[症例報告]Alpha-fetoprotein producing gastric cancer : A case report and a brief literature review

Alpha-fetoprotein producing gastric cancer : A case report and a brief literature review

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ABSTRACT

A case of AFP-producing gastric cancer in a 66-year-old female is herein reported. The patient was admitted to the university hospital in July 1997. The laboratory data showed the serum AFP to be 2,376 ng/dl. An endoscopic examination showed a big, broadbased, polypoid tumor with an ulceration in the gastric body. She underwent a distal gastrectomy with a nodal dissection (a curative operation). The tumor was composed of three histologic types of cancer including poorly differentiated medullary adenocarcinoma, moderately differentiated tubular adenocarcinoma and hepatoid adenocarcinoma. Immunohistochemically, tubular adenocarcinoma was positive for CEA, and hepatoid adenocarcinoma was positive for AFP and hCG. After the operation, the serum AFP level decreased to the normal range. The patient has been doing well since surgery. Patients with AFP-producing gastric cancer tend to show a poor prognosis. Therefore, they should be regularly and closely followed up. *Ryukyu Med. J., 17(4)229~232, 1997*

Key words: AFP-producing gastric cancer, histopathology, immunohistochemistry

INTRODUCTION

Alpha-fetoprotein (AFP)-producing gastric cancer is a rare and special entity of disease with a high incidence of liver metastasis and a poor prognosis which differentiates this disease from other common types of gastric cancer[1-5]. Since there is yet to be sufficient date to evaluate the clinicopathologic features of AFP-producing gastric cancer, more information on this disease is needed in order to make an accurate diagnosis and select the most appropriate treatment. The rarity of this disease has prompted us to report a case of AFP-producing gastric cancer.

CASE REPORT

A 66-year-old female presented with an attack of upper abdominal pain in June 1997. She was initially seen at her local hospital. Gastrointestinal fiberendoscopy revealed a large tumor with an ulceration in the gastric body. She was thereafter referred to the university hospital in July 1997. On admission, her physical examination showed no abnormality except for anemia. The laboratory findings on admission showed the hemoglobin to be 5.1g/dl and the serum AFP to be 2,376ng/dl. All other data were within the reference ranges. In addition, an endoscopic examination revealed a large sessile tumor with ulceration on the anterior wall of the gastric body and the biopsy findings indicated poorly differentiated adenocarcinoma. An abdominal CT scan demonstrated a sessile exophytic tumor involving the regional lymph nodes along the lesser curvature. She was diagnosed as having advanced gastric cancer in addition to anemia and poor general condition. The patient's anemia and poor nutrition were improved with parenteral nutrition and blood transfusion, meanwhile she recieved neoadjuvant chemotherapy (5-FU 250mg/day) orally for 10 days preoperatively.

A partial gastrectomy with a nodal dissection (a curative operation) was performed. Her gastric cancer Ctage was IIIa (T2, N2, H0, M0) according to the criteria of the Surgical Stage Grouping[6]. The patient was treated with adjuvant chemotherapy (5-FU 250mg/day, CDDP 5mg/day) for two weeks. Her postoperative course was uneventful and she was discharged two months after admission. Her serum AFP level decreased to 611ng/dl on the 5th postoperative day, to 89ng/dl on the 14th post operative day and to 22 ng/dl at discharge. After 3 months of operation, her serum AFP level was within the reference range.

