

Alpha-fetoprotein and carcinoembryonic antigen in a case of liver metastasis from gastric cancer

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A considerable number of reports have been made indicating that AFP was found even in the serum of patients with cancer other than hepatoma¹⁾. To our knowledge, these cases were mostly gastric cancer with liver metastasis²⁾. Furthermore, cases of AFP positive gastric cancer without liver metastasis were also reported^{3,4)}. On the other hand, CEA originally described by P. Gold⁵⁾ was found not only in colonic carcinoma but also in cancers of other parts of the digestive tract and in cancer of the breast, cancer of the lung and cancer of the urogenital tract⁶⁻⁹⁾. A fact that these cancer cells, whether originated entodermally or ectodermally, possess the same embryonic protein may suggest the multipotency of cancer cells. In the present paper, a report was made on a case of recurrent gastric carcinoma with liver metastasis, which contained both AFP and CEA significantly in the serum. Recently, Bierfeld reported a case of gastric carcinoma metastatic to the liver having both AFP and CEA¹⁰⁾.

The patient was a 34-year-old female. She was admitted to the Center for Adult Diseases, Osaka in March 1968, with a chief complaint of epigastralgia. An upper G-I series showed an irregular lesion of the prepyloric region. The endoscopic examination revealed a Borrmann's type II tumor of the prepyloric area. Endoscopic biopsy specimens showed papillotubular adenocarcinoma.

In a resected stomach, tumor was found in the prepyloric region and was about 2.5 cm × 2.0 cm in diameter. Operation findings showed neither hepatic nor peritoneal metastasis. Only subpyloric lymph nodes were found to be metastatic.

The postoperative course was uneventful. Her second admission was in Feb. 1971 with an enlarged abdominal mass, probably of liver metastasis. This metastatic liver tumor was progressively enlarged. The patient expired on the 29th May 1971. Postmortem examination revealed no recurrent or no metastatic lesion in the peritoneal cavity and the operated

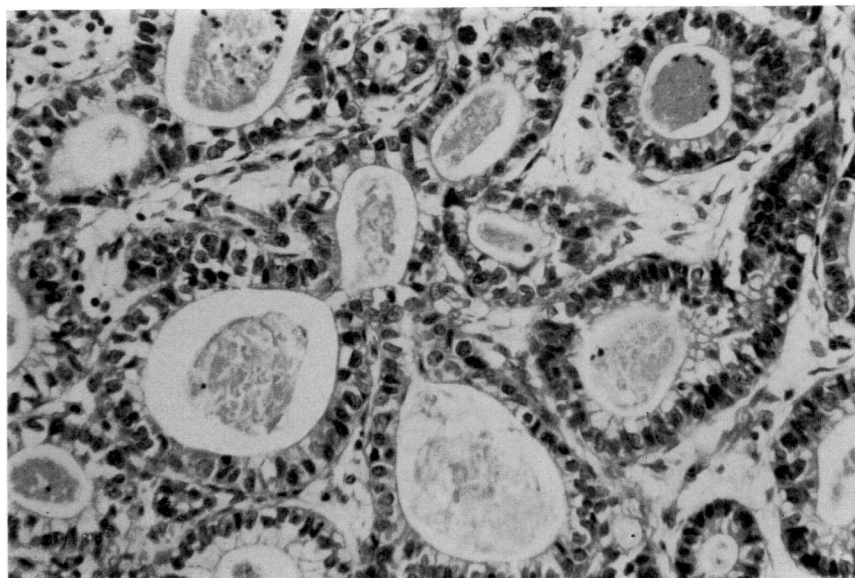
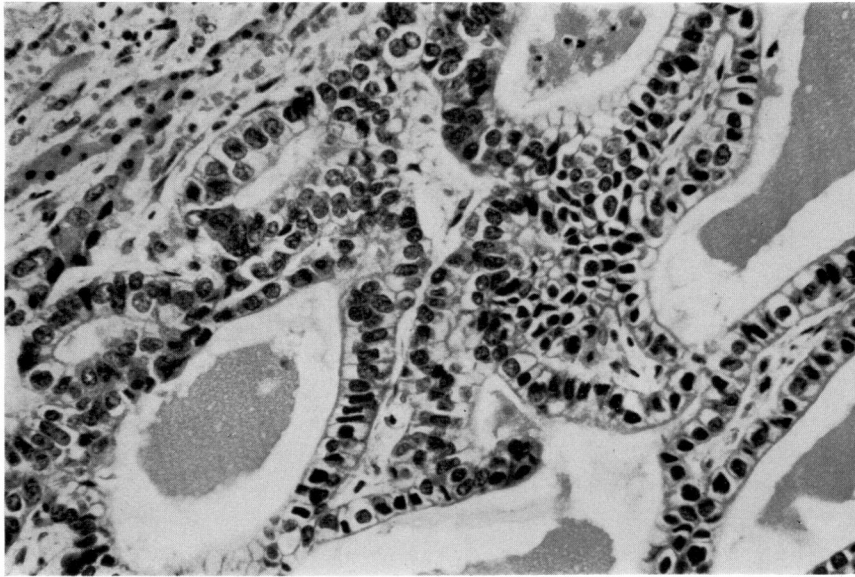


