Case report

Primary squamous cell carcinoma of the stomach

SHIGERU MARUBASHI, HIROSHI YANO, TAKUSHI MONDEN, HIDEO TATEISHI, TOSHIYUKI KANOH, TAKASHI IWAZAWA, SHIGEO MATSUI, YOSHIKI NAKANO, MASAKATSU KINUTA, HIDENORI TAKAHASHI, and JUN OKAMURA

Department of Surgery, Osaka Teishin Hospital, 2-6-40 Karasugatsuji, Tennoji-ku, Osaka 543-0042, Japan

Abstract:

Primary squamous cell carcinoma (SCC) of the stomach is extremely rare; only 32 cases are found in the Japanese literature. The pathogenesis of this neoplasm remains obscure and controversial. Furthermore, the optimal treatment, including adjuvant chemotherapy, remains unclear. We report herein a case of SCC of the stomach in a 70-year-old male with amazing effectiveness of neoadjuvant chemotherapy, low-dose FP chemotherapy. To our knowledge, no case of this disease has ever been reported that was given neoadjuvant chemotherapy and histologically showed its effectiveness. Our case demonstrated a striking effectiveness of chemotherapy in the neoplasm both radiologically and histologically.

Key words: squamous cell carcinoma, stomach, neoadjuvant chemotherapy

Introduction

Squamous cell carcinoma (SCC) of the stomach is defined as a pure SCC neoplasm arising in gastric epithelium. It is extremely rare and its incidence ranges between 0.04% and 0.09% [1,2] of all gastric cancers. Only 31 cases were found in the Japanese literature and only about 80 cases are known in the world [3]. Until now, there has been no adjuvant chemotherapy recommended that demonstrated effectiveness in the course of the treatment.

Case report

A 70-year-old man who suffered non-insulin-dependent diabetes mellitus and Korsakoff disease was referred to

our hospital because of a gastric neoplasm and pyloric stenosis. He had no complaint. Before his admission, it was revealed that he had Fe-deficient anemia, and his physician examined him and found the tumor. Because of the pyloric stenosis, he took only water orally and was supplied with IVH on his admission. He had no symptoms such as abdominal pain, nausea, vomiting, or melena. His height was 153 cm and his weight 41 kg; his weight had not changed. He had severe emaciation and his nutrition was poor. On physical examination, no abnormal sign was found except his anemic conjunctive palpebra. Laboratory values on admission showed anemia (RBC $313 \times 10^4/\text{mm}^3$; Hb 9.8 g/dl; Ht 29.5%), low albuminemia (serum albumin 3.2 g/dl), leucocytosis (WBC $10000/\text{mm}^3$), and a high serum SCC value, 14.0 (normal, 0–2 ng/ml).

Gastric fluoroscopy with Gastrografin illustrated a round and elevated lesion on the antrum of the stomach (Fig. 1a). The surface of the lesion was slightly rough and the margin was not clear. Endoscopic examination revealed a type 1 tumor on the lesser posterior wall of the antrum; the top of the surface was ulcerated and covered by fur (Fig. 2a). The scope could not be passed through the pylorus ring because of the stenosis. It was proved SCC by a biopsy. In addition to this lesion there were some hyperplastic polyps on the corpus of the stomach.

CT scan showed a solid and enhanced tumor around the antrum and duodenal bulb (Fig. 3a). Its diameter was about 5 cm and possible involvement into the pancreas head was shown. An angiography showed a hypervascular tumor that measured 7 cm and was supplied with a main feeding artery from the branch of the gastroduodenal artery (Fig. 4). The portal vein was patent. Despite of the result of the biopsy, which produced a diagnosis of SCC, these radiological findings still made us suspect that this tumor was derived not from epithelial cells but from interstitial cells, such as a leiomyosarcoma or malignant lymphoma.

