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Resection of Liver Metastasis from Alpha-Fetoprotein-Producing Early Gastric Cancer: Report of a Case

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Abstract: We herein present a case of resected synchronous solitary liver metastasis from alpha-fetoprotein (AFP)-producing early gastric cancer. A 61-year-old woman, who was diagnosed at a routine medical checkup as having early gastric cancer with a liver tumor, came to our hospital for surgery. Her serum AFP level was high at 910 ng/ml. An examination was performed to determine whether the liver tumor was primary hepatocellular carcinoma or metastasis from early gastric cancer. She had no evidence of either a hepatitis B or C virus infection, and her liver function was normal. A biopsy specimen from the gastric cancer predominantly revealed moderately differentiated adenocarcinoma, but a focally trabecular pattern compatible with AFP-producing gastric cancer was also observed. Preoperatively, it was concluded that the liver tumor was metastasis from an AFP-producing early gastric cancer. We thus performed distal gastrectomy and a posterior segmentectomy of the liver. Her serum AFP level decreased to the normal range within 2 weeks after the operation. An immunohistological examination revealed that AFP-positive cells were present in both the gastric cancer and liver tumor. One year after the operation, there was no sign of recurrence.

Key Words: AFP-producing gastric cancer, liver metastasis

Introduction

Alpha-fetoprotein (AFP) is a useful marker for hepatocellular carcinoma and yolk sac tumors. Furthermore, the serum AFP level is also sometimes elevated in other diseases. Gastric cancer is one such disease. Although case reports of AFP-producing gastric cancer have been increasing, to our knowledge, only a total of 23 such cases of early gastric cancer have so far been reported. Among those cases, liver metastasis was frequently observed even in the early stage. But the rate of curative resection of the liver metastasis in those cases was low. We herein report a case of successful resection of a metastatized liver tumor from an AFP-producing early gastric cancer.

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Case Report

A 61-year-old woman with epigastralgia visited another hospital. Ultrasonography (US) revealed a liver tumor and early gastric cancer was discovered by gastroendoscopy. She was admitted to our hospital for surgery. Her serum alpha-fetoprotein (AFP) level was elevated to 910 ng/ml, but her serum carcinoembryonic antigen (CEA) level was within the normal range. The possibilities to be considered included synchronous double cancers in the stomach and the liver, or liver metastasis from early gastric cancer. US revealed a hypoechoic lesion in the posterior segment of the liver. Dynamic computed tomography (CT) showed a tumor enhanced by contrast medium (Fig. 1). These findings were compatible with hepatocellular carcinoma, but there were no findings of either hypervascularity or tumor stain by hepatic angiography. Serum hepatitis B and C viral markers were both negative. Biopsy specimens taken from the stomach predominantly revealed moderately differentiated adenocarcinoma, but a focally trabecular pattern, consistent with AFP-producing gastric cancer, was seen. Based on these findings, AFP-producing early gastric cancer with solitary liver metastasis was diagnosed preoperatively and thus a distal gastrectomy and posterior segmentectomy of the liver were performed. The serum AFP level decreased remarkably to 19 ng/ml by the 14th postoperative day. The patient was discharged on the 34th postoperative day. For more than 1 year after the operation, there has been no sign of recurrence, and her serum AFP level has also remained within the normal range.

Fig. 1. Dynamic computed tomography. The tumor was enhanced by contrast medium in the rapid phase

Fig. 2. Gross appearance of the primary tumor in the stomach, showing a small depressed lesion with marginal elevation in the antral lesion

