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A Case of Early Adenosquamous Carcinoma of the Stomach

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Abstract

Adenosquamous carcinoma of the stomach is very rare ; at present, there are only seven published reports. We report here an eighth case involving a 77-year-old Japanese man who was diagnosed with gastric cancer by upper endoscopy and computed tomography (CT). He underwent laparoscopic-assisted distal gastrectomy for early gastric cancer and the resected specimen was diagnosed as adenosquamous carcinoma limited to the submucosal layer. Only one lymph node metastasis was noted. Seven months later, liver metastasis (3 tumors, 15 mm maximum in diameter) was detected by abdominal CT. He was started on chemotherapy with S-1 and cisplatin (CDDP) and is alive 14 months after surgery. Almost all cases of adenosquamous carcinoma of the stomach are diagnosed in advanced stages and carry a very poor prognosis. Most patients with early adenosquamous carcinoma of the stomach survive for 2 or more years without recurrence, however our patient experienced recurrence 7 months after surgery. Therefore, future treatment for recurrent adenosquamous carcinoma of the stomach should be considered.

Key words : Early Adenosquamous carcinoma · Gastric cancer · Chemotherapy

Introduction

Gastric cancer is one of the most common solid neoplasms in Japan. However, adenosquamous carcinoma of the stomach is rare and is classified as a special type histologically. The diagnosis of adenosquamous carcinoma requires that 25% or more of the entire tumor contains squamous cell carcinoma. In the Japanese classification of gastric cancer, early gastric cancer is classified as tumor

invading the mucosal or submucosal layer with or without lymph node metastasis¹⁾.

Although many cases of adenosquamous carcinoma have been reported, almost all cases were diagnosed at an advanced stage. There are some reports of early gastric adenosquamous carcinoma, among which some already showed liver metastasis. There are only seven cases of early adenosquamous carcinoma of the stomach that meet the classification criteria. We report here an

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eighth case of early adenosquamous carcinoma of the stomach, review the literatures, and discuss the clinical features and treatment of the disease.

Case Report

A 77-year-old Japanese man was diagnosed with gastric cancer by upper endoscopy. Endoscopy revealed an elevated and depressed lesion (0-IIa + IIc) located in the mid lesser curvature of the stomach and the tumor was diagnosed as early cancer (Fig. 1). Pathological examination of the endoscopic biopsy specimen showed adenocarcinoma. Computed tomography (CT) revealed neither lymph node involvement nor distant

metastasis. Laparoscope-assisted distal gastrectomy and Billroth I reconstruction was performed. The patient's postoperative course was uneventful and he was discharged 14 days after surgery.

The specimen was a 2-cm elevated lesion with a central depression (Fig. 2). Microscopically, the tumor was composed of both adenocarcinoma and squamous cell carcinoma with keratinization. Squamous cell carcinoma occupied 30% of the tumor, so this case was compatible with adenosquamous carcinoma. The tumor had invaded the submucosal layer with venous and lymphatics invasion, and one lymph node metastasis was

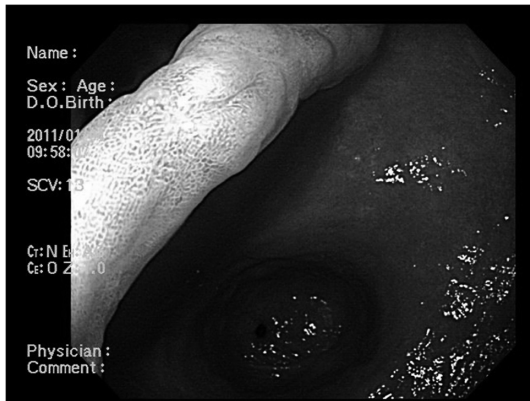


Fig. 1 Gastrointestinal endoscopy showing an elevated and depressed lesion (0-IIa + IIc) located in the middle and lesser curvature of stomach.