Offprint requests to: H. Yano

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Fig. 1. **a** *Left:* Gastric swallow before low-dose FP chemotherapy shows an elevated lesion around pylorus ring (arrowheads). **b** *Right:* UGI series after chemotherapy show remarkable reduction of the tumor (white arrowheads)

Fig. 2. **a** *Left:* Endoscopic examination before chemotherapy shows a type 1 lesion whose top is ulcerated and covered with fur. After chemotherapy (**b**), endoscopy shows remarkable reduction of the tumor

We scheduled an elective operation, but the patient's condition became worse and he ran a spike fever; WBC in peripheral blood rose to 20000/mm³, and he acquired moniliasis in the oral cavity. His condition was so poor that we could not perform the operation. After he recovered from these complications, we started low-dose 5-FU + CDDP chemotherapy [5-fluorouracil (5-FU), 500mg/body/day plus cisplatin (CDDP), 5mg/body/bolus, 5 days/week $\times$ 6 cycles], which was administered via a peripheral vein. No side effect occurred,

and he completed all the cycles of chemotherapy without any complication.

The radiological studies after chemotherapy showed remarkable reduction of the tumor (Figs. 1b, 3b). Endoscopic examination showed that the tumor had been remarkably reduced and the duodenum could be observed without invasion of the tumor (Fig. 2b). Serum SCC level fell within normal limits (1.4ng/ml).

At laparotomy, there was a 3-cm gastric tumor in the antrum with no adherence to adjacent tissues. A radical

Fig. 3. **a** *Upper:* CT scan before chemotherapy shows round, solid, and enhanced lesion of about 5 cm around the pylorus ring. Probable invasion into the pancreas head is also seen. **b** *Lower:* CT scan after chemotherapy shows remarkable reduction of the tumor

distal gastrectomy (D2 lymph node dissection) with cholecystectomy was performed. His postoperative course was uneventful and he was discharged. He is well, and is now taking Tegafur-Uracil (UFT) 300 mg/day orally; there is no evidence of recurrence after a follow-up period of 10 months.

On pathological examination, there was a 2.5×1.5 cm, type 1 tumor in the antrum with an ulcer on its top (Fig. 5). There were also some polyps in the antrum and corpus. The tumor was growing and expanding mainly in the submucosal layer. On histological examination, a moderately differentiated squamous cell carcinoma with invasion to the muscularis propria was seen (Fig. 6a). In all sections, there was neither adenocarcinoma nor squamous dysplasia. Sections stained with CEA, CA19-9, PAS, Alcian blue, and

Fig. 4. Angiography shows a hypervascular tumor (arrowheads) in the antrum of the stomach or pancreas head. The feeding artery (arrow) diverges from the gastroduodenal artery. Tumor size was about 7 cm

Fig. 5. Photomicrograph of the tumor shows a type 1 tumor, whose top is ulcerated and covered with fur, in the antrum. Size is 2.5×1.5 cm

mucicarmin showed no evident of a component of adenocarcinoma. The sections stained with cytokeratine 5, 6, 8, 17, and 19 were positive, stressing that the cancer cells were derived from epithelial cells. These findings confirmed that it was pure SCC of the stomach and that there was no evidence of transition from adenocarcinoma or squamous dysplasia. All the polyps in the antrum and corpus were benign hyperplastic polyps; 6 lymph nodes were involved (2/3) with pure SCC and 8a lymph node was also involved (1/3) with pure SCC. Lymph vessel involvement was seen (ly2). The conclusive stage was IIIa. The curability was B and there was no residual tumor (R0). The cancer cells in most of the tumor changed into necrotic

Fig. 6a–c. Photomicrographs of the surgical specimen. **a** Pure and moderately differentiated squamous cell carcinoma (SCC) is surrounded with marked inflammatory cell infiltration. H&E, $\times 100$. **b** Vacuolation or ballooning of cancer cells with pyknosis of nuclei. H&E, $\times 400$. **c** Most of the SCC was changed into coagulative necrosis of the tumor. H&E, $\times 40$. These findings are compatible with grade 2 of histological changes

granulation and the remaining cancer cells were dying, surrounded with infiltrating lymphocytes (Fig. 6b,c). We could conclude that the preoperative chemotherapy had a remarkable effect on the tumor both radiologically and histologically.

