Case report

Gastric carcinosarcoma presenting as a huge epigastric mass

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Abstract

Gastric carcinosarcoma often presents with an elevated lesion or increased thickness of the stomach wall. Histological diagnosis is achieved using conventional hematoxylin and eosin staining to confirm the coexistence of both epithelial and mesenchymal elements. We report a case of gastric carcinosarcoma presenting as a large mass in the epigastric region. Specimens obtained by endoscopic biopsy and surgical excision showed diffuse proliferation of atypical cells in sheet formation. No mucus production or glandular structures were apparent, but immunoreactivity for both epithelial and mesenchymal markers was noted. These findings led to a definitive diagnosis of gastric carcinosarcoma. Immunohistochemical analysis is useful for the early diagnosis and treatment of gastric carcinosarcoma.

Key words Gastric carcinosarcoma · Immunohistochemistry

Introduction

Carcinosarcoma is a malignant tumor comprising both epithelial and mesenchymal elements, and it typically occurs in the uterus, esophagus, and breasts, but rarely in the stomach [1]. Characteristics of gastric carcinosarcoma include marked thickening of the stomach wall [2,3], and a protruded or polypoid form of the tumor [1,3–11]. Histological identification of the coexistence of carcinomatous and sarcomatous components in the tumor is indispensable for diagnosis. In all reported cases this coexistence has been confirmed by using conventional hematoxylin and eosin (H&E) staining, with the additional use of immunohistochemical analyses in some cases [10,12–14].

We report herein a case of gastric carcinosarcoma presenting as a large epigastric mass as the first clinical finding, with the patient displaying a rapidly deteriorating course. Immunohistochemical analysis was useful for a definitive diagnosis of carcinosarcoma.

Case report

A 70-year-old Japanese woman presented with a 10-cm, elastic mass in the epigastric region and was admitted to our hospital. She reported a history of epigastric discomfort that had lasted for about 1 year before admission. Fever of around 39°C developed when she was admitted, and her activities of daily life corresponded to a performance status of 3 according to Eastern Cooperative Oncology Group criteria. Emaciation was extremely marked, with her weight being only 31 kg. Laboratory examinations revealed severe anemia (hemoglobin, 7.3 g/dl) and increased serum levels of carbohydrate antigen (CA) 19-9, at 71 IU/ml (normal, <37 IU/ml) and CA125, at 47 IU/ml (normal, <32 IU/ml). Computed tomography (CT) revealed a 21 × 14 × 8-cm upper abdominal mass adjacent to the lesser curvature of the stomach (Fig. 1). Gastrofiberscopy revealed a submucosal tumor with an open ulcer in the anterior wall of the gastric cardia (Fig. 2).

The high fever continued after admission, probably due to tumor necrosis, and her general malaise progressed. Considering the probability of incomplete tumor resection and intolerance to major surgery because of her poor general condition, early surgical intervention was regarded as unfavorable. On day 7 after admission, however, the tumor was exposed on the upper abdominal skin and was partially necrotized. Drainage surgery was conducted, and fragile tumor tissues were removed to the fullest extent possible. Although the administration of anticancer drugs, such as platinum compounds or fluorouracil, was considered, uncon-

Fig. 1. Computed tomography showed a huge mass, 21 × 14 × 8 cm, in the upper abdominal region

Fig. 2. Gastrofiberscopic examination revealed a submucosal tumor-like lesion with an open ulcer on the anterior wall of the gastric cardia

trolled cancer pain developed along with rapid tumor growth. We concluded that best supportive care was appropriate. The patient subsequently displayed rapid deterioration and died 16 days postoperatively. No autopsy was performed.