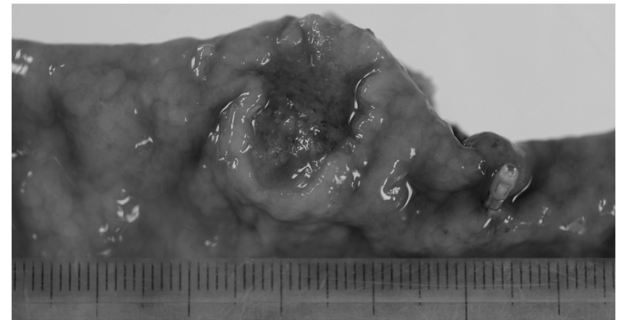


Fig. 2 Resected specimen showing a 0-IIa + IIc tumor in 2cm diameter.

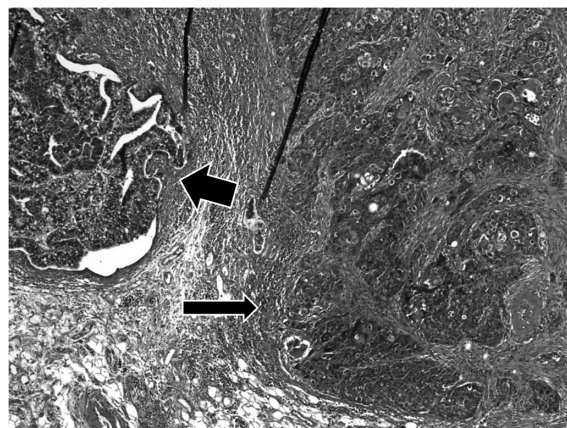


Fig. 3 Microscopic findings of adenosquamous carcinoma (hematoxylin and eosin staining: H. E. x40): Narrow arrow shows component of squamous cell carcinoma with keratinization and bold arrow shows adenocarcinoma component (black arrow).

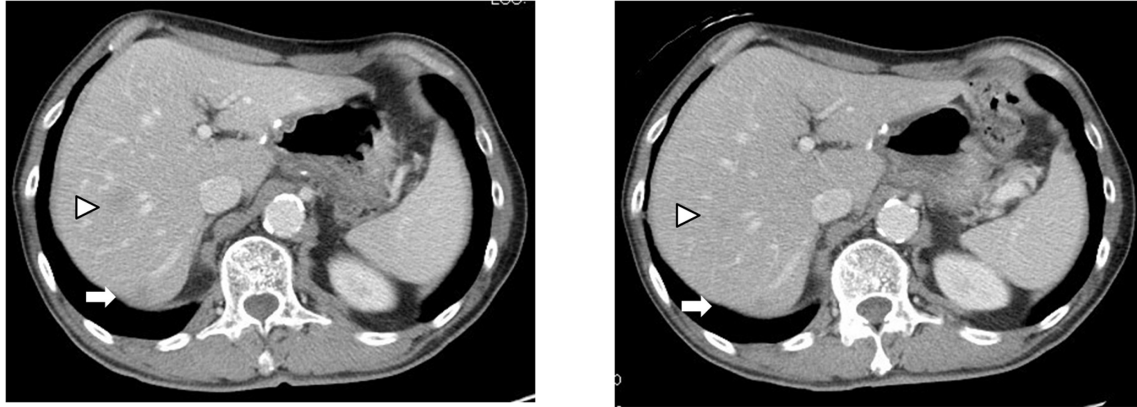


Fig. 4 A. CT showed two tumor 15mm and 10mm, low density lesion located S8 and S7, respectively.
B. CT showed two tumor 6mm and 9mm located S8 and S7, respectively, and which was decreased after chemotherapy.

noted (Fig. 3).