Discussion

The lesion described was a primary squamous cell carcinoma of the stomach, because it was pure SCC of the stomach and no other neoplastic lesion was found in the series of examinations. SCC of the stomach is defined as a tumor that consists entirely of SCC on the Japanese Classification of Gastric Carcinoma [4]. In SCC involving the esophageal junction, the evidence of its gastric origin should be present. This disease is extremely rare, and the incidence has been reported as 0.04% to 0.09% [1,2]. Since Rörig [5] first described this disease in 1895, only about 80 cases of true SCC of the stomach have been reported in the world literature [3]. In Japan, only 31 cases have ever been reported and our case was the 32nd case of SCC of the stomach (Table 1).

The clinicopathological features of these 32 cases, including our case, are reviewed. Age ranged from 29 to 81 years (mean, 60.7). Men were affected about four times as often as women. Most patients were symptomatic, most frequently with epigastralgia (53.1%). The location of the tumor was on the cardia of the stomach in more than half of all cases. The size of the tumor ranged from 2.5 to 13 cm (mean, 6.4 cm). Depth of invasion was T4 (SI) or t4 (si) in about one-half of all cases. Because of the deep invasion of these cases, surgical or conclusive stage was IVa or IVb in more than 40% of all cases in spite of rare involvement into liver or peritoneal dissemination. Therefore the surgical curability tended to be poor in many cases. We could consider from these clinicopathological features that surgical resection alone might be inadequate for the treatment for SCC of the stomach and that we should add adjuvant therapy before or after the surgery. A standard chemotherapy for this disease has not yet been established, however, and no case has previously received neoadjuvant chemotherapy and been studied concerning the effectiveness of chemotherapy to SCC of the stomach. It was certain that there were some cases who received chemotherapy postoperatively, but the effectiveness was still unclear in all cases. To our knowledge, our case is the first that received chemotherapy and showed the amazing effectiveness of chemotherapy histologically.

The pathogenesis of SCC of the stomach has been argued in many reports, and there are several theories about its development: SCC of the stomach originates from (1) foci of heterotopic squamous epithelium, (2) squamous metaplasia, (3) totipotent stem cells, and (4) overgrowth of squamous element in a primary adenocarcinoma. In recent reports [6,7], adenocarcinoma-related antigen such as CA19-9 was found in SCC of the stomach and these authors believed the fourth theory, that the tumor originates from adenocarcinoma and changes to SCC. As for our case,

Table 1. Clinicopathological features of squamous cell carcinoma of the stomach in the Japanese literature