Pathological examination

Specimens obtained from the ulcer base at gastrofiberscopy revealed diffuse proliferation of polygonal and spindle-shaped atypical cells with strongly eosinophilic nucleoli and weakly eosinophilic cytoplasm, demonstrating a sheet-like appearance, but with no mucus production or glandular structures (Fig. 3). Specimens from the surgical excision showed histological findings similar to those from the biopsy, with mitotic indices of 2.4 and 1.8 per 10 high-power fields, respectively. How-

Fig. 3. Biopsy specimens from the ulcer base revealed diffuse proliferation of atypical spindle-shaped and polygonal cells in sheet formation, demonstrating enlarged nuclei with prominent nucleoli and slightly eosinophilic cytoplasm. Mitotic figures were obvious. H&E, ×400

ever, while these characteristics suggested the possibility of carcinosarcoma, no definitive diagnosis could be reached using conventional H&E staining alone. Immunohistochemical analysis was therefore performed. The tumor was positive for the epithelial marker cell adhesion molecule (CAM) 5.2 (Fig. 4) and the mesenchymal marker vimentin (Fig. 5), but was negative for calretinin, a mesothelial marker, and CD117 (c-kit) and CD34, markers of gastrointestinal stromal tumor (GIST; Table 1). In a biopsy specimen, muscular markers HHF35 (Fig. 6), and α -smooth muscle actin (SMA; Fig. 7) were focally positive. Epithelial and mesenchymal components were intermingled with each other in the tumor nest, leading to a diagnosis of carcinosarcoma.

Discussion

Gastric carcinosarcoma presents with an elevated lesion or increased stomach wall thickness in 83%–91% of all reviewed cases [1,2,4]. To the best of our knowledge, no previous report has described gastric carcinosarcoma as a huge epigastric mass at early clinical presentation. This tumor is generally classified into two types: “true carcinosarcoma” and “so-called carcinosarcoma”. True carcinosarcoma is a mixed tumor comprising carcinoma and genuine sarcoma, usually with relatively sharp demarcation between the two neoplastic components. In contrast, so-called carcinosarcoma consists of carcinoma and a sarcomatous part originating from the carcinoma with transitional features. The present case demonstrated a mixture of epithelial and mesenchymal

Table 1. Immunohistochemical findings of the specimens

Antibody	Clone	Manufacturer	Dilution	Positivity	
				A	B
Ki67	MIB-1	DAKO	1:500	++	++
CAM5.2	CAM5.2	Becton Dickinson	1:6	++	+
Vimentin	V9	DAKO	1:50	+	++
c-kit	Polyclonal	DAKO	1:50	–	–
CD34	QBEND10	Immunotech	1:500	–	–
Desmin	D33	DAKO	1:100	NA	–
α -SMA	A2547	Sigma	1:400	+	–
Actin	HHF35	DAKO	1:500	+	–
Calretinin	Polyclonal	Novocastra	1:100	–	–
CEA	II-7	DAKO	1:100	–	–
LCA	2B11, PD7/26	DAKO	1:100	NA	–
p53	DO-7	DAKO	1:500	NA	+
bcl-2	Polyclonal	DAKO	1:50	NA	–
S-100	2A10	IBL	1:200	–	–
EMA	E29	DAKO	1:400	NA	–

A, Specimens from ulcer base obtained at gastroscopy; B, specimens obtained by surgery; ++, strongly and diffusely positive; +, positive; –, negative; CAM, cell adhesion molecule; CEA, carcinoembryonic antigen; EMA, epithelial membrane antigen; LCA, leucocyte common antigen; NA, not analyzed; SMA, smooth muscle actin

Sources of the antibodies: DAKO, Glostrup, Denmark; Becton Dickinson, San Jose, CA, USA; Immunotech, Marseille, France; Sigma, St Louis, MO, USA; Novocastra, Newcastle, UK; IBL, Gunma, Japan

Fig. 4. Diffuse positive staining for cell adhesion molecule (CAM) 5.2 in a biopsy specimen. **Fig. 5.** Diffuse positive staining for vimentin in a biopsy specimen. $\times 400$

components with immunoreactivity for both cytokeratin and vimentin. Moreover, the tumor revealed no apparent sarcomatous foci with differentiation into osteoid, chondroid, rhabdoid, or lipoid tissue. Given these histological and immunohistological findings, this case was classified as so-called carcinosarcoma.