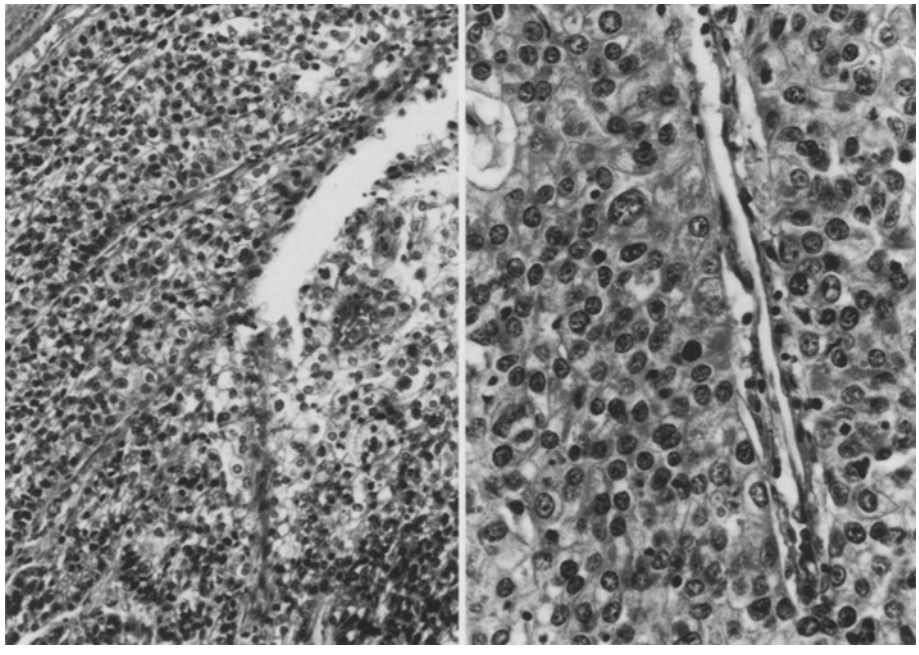

Fig. 3. **a** Histological photomicrograph of the primary lesion showing polygonal cells with abundant eosinophilic cytoplasm, arranged in a trabecular pattern, infiltrating into the submucosal layer (HE ×200). **b** Photomicrograph of the metastatic tumor showing large polygonal cells with abundant eosinophilic cytoplasm, in the same histologic pattern as the primary lesion (HE ×400)

Pathological Findings

Macroscopically, the gastric tumor was located in the antrum, and was observed to consist of a small depressed lesion with a marginal elevation, measuring 2.1 × 1.8 cm in diameter (Fig. 2). Microscopically, the tumor was composed of polygonal cells with abundant eosinophilic cytoplasm, arranged in a trabecular pattern characteristic of hepatocellular carcinoma (Fig. 3a). The depth of tumor invasion was limited to the submucosal layer, but a remarkable degree of venous involvement was observed. The resected liver measured 9 × 8 × 7 cm and weighed 300 g. The cut surface of the liver showed a solitary, well-defined tumor (Fig. 4). Microscopically, the liver tumor showed the same histology as the gastric cancer (Fig. 3b). An immunohistological study indicated that AFP-positive cells were present in both the primary lesion and the metastatized liver tumor.

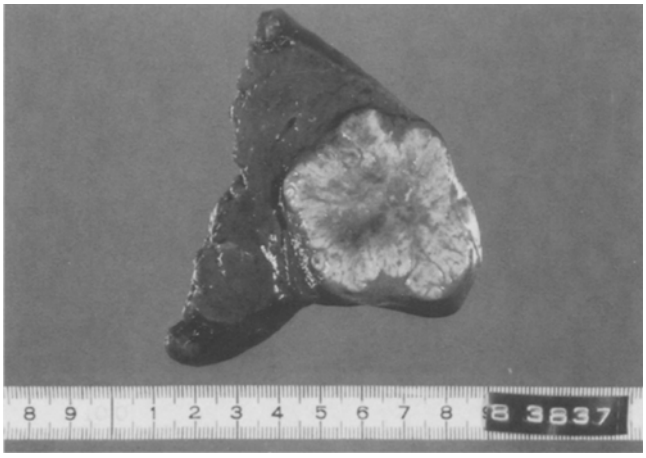

Fig. 4. Cut surface of the liver shows a well-defined tumor with central fibrosis

Discussion

AFP is a useful marker for screening and monitoring patients with hepatocellular carcinoma or yolk sac tumors. However, several investigations have revealed that some other types of tumors could also produce AFP, with gastric cancer being the most common among them.[1]