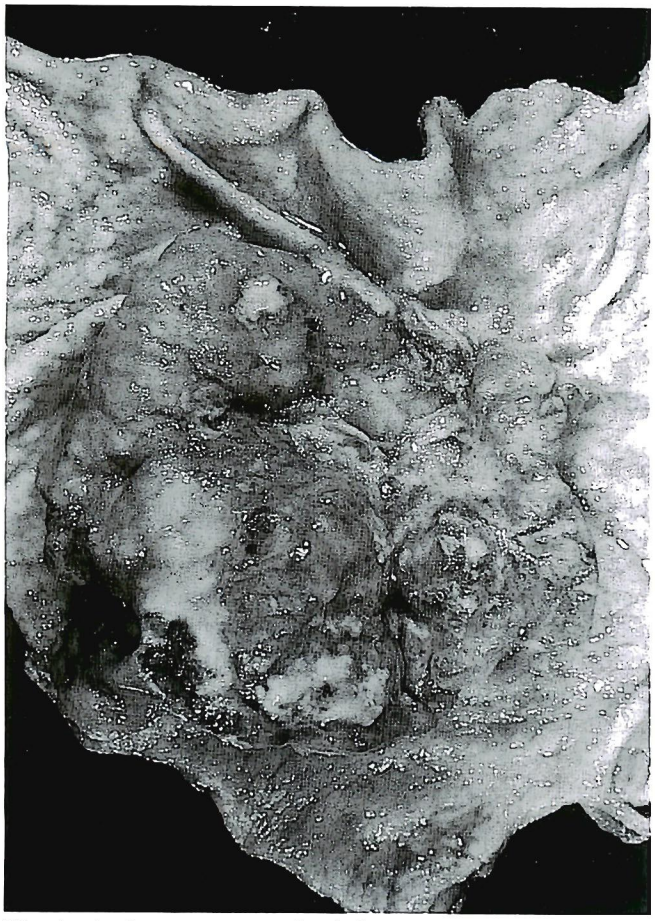

Fig. 1 A photomacrograph of the resected stomach showing a big, broadbased, polypoid tumor with ulceration at the left upper quadrant of the dome of the mass.

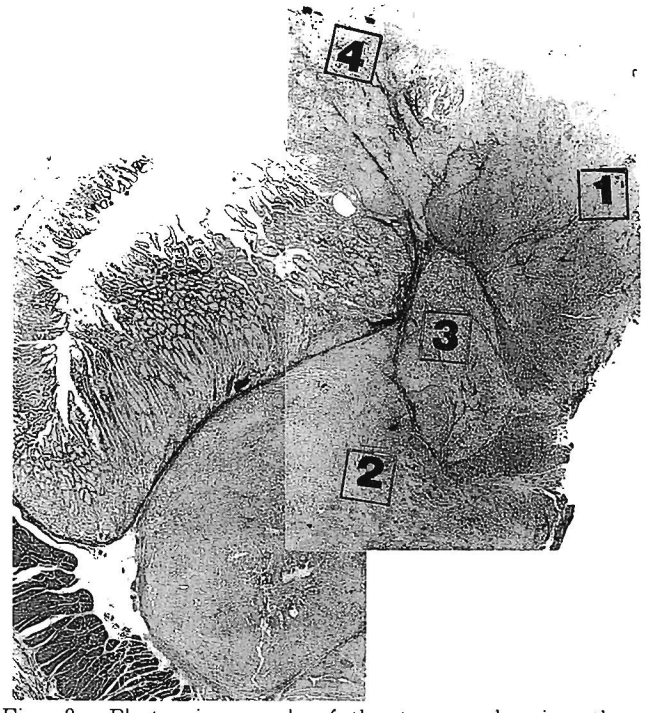

Fig. 2 Photomicrograph of the tumor showing three histologic types relatively clearly separated by thin, fibrous tissue: 1 and 3 indicate poorly differntiated adenocarcinoma; 4, moderately differentiated tubular adenocarcinoma with clear cytoplasm; 2, hepatoid adenocarcinoma.

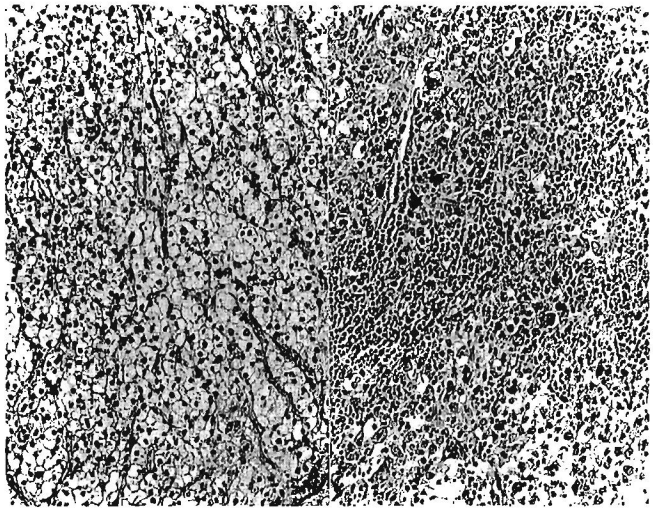

Fig. 3 Photomicrophotographs of the tumor showing poorly differentiated medullary adenocarcinoma (HE, X25). Both were negative for AFP and CEA.

