver disease such as abdominal distension, jaundice or encephalopathy. There was no history of blood transfusion or prior surgery. On physical examination, he was anicteric and had no lymphadenopathy or pedal edema. Liver was palpable, which was hard in consistency with irregular margin. Routine blood investigations revealed hemoglobin of 9.1 g/dL, total leucocyte count of 11,100 per cu mm and a platelet count of 181,000 per cu mm. The liver and renal function tests were within normal limits. Serum AFP was markedly elevated (58,618 ng/ml). Multiphasic MRI abdomen revealed diffuse gastric wall thickening involving the body and the antral region with multiple lesions in the right lobe of liver that were heterogenously enhancing. Conglomerate of enlarged lymph nodes were present in the lesser and greater omentum, subpyloric region and the splenic hilum with omental and peritoneal metastases. (**Figure 1,2**) Based on the elevated serum AFP level and MR imaging, a possibility of hepatocellular carcinoma was kept. Further, upper gastrointestinal endoscopy confirmed the findings

Table 1: Non-hepatic tumors producing AFP

Site and type of Tumors	Authors, Year	Serum AFP level (ng/ml)
Renal Cell carcinoma	[3] Saito S et al, 1989	418
Carcinoma gall bladder	[4] Ng WK et al, 1995	256
Adenocarcinoma Lung	[5] Yoshino I et al, 1996	696
Pancreatic carcinoma	[6] Mueller SB et al, 2005	3000
Collecting duct carcinoma	[7] Blandamura S et al, 2005	102
Wilms tumor	[8] Crocoli A et al, 2008 (3 cases)	9800 5515 126.8
Transitional cell carcinoma bladder	[9] Lu CH et al, 2009	1428

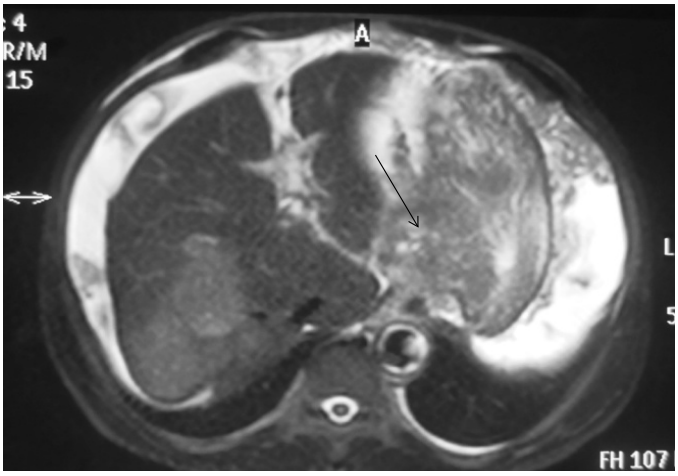

Figure 1: Axial T2W MR image showing a heterogeneous mass in the gastrohepatic region (arrow) and a large hyperintense mass lesion in the right lobe of liver (arrow head) with gross ascites (black arrow).

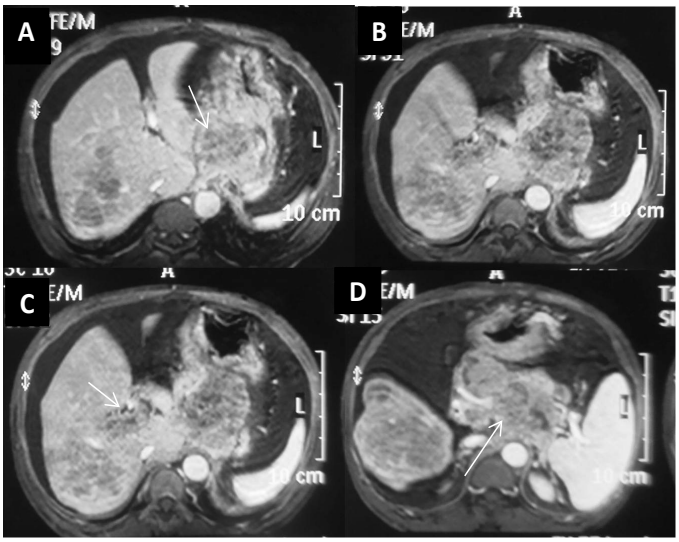

Figure 2: **(A-D) Axial post gadolinium MR images showing large heterogeneously enhancing mass lesion arising from lesser curvature of stomach (A) extending into gastrohepatic region (arrow), with large mass lesion in right lobe of liver (B) with contiguous extension of tumor thrombus in to main portal vein (C) (arrow), with involvement of the celiac axis by the stomach mass (D) (arrow).**