As for differential diagnoses, GIST and mesothelioma were considered in our patient. Actually, the use of imatinib mesylate was considered as empiric treatment, because GIST often presents as a huge intraabdominal tumor (such as that in our patient) and GIST sometimes consists of spindle-shaped or epithelioid cells [15,16].

However, the tumor in our patient showed no immunoreactivity for CD117 or CD34. Furthermore, the tumor did not demonstrate papillary or glandular structures on H&E sections, such as those usually observed in malignant mesothelioma [17], and calretinin, a mesothelial cell marker, was negative.

At least 45 cases of gastric carcinosarcoma have been reported around the world [1–6,8–14,18–27], with the majority from Japan [13] (Table 2). As gastric carcinosarcoma is very rare, the effects of chemotherapy or radiotherapy have not yet been reported. Ashida et al. [4] reported a patient with gastric carcinosarcoma who

Table 2. Previously reported cases of gastric carcinosarcoma

No.	Author	Year	Age (years)	Sex	Symptom	Appearance	Size (cm) ^a	IHC	Treatment	Prognosis (survival period)
1	Saito [4]	1916	29	M	Fatigue	ND	15	NA	ND	DOD (7 days)
2	Shimo [4]	1938	37	M	Abdominal pain	Ulcerated	ND	NA	ND	DOD (6 days)
3	Furukawa [4]	1946	46	F	Abdominal pain	Polypoid	ND	NA	ND	ND
4	Nagashima [4]	1948	49	M	Abdominal pain	Ulcerated	ND	NA	ND	ND
5	Kitamura [2]	1950	64	F	Abdominal fullness	Protruded	ND	NA	R	NED (28 days)
6	Kitamura [2]	1950	40	F	Heartburn	Protruded	ND	NA	NT	NED (1 year)
7	Nakatani [4]	1951	45	M	Abdominal pain	ND	ND	NA	ND	DOD (16 days)
8	Hara [4]	1953	40	M	Abdominal fullness	ND	8	NA	ND	NED (6 months)
9	Kyogoku [4]	1960	49	M	Abdominal fullness	ND	ND	NA	ND	DOD (3 years)
10	Arganaras and Rigdon [18]	1963	70	M	Appetite loss	Ulcerated	5.5	NA	NT	DOD (7 months)
11	Tanimura [1]	1967	65	F	Anemia	Polypoid	8	NA	R	NED (7 months)
12	Watanabe [11]	1975	69	F	Abdominal pain	Polypoid	9.2	NA	R	DOD (6 months)
13	Tominaga [4]	1976	63	M	Abdominal discomfort	Ulcerated	6	NA	R	NED (5 years)
14	Tokunaga [4]	1979	66	M	Abdominal pain	Ulcerated	8	NA	ND	DOD (3 months)
15	Machida [4]	1981	39	F	Anemia	Ulcerated	7	NA	R	DOD (5 months)
16	Ooi [9]	1982	80	M	Abdominal pain	Polypoid	4.5	NA	R	NED (1 month)
17	Bansal [3]	1982	71	M	Dysphagia	Polypoid	11.5	NA	R	DOD (6 months)
18	Yamagiwa [4]	1983	61	M	Vomiting	Ulcerated	ND	NA	R	ND
19	Yamagiwa [4]	1983	69	M	Dysphagia	Polypoid	ND	NA	R	ND
20	Yamagiwa [4]	1983	73	F	Melena	Polypoid	ND	NA	R	ND
21	Minamoto [8]	1984	70	M	Abdominal pain	Ulcerated	5.6	NA	R	DOD (51 days)
22	Kumagai [4]	1984	47	M	Hematemesis	Polypoid	4	NA	R	DOD (2 years)
23	Hanada [5]	1985	70	F	Abdominal pain	Ulcerated	8	CEA	R	ND
24	Dundas [19]	1988	50	M	Epigastralgia	Polypoid	9	CEA, CAM5.2, vimentin, desmin	R	NED (6 months)
25	Siegal [20]	1988	72	M	Tarry stool	Polypoid	10	CEA, EMA, desmin	R	DOD (6 months)
26	Cho [21]	1990	66	M	Epigastralgia	Ulcerated	4	CEA, S-100	R	NED (6 months)
28	Ito [4]	1991	72	M	Appetite loss	Polypoid	12.7	CEA, EMA, desmin	R	ND
29	Sugai [4]	1991	78	M	Abdominal pain	Polypoid	9	EMA, CEA, desmin, myoglobin	R	DOD (6 months)
30	Cruz [22]	1991	67	M	Appetite loss	Polypoid	10	EMA, CEA, chromogranin A	R	DOD (4 months)
31	Kawabata [14]	1993	72	M	Hematemesis	Polypoid	12.7	CEA, vimentin, desmin, S-100	R	DOD (5 months)
32	Muroya [4]	1992	70	F	Epigastralgia	Ulcerated	8	NA	R	NED (10 years)
33	Muroya [4]	1992	68	M	Epigastralgia	Ulcerated	ND	NA	R	DOD (4 months)
35	Miyauchi [4]	1994	65	M	Hematemesis	Ulcerated	5.5	CEA, CA19-9, EMA, desmin	R	NED (1 year)
36	Melato [23]	1993	73	M	Epigastralgia	Ulcerated	8	CEA, EMA, desmin, myoglobin	R	DOD (6 months)
37	Ashida [4]	1995	74	M	Anemia	Ulcerated	12	NA	R	NED (7 years)
38	Nakayama [6]	1997	69	M	Epigastralgia	Polypoid	20	Cytokeratin, desmin, myoglobin	R	DOD (1 month)
39	Matsukuma [24]	1997	74	M	Appetite loss	Polypoid	15	Cytokeratin, desmin, myoglobin	R	DOD (5.5 months)
40	Inoue [25]	1998	74	F	Dysphagia	Ulcerated	7.8	Keratin, S-100	R	DOD (10 months)
41	Tsunezawa [13]	1999	63	M	Malaise	Polypoid	7	EMA, CEA, desmin, myoglobin	R	NED (10 months)
42	Sato [10]	2001	67	F	No symptom	Polypoid	8	Cytokeratin, desmin, myoglobin	R	NED (11 months)
43	Teramachi [12]	2003	62	M	Epigastralgia	Ulcerated	10	CAM5.2, EMA, α -SMA, desmin	R	NED (20 months)
44	Yamazaki [26]	2003	56	M	Dysphagia	Ulcerated	9	CAM5.2, α -SMA, desmin	R	DOD (2 months)
45	Kuroda [27]	2006	59	M	No symptom	Polypoid	9.2	CAM5.2, α -SMA, S-100	R	ND