Seven months later, abdominal CT revealed liver tumors 15 mm in maximum diameter in segment 8 (S8), 10 mm in S7 (Fig. 4-A) and 12 mm in S5; there was no evidence of metastasis in other organs. Fluorodeoxyglucose positron emission tomography (FDG-PET) revealed metastatic liver tumors more clearly. Serum carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 were negative from before the operation to the time of recurrence. Chemotherapy consisted of oral S-1 (80 mg/body) daily for 21 days and intravenous infusion of CDDP (100 mg/body) on day 8. He had grade 1 nausea but no other side effects such as bone marrow suppression or renal failure. After 2 courses of the regimen, the liver tumors in S8 and S7 had decreased to 6 mm and 9 mm, respectively (Fig. 4-B); the S5 tumor was no longer detected on CT. We are continuing with the same chemotherapy more 2 cycles and he is alive 14 months after surgery.

Discussion

Adenosquamous carcinoma is rare and accounts for around only 0.5% of gastric cancers²⁾. Recent analysis of the Japanese Gastric Cancer Association's nationwide registry revealed that 41 cases (0.5%) were classified as "other histological types" among 7935 resected cases³⁾. Although the

rate of adenosquamous carcinoma is unknown among the 41 cases, it can be said that it is 0.5% or less.

To our knowledge, seven cases of early gastric adenosquamous carcinoma that meet the Japanese classification criteria have been reported, and all were from Japan. Although there are other reports of early gastric adenosquamous carcinoma, some cases involved bulky lymph node metastasis or liver metastasis and therefore should be excluded in accordance with the Japanese classification. The other case already had liver metastasis from adenosquamous carcinoma limited to the submucosal layer⁴⁾. The first report of early gastric adenosquamous carcinoma, by Samejima et al., described lymph node metastasis but not the prognosis⁵⁾. Other cases of early gastric adenosquamous carcinoma are shown in Table 1. Three of the seven reports did not describe lymph node metastasis, recurrence, or prognosis⁵⁾⁶⁾⁸⁾, however, all the known cases have passed without a reported recurrence⁷⁾⁹⁾⁻¹¹⁾.

It is said that prognosis of gastric adenosquamous carcinoma is poor. Mori et al.¹²⁾ reported that the 5-year survival rate was 0% in 24 cases. They encountered 9 cases of advanced adenosquamous carcinoma among 976 cases at their institution, but none among 1028 cases of early cancer.

The prognosis of gastric adenosquamous carci-

Table 1 Reported cases of early adenosquamous carcinoma of stomach

Authors	Year (Reported)	Patient Age	Sex	Type	Depth	Location	N	Recurrence (after surgery)	Prognosis
Samejima et al.	1974	44	M	0-IIc	sm	L	positive	no discription	
Watanabe et al.	1976	72	F	0-IIa + IIc	sm	LM	unknown	no discription	
Horikawa et al.	1987	56	F	0-IIc + III	sm	M	negative	none	2y4m
Yasuda et al.	1991	63	M	0-I	m	M	negative	no discription	
Ho et al.	1996	52	M	0-I + IIa + IIc	sm	L	positive	none	4y
Nishidoi et al.	1996	80	M	0-IIa + IIc	m	M	negative	none	2y6m
Sasada et al.	2011	60	F	0-IIc	sm	M	negative	none	1y
Current case	2013	77	M	0-IIa + IIc	sm	L	positive	6months	1y7m

noma is not well understood for the following reasons. First, of the few reports available, adenosquamous carcinoma was diagnosed at an advanced stage, such as with liver metastasis or bulky lymph nodes metastasis. Second, metastatic recurrence was early in the postoperative course, as in the present case⁴⁾¹³⁾. Furthermore, the disease course may be related to biological behaviors of the metastatic cells. Faria et al.¹³⁾ reported a Caucasian woman diagnosed with gastric adenosquamous carcinoma with lymph node and liver metastasis. In that case, the nodal and hepatic metastasis showed both cellular lines but the majority were squamous. In another case, right hepatectomy was performed for multiple liver metastasis from advanced gastric adenosquamous carcinoma 6 months after the primary operation¹⁴⁾. Pathological examination showed that the liver tumors were composed of only well-differentiated adenocarcinoma. These two cases suggest that the metastatic site is dependent on the cells that invade, and chemotherapy has to be prescribed with consideration for the histological component. Three of eight reported cases of early adenosquamous carcinoma of the stomach survived for 2 or more years, the prognosis is not so poor that if it is discovered early stage.

