#### **Case Report**

# Coexistence of Choriocarcinoma and Hepatoid Adenocarcinoma in Early Gastric Cancer

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Abstract: We report here the first case of early gastric carcinoma showing the histological features of choriocarcinoma and hepatoid adenocarcinoma. A 68-year-old woman was admitted to our hospital for treatment of gastric cancer detected by her primary care physician. X-ray examination of the stomach and esophagogastroduodenoscopy revealed a 0-I type,  $25 \times 20$  mm tumor occupying the greater wall of the upper gastric body. The biopsy specimens obtained from the tumor revealed a poorly differentiated adenocarcinoma, and a total gastrectomy with lymph node dissection was carried out. Macroscopically, there was a protruding lesion (0-I type) measuring  $25 \times 20$  mm in size in the upper third of the greater curvature of the stomach. Microscopically, features of choriocarcinoma and hepatoid adenocarcinoma were present in the tumor. Immunohistochemically, the choriocarcinoma component was positive for the  $\beta$ -subunit of human chorionic gonadotropin and human placental lactogen. The hepatoid carcinoma component was positive for  $\alpha$ -fetoprotein. To the best of our knowledge, there is only one similar case report of advanced gastric cancer, the our present patient is the first case of early gastric carcinoma showing the coexistence of choriocarcinoma and hepatoid carcinoma. This patient is still alive 19 months after surgery, without recurrence.

# Key words: choriocarcinoma, combined carcinomas, hepatoid carcinoma gastric cancer

#### Introduction

Gastric carcinoma has various histological features. Gastric hepatoid adenocarcinoma is relatively rare<sup>1-3)</sup> and choriocarcinoma is very rare<sup>4)</sup>. Furthermore, there has been only one previous case report showing coexistence of choriocarcinoma and hepatoid carcinoma in advanced gastric cancer<sup>5)</sup>. We report here the first case of early gastric carcinoma combined with choriocarcinoma and hepatoid adenocarcinoma.

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#### **Case Report**

A 68-year-old woman was admitted to our hospital for treatment of gastric cancer detected by her primary care physician. No specific family history was identified. Hemato-logical examination and biochemical test results were within normal limits. Levels of tumor markers such as carcinoembryonic antigen, carbohydrate antigen 19-9 and  $\alpha$ -fetoprotein were within normal limits (Table 1). X-ray examination of the stomach and esophagogastroduo-denoscopy demonstrated a protruding lesion (0–I type) of approximately 25 mm in diameter in the upper third of the greater curvature of the stomach (U area) (Fig. 1A, B). The biopsy specimens obtained from the tumor revealed a poorly differentiated adenocarcinoma. Computed tomography of the abdomen showed no other lesions. Endoscopic ultrasonography with a miniature probe of 20 MHz frequency using the water filling method revealed that the third layer of the gastric wall was uneven (Fig. 1C). The tumor was diagnosed as involving the submucosal tissue. The patient underwent a total gastrectomy with lymph node dissection.

#### Gross findings

The resected specimen included a protruding tumor measuring  $25 \times 20$  mm, located in the upper body of the stomach (Fig. 2). The cut surfaces of the tumor showed two different features, a hemorrhagic brown area and a whitish-yellow area.

#### Histopathological findings

The gastric tumor exhibited two histological patterns, choriocarcinoma (Fig. 3A, B) and hepatoid adenocarcinoma (Fig. 4A, B). The choriocarcinoma component was composed of both cytotrophoblastic and syncytiotrophoblastic cells, which showed a solid irregular pattern with hemorrhage. The hepatoid adenocarcinoma cells were polygonal in shape, and had an abundant eosinophilic granular cytoplasm. Although bile production was not confirmed, the tumor cells occasionally formed a sinusoidal structure. The tumor cells showed invasive growth to a depth of 500  $\mu$ m in the submucosal tissue, but did not reach the muscularis propria.

## Immunohistochemical findings

The choriocarcinoma cells were positive for the  $\beta$ -subunit of human chorionic gonadotropin and human placental lactogen mainly in syncytiotrophoblastic cells. The hepatoid adenocarcinoma cells were positive for  $\alpha$ -fetoprotein. From these results, we diagnosed the patient as follows:

Early gastric cancer; U, Gre, pType 0–I,  $25 \times 20$  mm, choriocarcinoma + hepatoid adenocarcinoma (C·H adenocarcinoma), pT1 (SM 500  $\mu$ m), med, INF  $\alpha$ , ly1, v0, pN0, pPM(–), pDM(–). STAGE IA (T1 N0 M0).