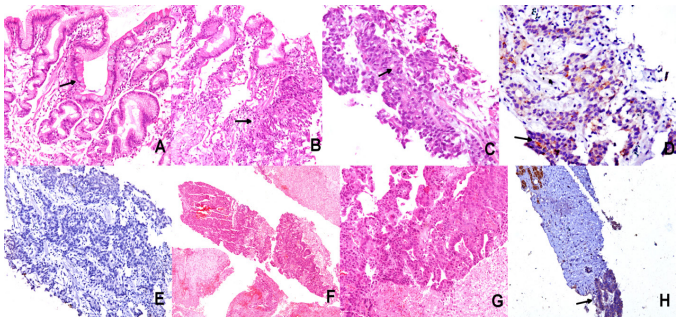

Figure 3: **(A-H) Photomicrograph shows gastric biopsy with focal intestinal metaplasia (arrow) [Fig A, H&E x100]. Focally an infiltrating moderately differentiated adenocarcinoma (arrows) was noted [Fig B, H&E x 40]. Higher power photomicrograph shows the focal acinar arrangement within the tumor [Fig C, H&E x100]. Immunohistochemical stains for alphafeto protein was positive focally in the tumor cells (arrows) [Fig D, AFP x100] and Arginase-1 was negative [Fig E, Arginase-1 x40]. Liver biopsy shows features of a metastatic adenocarcinoma with foci of necrosis [Fig F, H&E x100], showing acinar arrangement pattern [Fig G, H&E x100]. Hep Par-1 stain while was positive in the benign hepatocytes, the tumor cells (arrow were negative [Fig H, Hep Par 1 x40].**

of MRI and a pyloric antral biopsy was done. This showed moderately differentiated adenocarcinoma, with predominant diffuse sheets of tumor cells resembling fetal hepatocytes and focal acinar arrangements. Subsequently, an ultrasound guided biopsy of the liver mass was performed which revealed features of adenocarcinoma. Immunohistochemical stains performed in the gastric biopsy showed focal positivity for alpha-fetoprotein and CdX2 and the cells were negative for Arginase-1. Liver biopsy showed features of a metastatic adenocarcinoma with acinar arrangement, along with foci of necrosis. The hepatic tumor was negative for HepPar-1 and CK.[7] (**Figure 3**) Diagnosis of AFP producing gastric carcinoma with disseminated metastases was made. The patient was very sick and once the diagnosis and prognosis was revealed, he opted for palliation alone.

Discussion

AFPGC generally occurs in the sixth to seventh decade and pyloric antrum is the most frequent site. AFPGC has multiple phenotypes including gastric hepatoid, intestinal and signet ring type.[11] Liver metastasis (14.3%-75.6%) is one of the main features of hepatoid variant. Gastric hepatoid adenocarcinoma (GHA) has a striking morphologic similarity to hepatocellular carcinoma (HCC).[11] The tumor cells in the hepatoid foci resemble the morphology of HCC, and the immunohistochemistry can be positive for AFP, PIVKA-II, alpha-1 antitrypsin, alpha-1 antichymotrypsin and albumin. AFP production in AFPGC is thought to be due to hepatoid differentiation of tumour cells.[11] SALL4 (Sal-like protein 4) is an oncofetal protein similar to AFP and represents fetal gut differentiation in gastric carcinoma. SALL4 is a sensitive marker for AFP-producing gastric carcinoma and is especially useful to distinguish hepatoid gastric carcinoma from hepatocellular carcinoma.[12] Various reports have shown that AFP producing carcinoma of the stomach has a more aggressive behavior than the common

gastric cancers in the form of higher incidence of vascular invasion, lymph node and liver metastasis.[13]

Data regarding optimum therapy of AFPGC is sparse. The treatment is similar to that of common gastric adenocarcinoma. Surgical management of an early primary tumor, if feasible, is the indicated approach. Adjuvant chemotherapy and radiotherapy should be given according to current gastric cancer indications, despite the fact that no specific data on adjuvant treatment of AFPGC is available.

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