Most of the case reports for adenosquamous carcinoma have discussed epidemiology or pathological features and have seldom discussed chemotherapy. Ikeda et al.¹⁵⁾ reported a patient with gastric adenosquamous carcinoma invading the pancreas who received S-1, CDDP, and

docetaxel as neoadjuvant chemotherapy. After two courses of chemotherapy, total gastrectomy and distal pancreatectomy were performed. The patient survived at least 13 months without recurrence despite having advanced disease. Takahashi et al.¹⁶⁾ reported a case of advanced gastric cancer diagnosed as adenosquamous carcinoma by endoscopic biopsy, which was treated with 3 courses of S-1 and CDDP before surgery. The postoperative pathological examination revealed that the remaining tumor consisted of squamous cell carcinoma and was free of any adenocarcinoma component.

In our case, the patient was diagnosed as StageIB¹⁾ and he did not taken adjuvant chemotherapy under Japanese gastric cancer treatment guideline¹⁷⁾. Our patient's cancer recurred 7 months after surgery and we started chemotherapy with S-1/CDDP following the results reported by the SPIRITS trial for adenocarcinoma¹⁸⁾. As there is no evidence of the efficacy of chemotherapy for adenosquamous carcinoma, simultaneous treatment with 5-FU, CDDP, and taxanes could be started or, if possible, pathological diagnosis by biopsy of a metastatic site could be performed to help decide which chemotherapy regimen to use. For primary adenosquamous carcinoma of the stomach with lymph node metastasis or venous or lymphatic invasion, it may be better to consider adjuvant chemotherapy even if the neoplasm does not invade beyond the submucosal layer.

An adequate screening strategy needs to be devised and a larger number of cases should be investigated.

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(和文抄録)

胃の早期腺扁平上皮癌の一例

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【はじめに】胃腺扁平上皮癌はまれな疾患であり、報告は様々だがおよそ胃癌の0.5%といわれている。早期癌に関する報告は非常に少なく、現在7例報告されているのみである。今回我々は本邦で8例目となる早期胃腺扁平上皮癌を経験したので報告する。

【症例】77歳男性で上部消化管内視鏡検査で、胃角部に0-IIa + IIc病変を指摘され、生検では腺癌の診断であった。腹腔鏡補助下幽門側胃切除施行され、病理組織診断では胃腺扁平上皮癌、T1b (SM) N1 M0 StageIBと診断された。術後6か月目のCTで肝臓に3か所の転移を指摘され、再発に対してS-1/CDDP療法が施行された。現在1年7か月生存中である。

【考察】腺扁平上皮癌とは腺癌と扁平上皮癌が共存しており、うち扁平上皮癌が4分の1以上存在することが必要とされている。腺扁平上皮癌の報告は多数あるが、ほとんどの症例は肝転移や多発リンパ節転移を伴った進行した状態で発見されている。また症例が少なくまだ不明なことが多いが、基本的には予後不良といわれている。理由としては①多発肝転移や多発リンパ節転移を伴った進行癌で発見されている、②早期胃腺扁平上皮癌でも早期に再発する、ということが挙げられる。しかし、これまでの7例の早期癌症例において3例は言及されていないが、4例は無再発であり、4年以上生存している症例もあるため、胃腺扁平上皮癌が生物学的な特徴を有している可能性がある。本症例のように早期癌であってもわずか6か月で再発をきたした症例もあることから、通常の腺癌よりは嚴重な経過観察が必要であると考えられた。