Fig. 1. Sections of gastric carcinoma (the left) and of metastatic liver tumor (the right). $\times 200$. Stained by hematoxylin and eosin.

stomach except for huge and multiple liver metastases. The liver was around 8 kg in weight, and almost all of the bilateral lobes were occupied by tumorous nodules, non-cancerous tissue was seen only in a very little part of the left lobe, but no cirrhotic change was found.

The photograph shows microscopic sections of the tumor of the resected stomach and the autopsy specimen of the liver metastasis (Fig. 1).

Serum AFP was positive in April 1971. AFP in concentrated urine and ascites was also positive. For the determination of AFP in cancerous parts and non-cancerous parts of the liver, the Ouchterlony method and a single radial immunodiffusion by Mancini were used. Positive precipitin line against anti-AFP was observed with 2.5% tissue homogenate from both cancerous and non-cancerous parts of the liver tissues. AFP in the serum was determined to be 6.1 mg/100 ml and 31.0 mg/100 g in the cancerous part and 25.0 mg/100 g in the non-cancerous part of liver on SRID. The concentration of AFP in the tumor was 5 times as much as in the serum (Table 1).

Table 1. *AFP and CEA in the serum and the liver of patient H.S.*

	Serum	Liver	
		Cancerous parts	Non-cancerous parts
AFP (SRID-Mancini) BPCJ	6.1 mg/dl	31.0 mg/100g (wet weight)	25.0 mg/100 g (wet weight)
CEA (dry weight)	1.6 mg/dl	0.8 mg/100 g (wet weight)	

Extraction and purification of CEA was performed by the method of Krupey¹¹⁾. Liver tissue and serum were extracted using 0.6 M PCA solution and then applied to Sephadex G-200 chromatography, followed by agar gel zone electrophoresis. Each fraction was tested against rabbit anti-CEA antiserum to determine whether it contained CEA or not. Finally, CEA was separated by using polyacrylamide gel disc electrophoresis. Thus extracted and purified CEA was lyophilized and weighed. CEA from the serum was 1.6 mg/100 ml and from the tissue was 0.8 mg/100 g tumor (Table 1).

The CEA extracted from this patient's serum formed a precipitin line identical with CEA extracted from the liver tumor of this patient against goat anti-CEA antiserum which was prepared in our laboratory using extracted CEA from this patient's serum as an antigen.

A comparison of anti-CEA antiserum prepared in our laboratory with antiserum supplied by Dr. P. Gold, indicated a complete line of identity against CEA. CEA was not detected from the non-cancerous parts of the liver using our anti-CEA antiserum by the Ouchterlony method.

The extracted CEA was analysed by disc electrophoresis using 7.5% polyacrylamide gel. A faint broad band was observed near the origin. The patient's serum was also analysed by immunoelectrophoresis using anti-AFP and anti-CEA. Two precipitin lines were observed; one against anti-AFP and the other against anti-CEA (Fig. 2).