The incidence of AFP-producing gastric cancer is reported to range from 1.8% to 9.3%.[2] But as seen in our case, AFP-producing early gastric cancer is very rare, and has only been reported in 23 cases,[2–5] which are summarized in Table 1. The majority of such patients were males (16 of 23), ranging in age from 48 to 78 years. The serum AFP levels ranged from 16 to 245600 ng/ml. The depth of tumor invasion in all these cases was limited to within the submucosal layer. Histopathologically, typical features of AFP-producing gastric cancer were undifferentiated cancer cells with clear or slightly eosinophilic, abundant cytoplasm and pleomorphic large round nuclei, based on the *General Rules for Gastric Cancer Study* proposed by the Japanese Research Society for Gastric Cancer.[6] However, most cases were recognized as poorly differentiated adenocarcinoma with medullary proliferation. Nine of the cases had liver metastasis. There was no relation between the serum AFP level at the initial operation and liver metastasis. Most of the liver metastases (6 of 9) occurred within 2 years after surgery, and curative resection of these metachronous metastatic tumors could not be performed because of multiple lesions in the liver. Synchronous liver metastases were seen in 3 cases, and a curative resection could be carried out in 2 of them, including our case. However, regarding the other case of resected liver metastasis, the metastatic lesion was only a tiny nodule (about 2 mm in diameter), that was incidentally discovered while gastrectomy was being performed, and thus was extirpated.[5]

Table 1. Reported cases of AFP-producing early gastric cancer

No	Author	Year	Sex	Age	Gross type	Depth	Histology	Serum-AFP (ng/ml)	AFP staining	Liver metastasis	Prognosis
1	Kondo	1983	M	62	?	sm	por	>10000	(+)	(+)	?
2	Kondo	1983	M	67	?	sm	tub2	209	(+)	?	?
3	Yokota	1985	F	48	I	sm	por	1480	(+)	(−)	3Y2M alive
4	Nishikawa	1985	M	59	IIa + IIc	sm	?	105	(+)	(−)	10M alive
5	Hirato	1986	M	54	IIa + IIc	sm	pap	245600	(+)	(+)	3Y7M died
6	Takahashi	1987	F	73	IIa + IIc	sm	tub2	187	(+)	(−)	2M alive
7	Tanaka	1988	M	55	IIa + IIc	sm	por	39000	(+)	(+)	6M died
8	Ohta	1989	F	73	IIa + IIc	sm	tub2	187	(+)	(−)	2Y alive
9	Chang	1990	F	62	IIa	sm	pap + por	146	(+)	(+)	10M died
10	Chang	1990	M	59	IIc	sm	tub + por	4800	(+)	(+)	2Y died
11	Chang	1990	M	65	IIa	sm	pap	<1	(+)	(+)	2Y died
12	Kato	1990	M	58	IIa + IIc	sm	por	91.3	(+)	(+)[a]	5M alive
13	Takiguchi	1991	M	61	IIa + IIc	sm	por	121.1	(+)	(−)	10M alive
14	Kubo	1992	M	60	IIa + IIc	sm	tub1	44.9	(+)	(−)	2Y3M alive
15	Kubo	1992	F	72	IIa + IIc	sm	por	21.5	(+)	(−)	1Y2M died
16	Shirasaki	1992	M	41	IIa + IIc	sm	?	23	(+)	(−)	2M alive
17	Kurita	1993	M	61	IIa + IIc	sm	por	51.2	(+)	(−)	1Y6M alive
18	Itoh	1993	F	78	I	sm	por	10715	(+)	(−)	3M alive
19	Umekawa	1994	M	61	IIc	sm	por	52	(+)	(−)	2Y7M died
20	Yoshizumi	1995	M	73	IIa + IIc	sm	tub2	162	(+)	(−)	3Y2M alive
21	Suganuma	1995	M	61	IIc	sm	por1	16 → 600	(+)	(+)	8M died
22	Nakazaki	1995	M	57	IIa + IIc	sm	tub2	17208	(+)	(−)	3M alive
23	Tsurumachi	1995	F	61	IIc	sm	por1	917	(+)	(+)[a]	10M alive

AFP, alpha-fetoprotein; sm, submucosal
[a] Cases of resected liver metastasis.

As for the production of AFP by gastric cancer, the main theory to explain this phenomenon is based on the morphological similarity between AFP-producing gastric carcinoma and the other tumors that produce AFP, especially yolk sac tumors and hepatocellular carcinoma.[7] Accordingly, AFP-producing gastric cancer has been divided into two types, one comprising the yolk sac tumor-type AFP-producing gastric cancer, and the other the hepatoid type.[7,8] The stomach and liver are derived from the foregut which is supposed to be in direct continuity with the yolk sac at the primitive stage of development.[9] It is thus said that the hepatoid type is the most common type among AFP-producing gastric cancers, and most of the hepatoid type seem to be highly malignant.