Case no.	Author	Reported year	Age	Sex	Location	Size (cm)	Depth of invasion (involved organ)	Lymph node metastases	Distant metastases	Postoperative chemotherapy	Effect of chemotherapy	Surgical curability ^a	Residual tumor classification ^b	Prognosis
1	Seta	1967	57	M	A	n.m.	SE	n1	No	MMC 60 mg	Unknown ^c	B	R0	1 y 7 m alive
2	Yamaguchi	1969	39	F	M	n.m.	Si	n.m.	Multiple	—		—	—	Autopsy
3	Uchida	1971	67	F	CM	10	se	n.m.	No	Nothing	No	n.m.	n.m.	4 y 4 m alive
4	Kitamura	1975	68	M	M	6.5	ss	n.m.	No	Nothing		n.m.	n.m.	5 y no recurrence
5	Shimizu	1976	72	M	A	6	si (pancreas)	n1	No	Nothing		C	R2	3 m death
6	Nakaizumi	1983	30	F	C	6	se	n0	No	HA: MMC, bleomycin	NC-PD	n.m.	n.m.	10 m death
7	Kataoka	1983	69	M	AM	n.m.	si (pancreas, colon)	N2	H1	5-FU, bleomycin, MMC	NC-PD	C	R2	5 m death
8	Mukaida	1984	56	M	C	8	si (liver, diaphragm)	N4	No	Nothing		C	R2	n.m.
9	Damouira	1984	75	M	C	4	si (diaphragm)	N2	No	Nothing		C	R2	1 y death
10	Matsuzaki	1984	56	F	C	5	n.m.	n.m.	n.m.	Nothing		n.m.	n.m.	6 y no recurrence
11	Takahashi	1984	56	M	C	7	si (spleen)	n2	No	Nothing		B	R0	Unknown
12	Kametani	1985	68	F	CM	6.5	si (pancreas)	N3	No	Nothing		C	R2	1 m death
13	Tanaka	1985	81	M	M	6	SE	N2	No	Nothing		n.m.	n.m.	4 m death
14	Hatayama	1987	75	M	C	4	mp	n0	No	Nothing		n.m.	n.m.	3 y no recurrence
15	Hatayama	1987	52	M	C	n.m.	se	n0	No	Nothing		n.m.	n.m.	4 y no recurrence
16	Hatayama	1987	64	M	C	8	si	n0	No	Nothing		n.m.	n.m.	11 y no recurrence
17	Ozeki	1988	56	M	AM	10	Si (pancreas)	N4	No	Nothing		C	R2	n.m.
18	Kaneko	1989	55	M	C	4	ss	n0	No	Bleomycin 100 mg	Unknown ^c	A	R0	2 y no recurrence
19	Mizutani	1989	59	M	M	7	si (pancreas, colon)	n2	No	Nothing		B	R1	8 m death
20	Miki	1991	50	M	M	10	si (pancreas, liver)	n0	H1	Nothing		C	R2	1 y 2 m death
21	Onoda	1991	68	F	A	4.5	mp	N2	No	Nothing	PR (liver) →PD	n.m.	n.m.	6 m death
22	Kurose	1992	75	M	M	4.7	si (colon)	N2	H2	HA: ADM, CDDP, Etoposide		C	R2	1 y 2 m death
23	Nakabachi	1993	63	F	A	4.5	mp	n1	No	CDDP 190 mg	NC-PD	C	R2	7 m death
24	Nakabachi	1993	58	M	C	13	si (diaphragm)	n0	No	CDDP 250 mg	Unknown ^c	B	R0	2 y no recurrence
25	Shimizu	1993	59	M	M	4.5	ss	n0	No	5-FU, CDDP	Unknown ^c	A	R0	n.m.
26	Tanaka	1994	59	M	C	7	si (diaphragm)	n4	No	CDDP 80 mg + FARM	NC-PD	C	R2	6 m death
27	Imahari	1994	29	M	MC	8	sm	n0	No	Nothing	PR (liver) →PD	A	R0	n.m.
28	Koide	1995	57	M	C	6	ss	n2	H3	HA: 5FU, epiADM, MMC		C	R2	3 m death
29	Aoki	1996	73	M	M	6.5	ss	n0	No	CDDP 100 mg orally	Unknown ^c	A	R0	1 y no recurrence
30	Watanabe	1997	62	M	C	5	si (pancreas)	n1	No	CDDP 50 mg + 5FU 250 mg	Unknown ^c	B	R0	2 y 4 m alive
31	Nozawa present	1997	64	M	C	5	se	n4	No	Nothing	Remarkably reduced	C	R2	4 m death ^d
32	Nakaizumi case	1998	70	M	A	2.5	mp	n2	No	Orally		B	R0	8 m no recurrence

n.m., not mentioned; HA, intrahepatic artery injection; total, total gastrectomy; distal, distal gastrectomy; Prox, proximal gastrectomy; PR, partial response; NC, no change; PD, progressive disease; y, year; m, month

^aJapanese Classification of Gastric Carcinoma

^bTNM-UICC

^cwe cannot evaluate the effect because there is no residual tumor

^dCaused by cerebral infarction

there could be identified no histological sign of adenocarcinoma in the tumor or squamous mataplasia in the gastric mucosa around the SCC. Therefore, we can speculate the pathogenesis of this case might be (1) foci of heterotopic squamous epithelium or (3) totipotent stem cells. We should accumulate more cases with SCC of the stomach and investigate them histologically or genetically to determine the histopathogenesis of SCC of the stomach.

Conclusion

Squamous cell carcinomas of the stomach are very rare, and no case of this disease has been reported that was given chemotherapy and histologically demonstrated the effectiveness of the chemotherapy on the neoplasm. We think, because of the present case, that low-dose FP chemotherapy might be very effective for SCC of the stomach and may improve the prognosis of patients with this disease.

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