Macroscopic Findings

The resected, opened stomach showed a large, solitary, well-circumscribed, broadbased polypoid tumor with severe ulceration at the left upper quadrant of the dome of the mass. The tumor measured 10×10 cm in size. After the fixation of the tissue, the tumor showed invasion into the submucosa on the cut section of the tumor. Several lymph nodes along the lesser curvature and around the celiac artery were involved by the cancer (Fig. 1).

Miroscopic Findings

The sections from the varigated portions of the tumor were essentially similar. The tumor was mainly composed of three histologic types consisting of: 1) poorly differentiated medullary adenocarcinoma, 2) moderately differentiated tubular adenocarcinoma with clear cytoplasm, and 3) the so-called hepatoid adenocarcinoma. The ratio of these three types of carcinoma was almost 1:1:1. Each section was separated by thin, fibrous tissue with a transition to each other (Fig. 2). The above mentioned histologic typing was described principally in accordance with the classification of the Japanese Research Society on Gastric Cancer[6].

The histologic description of each different tumor type was as follows: 1) poorly diffrentiated medullary adenocarcinoma; these relatively small and round tumor cells were arranged in a solid or medullary pattern. Half of them were tumor, cells with clear cytoplasm (1) and the remaining ones were infiltrated with lymphoid tissue

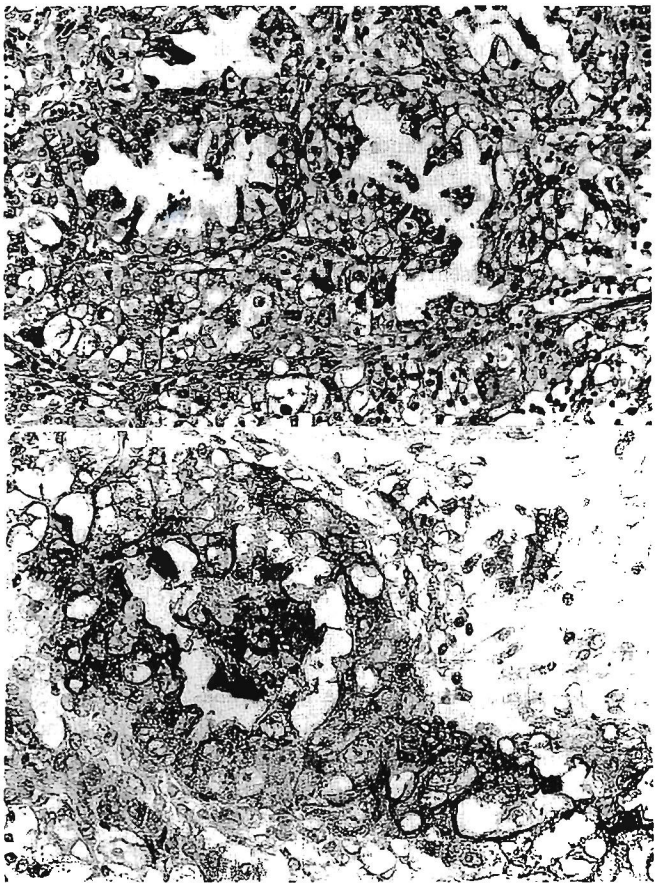

Fig. 4 Photomicrographs of the tumor showing moderately differentiated tubular adenocarcinoma with clear cytoplasm (top; HE, X 100). The tumor cells were positive for CEA (bottom; X 100).