Human AFP is a glycoprotein, and the structure of its carbohydrate chains varies slightly among AFP-producing tumors, thus resulting in different lectin-binding properties.[10] With the ConA-affinity column, AFP is separated into ConA-binding and -nonbinding fractions. The proportion of ConA-nonbinding AFP is generally high in AFP produced by the yolk sac and low in AFP produced by hepatocellular carcinoma. Each type of AFP-producing gastric cancer is thus distinguished by these characteristic lectin-binding properties.[7] As for our case, we did not perform ConA-affinity column chromatography, but hepatoid features were observed by H&E staining, and the immunohistochemical staining for AFP was positive. Based on these findings, it might be appropriate to consider the hepatoid type AFP-producing early gastric cancer.

It is generally considered that the prognosis of AFP-producing gastric cancer is poor because of frequent liver metastasis. In our case, although we believed that a curative resection was achieved since the venous involvement was especially remarkable, the careful monitoring of the serum AFP level must be carried out so as not to overlook any possible recurrence in the liver, even with early stage disease, as in our case. If a serum AFP elevation is observed, aggressive adjuvant chemotherapy should thus be considered. Generally speaking, systemic chemotherapy has not been very effective against AFP-producing gastric cancer with liver metastasis. However, Gonda et al.[11] did report one case with multiple liver metastases that was successfully treated with EAP (etoposide, Adriamycin, cisplatin) therapy.

To date, our case has shown no sign of recurrence after more than 1 year of observation.

References

1. Bourreille J, Metayer P, Sauger F (1970) Existence d'alpha foeto protéine aucours d'un cancer secondaire du foie d'origine gastrique. Presse Med 78:1277–1278
2. Yoshizumi Y, Morisaki Y, Sugiura Y, Tamai S, Tanaka S (1995) Alpha-fetoprotein-producing early gastric cancer: Report of a case (in Japanese with English abstract). Gann no Rinsho (Jpn J Cancer Clin) 41:843–847
3. Suganuama M, Funabiki T, Futawatari H, Ochiai M, Mori K, Morishita H, Sasayama Y (1995) A case of AFP-producing early gastric cancer metastasizing to the liver (in Japanese with English abstract). Nippon Shokaki Geka Gakkai Zasshi (Jpn J Gastroenterol Surg) 28:1086–1089
4. Nakazaki T, Tobinaga K, Taketomi K, Kimino K, Nakasone T (1995) A case of AFP-producing early gastric cancer (in Japanese with English abstract). Nippon Rinsho Geka Gakkai Zasshi (J Jpn Soc Clin Surg) 56:2089–2093
5. Kato M, Kinoshita K, Sawa T, Yoshimitsu S, Yonemura Y, Miwa K, Miyazaki I, Matsui Y (1990) Early gastric cancer of type IIa+IIc producing alpha-fetoprotein with liver metastasis — Report of a case (in Japanese with English abstract). Nippon Shokaki Geka Gakkai Zasshi (Jpn J Gastroenterol Surg) 23:2624–2628
6. Japanese Research Society for Gastric Cancer (1993) The general rules for the gastric cancer study in surgery and pathology, 13th edn, Kanehara, Tokyo, pp 1–89
7. Matsunou H, Konishi F, Roswelly EAJ, Yamamichi N, Mukawa A (1994) Alpha-fetoprotein producing gastric carcinoma with enteroblastic differentiation. Cancer 73:534–540
8. Ishikura H, Mizuno K, Shamoto M, Kirimoto K (1987) Hepatoid adenocarcinoma of the stomach (in Japanese with English abstract). I to Cho (Stomach Intestine) 22:75–83
9. Hamilton WJ, Massman HW (1972) Human embryology. Prenatal development of form and function, 4th edn. Williams and Wilkins, Baltimore
10. Tsuchida Y, Kaneko M, Fukui M, Sakasguchi H, Ischguro T (1989) Three different types of alpha-fetoprotein in the diagnosis of malignant solid tumors. J Pediatr Surg 24:350–355
11. Gonda T, Ishida H, Higuchi T, Hirukawa H (1994) A case of AFP-producing gastric cancer successfully treated with EAP (etoposide, Adriamycin, cisplatin) therapy (in Japanese with English abstract). Gan to Kagaku Ryoho (Jpn J Cancer Chemother) 21:1659–1663