< Hematological test $>$		< Blood chemistry >			
WBC	7660 / µl	TP	7.3 g / dl	GOT	15 IU / 1
(neutrophil 76.0%)		Alb	4.1 g / dl	GPT	7 IU / 1
RBC	$538  imes 10^4$ / $\mu l$	BUN	11.7 mg / dl	LDH	182 IU / 1
Hb	16.2 g / dl	UA	4.4 mg / dl	ALP	183 IU / 1
Ht	48.0%	Cre	0.7 mg / dl	T-chol	206 mg / dl
Plt	$24.7 \times 10^4$ / $\mu$ l	Na	141 mEq / l		
		Cl	105 mEq / l	CRP	< 0.2 mg / dl
< Tumor marker >		Κ	3.9 mEq / 1		
CEA	2.8 ng / ml	Ca	9.7 mg / dl		
CA19-9	5.1 U / ml				
AFP	$6 \text{ ng} / \text{ml} \ (< 20 \text{ ng} / \text{ml})$				

Table 1. Laboratory data on admission

#### Outcome

She is still alive 19 months after surgery, with no recurrence.

## Discussion

Gastric choriocarcinoma is a rare tumor, reported to account for approximately 0.08% of all gastric cancers<sup>4)</sup>. In total, approximately 140 cases have been reported in the English language literature. In one analysis of 53 cases, all patients with choriocarcinoma were found with advanced cancer, and the rates of lymph node, liver, peritoneal, and lung metastases were 87% (40/46), 45% (24/53), 23% (12/53), and 8% (4/53), respectively<sup>6)</sup>. Primary gastric choriocarcinoma is a rapidly growing neoplasm, and untreated patients have an average survival of only several months<sup>7)</sup>.

Gastric hepatoid adenocarcinoma is also well known as a highly malignant neoplasm, but lesions are relatively rare and account for approximately 2.7%–8.0% of all gastric tumors<sup>1-3)</sup>. However when limited to early gastric cancer, only 24 previous cases of hepatoid gastric cancer have been reported in the English and Japanese literature. Among these 24 cases, liver metastasis was observed in 2 patients (8%) and lymph node metastasis was found in 18 patients (72%), all detected upon diagnosis<sup>8)</sup>. Thus, even if gastric hepatoid adenocarcinoma could be detected in the early stage, liver and lymph node metastases may have already occurred<sup>9-12)</sup>.

Given these facts, coexistence of choriocarcinoma and hepatoid adenocarcinoma, namely C·H adenocarcinoma, in early gastric cancer is extremely rare. To the best of our knowledge, there is only one case report of C·H adenocarcinoma in advanced gastric cancer<sup>5)</sup>, and the present patient is the first to show early C·H adenocarcinoma. The prognosis is considered poor in C·H adenocarcinoma, but fortunately she is still alive 19 months after surgery with no sign of recurrence. The reason for this could be that the tumor had invaded only 500  $\mu$ m into the submucosa, which is considered to be an extremely early stage. Close



Fig. 1. Diagnostic images of the tumor. A: X-ray revealed an elevated lesion in the greater curvature of the U area. B: Gastric endoscopy revealed a hemorrhagic elevated lesion, measuring 25 mm in diameter. C: Endoscopic ultrasonography showed a hypoechoic protruding mass located mainly in the first and second layers of the gastric wall, with the third layer uneven. В



Fig. 2. Macroscopy of the resected specimen. The protruding tumor, measuring  $25 \times 20$  mm, was located in the upper body of the stomach.



Fig. 3. Histologic features of the choriocarcinomatous area A: The tumor was composed of cytotrophoblastic and syncytiotrophoblastic cells and contained hemorrhagic lesions (hematoxylin & eosin,  $\times 400$  magnification). B: Carcinoma cells were positive for  $\beta$ -human chorionic gonadotropin (immunohistochemistry,  $\times 400$  magnification).



Fig. 4. Histologic features of the hepatoid adenocarcinomatous area A: The tumor cells were polygonal in shape, had an abundant eosinophilic granular cytoplasm, and showed a trabecular pattern (hematoxylin & eosin,  $\times 400$  magnification). B: Carcinoma cells were positive for  $\alpha$ -fetoprotein (immunohistochemistry,  $\times 400$  magnification). The tumor includes abnormal cells with clear cytoplasm. The tumor cells showed positive immunoreaction for  $\alpha$ -fetoprotein.

follow-up and examination of serum human chorionic gonadotropin and  $\alpha$ -fetoprotein may improve the prognosis for survival. Further study is necessary to clarify the prognosis of C·H adenocarcinoma in such early stages.

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