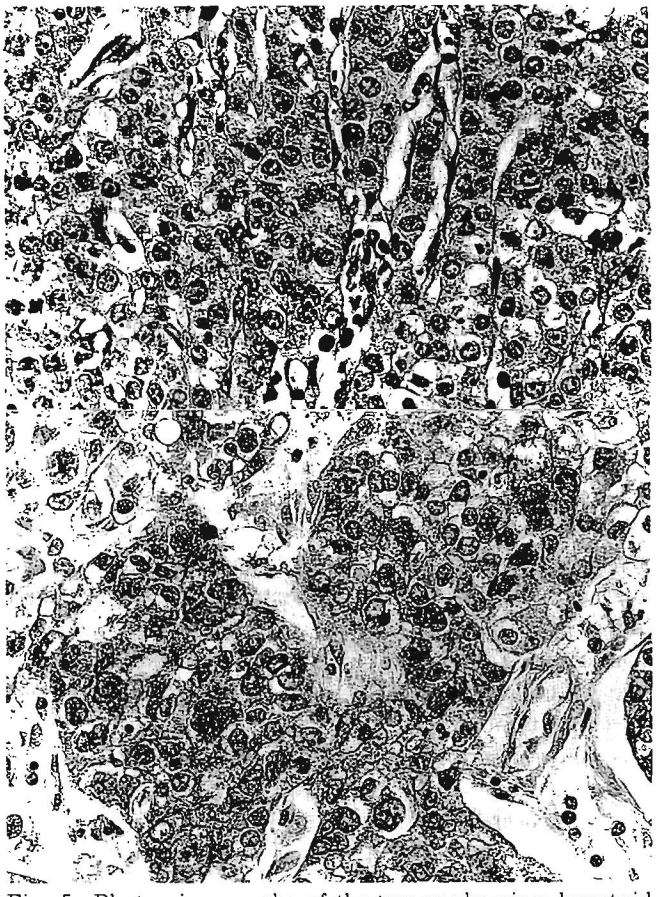

Fig. 5 Photomicrographs of the tumor showing hepatoid adenocarcinoma (top; HE, X 100) and positive AFP expression (bottom; X100).

(3) (Fig. 3). 2) moderately differentiated tubular adenocarcinoma with clear cytoplasm; the tumor cells were cuboidal to columnar in shape with abundant clear cytoplasm arranged in a tubular or glandular pattern. The tumor cells were positive for CEA (carcinoembryonic antigen)(2)(Fig. 4). 3) hepatoid adenocarcinoma; the tumor cells showed only a cuboidal shape with abundant eosinophilic, granular cytoplasm arranged in a trabecular pattern looked like Yolk sac tumor or embryonal carcinoma of ovary. The tumor cells were positive for AFP (alpha-fetoprotein) and hCG (human chorionic gonadotropin) (4) (Fig. 5). But syncytiotrophoblastic giant cell seen in embryonal carcinoma or Schiller-Duval body seen in Yolk sac tumor was not seen. Lymphatic and venous invasion in the gastric wall was moderate to severe, and the lymph nodes were invaded by poorly differentiated medullary adenocarcinoma.

The lectin-binding pattern of AFP showed a hepatocellular carcinoma type ellusion pattern, but no yolk sac tumor type.

DISCUSSION

Gastric cancer has close relationship to hepatocellular carcinoma because both the stomach and liver are embryologically derived from the primitive foregut. It is therefore not surprising that some gastric cancers contain foci of hepatocellular differentiation, producing AFP, albumin, and alpha-1 antitrypsin[3]. These gastric cancers have been designated as hepatoid cancers[4] or AFP-producing cancers[7]. However, no clear definition of AFP-producing gastric cancer has been established. Nowadays, the following criteria for AFP-producing gastric cancer has been accepted: (1) abnormally high serum AFP level throughout the clinical course, changing in parallel with the extent of the lesion, and (2) the tumor cells of gastric cancer are immunohistochemically positive for AFP[8]. These two criteria are essential for AFP-producing gastric cancer. Our case met all these criteria.

Since the first report of this disease, the accumulation of isolated case reports and relatively large series along with their analyses have gradually helped to elucidate its clinicopathological features. The incidence is reported to range from 1.3% to 15% in the literature[9-13].

AFP-producing gastric cancer is characterized by a far advanced tumor stage and a subsequent poor prognosis. When the clinicopathologic features of AFP-producing gastric cancer were compared with all gastric cancers[5], there was no substantial differences in sex, age, tumor location, or pathologic type. AFP-producing gastric cancer is characteristically far advanced at the time of diagnosis, and the far advanced tumor stage may thus be attributed to its poor prognosis.

Of the prognostic factors regulating Surgical Stage Grouping, liver metastasis characteristically occurs so frequently[1-5]. Generally, liver metastasis correlates closely with the tumor stage. However, even AFP-producing early gastric cancer may demonstrate liver metastasis[14]. These investigations thus suggest that AFP-producing gastric cancer is more malignant or aggressive. Indeed, the incidence of lymph node metastasis, lymphatic invasion, and venous invasion of the gastric wall have all been reported to be significantly higher in AFP-producing gastric cancer. In our case, the degree of lymphatic and venous invasion of the gastric wall was moderate to severe. In addition, the DNA of these tumors also showed an aneuploid pattern[5]. The above described evidence may thus indicate this disease to be biologically more aggressive than the usual gastric cancer.

The prognosis of AFP-producing gastric cancer is very poor. The factors responsible for a poorer prognosis also remain to be elucidated. As a result, further information on this disease still needs to be accumulated in order to more thoroughly elucidate its characteristic features.

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