CEA, carcinoembryonic antigen; CAM, cell adhesion molecule; DOD, died of disease; EMA, epithelial membrane antigen; IHC, immunohistochemistry; NA, not analyzed; ND, not described; NED, alive with no evidence of disease; NT, no treatment; R, resection; SMA, smooth muscle actin

^aMaximum diameter

Fig. 6. Focal positive staining for HHF35 in a biopsy specimen. $\times 400$

Fig. 7. Focal positive staining for α -smooth muscle actin (SMA) in a biopsy specimen. $\times 400$

survived for 7 years after surgery, and described the importance of surgical treatment. At present, surgery is regarded as the only curative treatment for gastric carcinosarcoma. However, this tumor tends to develop rapidly and to be diagnosed at an advanced clinical stage [14,26], resulting in poor prognosis [8]. Sato et al. [10] reported a mean survival of 10 months. Diagnosis and treatment as early as possible is, thus, crucial.

In conclusion, we reported a case of carcinosarcoma together with the procedure for achieving a definitive diagnosis, using immunohistochemical methods, despite the atypical macroscopic form and the patient's clinical course. Gastric carcinosarcoma should be taken into consideration when a giant tumor of unknown origin is

identified in the upper abdominal region. Immunohistochemical analysis is helpful in making an early diagnosis of carcinosarcoma, even for endoscopic material and tumors showing ambiguous pathological findings.

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