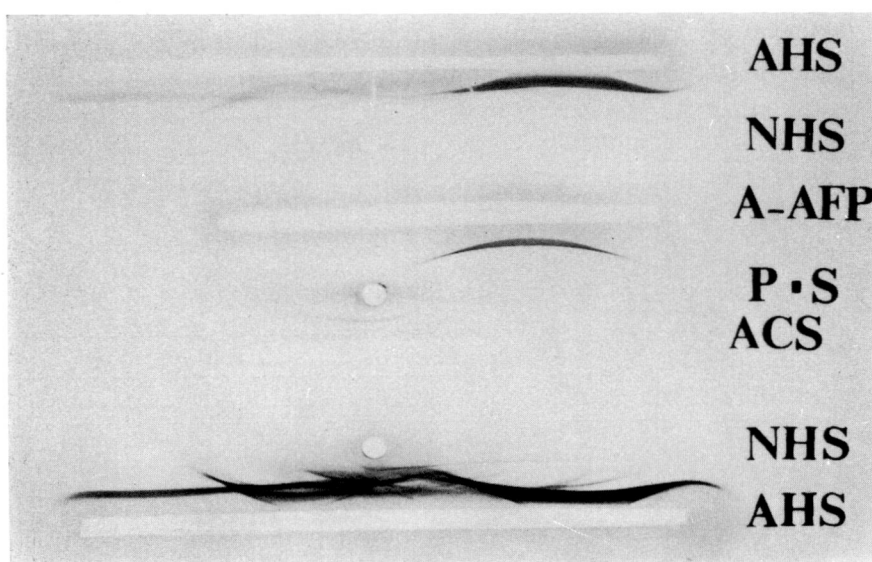


Fig. 2. Precipitin pattern of immunoelectrophoresis in agar gel (0.05 M veronal-acetate buffer at pH 8.6). The anode is to the right.
 AHS; Rabbit anti-human serum
 A-AFP; Horse anti-alpha-fetoprotein
 ACS; Goat anti-CEA antiserum
 P-S; Patient serum
 NHS; Normal human serum

The tissue extracts of a portion of the tumor and of the non-cancerous parts of the liver contained AFP amounting to 31.0 mg/100 g and 25.0 mg/100 g respectively. This result suggests the possibility that AFP can be produced by non-cancerous liver tissue in response to the metastatic gastric carcinoma as well as the cancerous portion of the liver.

On the other hand, CEA was found only in the extract of the cancerous portion of the liver.

REFERENCES

1. AKAI, S. and KATO, K.: Alpha-fetoprotein (AFP) and metastatic liver tumor. *Igaku-no Ayumi*, **80**, 819 (1972) (in Japanese).
2. TSUCHIYA, M., *et al.*: Positive alpha-fetoprotein in a case of gastric carcinoma with metastasis to the liver. *Jap. J. Gastroenterol.*, **70**, 475 (1973) (in Japanese).
3. KITAOKA, H., *et al.*: Alpha-fetoprotein content in tissues from gastric cancer patients. *Proc. Jap. Cancer Ass., the 32nd Annual Meeting*, 314 (1973) (in Japanese).
4. KURIYAMA, H. and OKAMURA, J.: Alpha-fetoprotein in patients of gastric carcinoma. *Proc. Jap. Cancer Ass., the 32nd Annual Meeting*, 316 (1973).
5. GOLD, P. and FREEDMAN, S. O.: Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. *J. Exp. Med.*, **121**, 439 (1965).
6. HOLYOKE, D., *et al.*: Carcinoembryonic antigen (CEA) in patients with carcinoma of the digestive tract. *Ann. Surg.*, **176**, 559 (1972).
7. DENK, H., *et al.*: Carcinoembryonic antigen (CEA) in gastrointestinal and extragastrointestinal tumors and its relationship to tumor-cell differentiation. *Int. J. Cancer*, **10**, 262 (1972).
8. REYNOSO, G., *et al.*: Carcinoembryonic antigen in patients with tumors of the urogenital tract. *Cancer*, **30**, 1 (1972).
9. PUSZTASZERI, G. and MACH, J. P.: Carcinoembryonic antigen (CEA) in non digestive cancerous and normal tissues. *Immunochemistry*, **10**, 197 (1973).
10. BIERFELD, J. L., *et al.*: Alpha-fetoprotein and carcinoembryonic antigen in a case of gastric carcinoma metastatic to the liver. *Am. J. Dig. Dis.*, **18**, 517 (1973).
11. KRUYEY, J., *et al.*: Purification and characterization of carcinoembryonic antigens of the human digestive system. *Nature*, **215**, 67 (1967).