Original paper

Histological heterogeneity and distributional difference of gastric carcinosarcoma: report of 4 cases and literature review

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Carcinosarcoma is a rare malignant neoplasm, consisting of both epithelial and mesenchymal component. Primary gastric carcinosarcoma is rare and poorly understood. We reported clinicopathologic features of 4 cases and analysis of 76 cases published in the literature. Clinical symptoms were nonspecific with epigastric pain, weight loss, and melena, as the most common complaints. The prognosis of patients was dismal with high mortality. The tumor commonly occurred in the upper stomach in Chinese patients, whereas, it was more prevalent at the lower stomach in Japanese and other populations. The two malignant components of this rare cancer showed considerable histological heterogeneity with a wide range of differentiation. We propose that carcinosarcomas be divided in two main subtypes: conventional carcinosarcoma and carcinosarcoma, not-otherwise-specified (NOS). Such distinction may provide useful information for targeted treatment of various sarcomatous components of this tumor. Immunohistochemistry should be routinely applied in the diagnosis of this rare tumor.

Key words: stomach, carcinosarcoma, gastric cardia, classification.

Introduction

Carcinosarcoma is a rare malignant neoplasm, consisting of both epithelial and mesenchymal component, which has been described as "carcinosarcoma, so-called carcinosarcoma, and sarcomatoid carcinoma" in the uterus, esophagus, and breasts, but seldom in the stomach [1]. Because of its rarity, carcinosarcoma of the stomach was listed only by name in the Chapter for Gastric Carcinoma of the most recent edition of the World Health Organization (WHO) Classification of Tumors of the Digestive System [2]. Until now, less than 100 gastric carcinosarcomas have been reported [3]. The two malignant components of this cancer show considerable histological heterogeneity with a wide range of differentiation, such as adenocarcinoma (AC), undifferentiated carcinoma, squamous cell carcinoma (SCC), and neuroendocrine carcinoma (NEC) in the carcinomatous component, and chondroid, osteoid, rhabdoid, fibrous, leiomyomatous differentiations as well as spindle, round, polygonal unclassifiable mesenchymoid cells in

the sarcomatous component [1, 3]. Herein, we report 4 cases of gastric carcinosarcoma in Chinese patients and a literature review.

Material and methods

Case selection

Electronic pathology archive of two hospitals (Drum Tower Hospital and Changzhou Second People's Hospital) over the period from January 2003 to December 2016 were searched for cases with a final diagnosis of gastric carcinosarcoma on radical gastrectomy specimens. A literature search was performed on the China National Knowledge Internet in Chinese, PubMed and Google Scholar in English, using the terms of "stomach, and carcinosarcoma". Eligible cases published between 1960 and 2017 were included. Sarcomatoid carcinomas and cases without a definite pathologic diagnosis were excluded.

Clinicopathological study

Clinicopathologic characteristics of all included cases were analyzed i.e. patient age, gender, symptoms at diagnosis, tumor location, size, gross appearance, histological type, and sarcomatoid differentiation, and post-resection survival. The carcinomatous component was divided into the common histology Lauren intestinal- or diffuse-type adenocarcinoma, and the uncommon types of SCC and NEC. The sarcomatous component was tabulated as chondroid, osteoid, rhabdoid, leiomyomatous, and fibrous differentiations. The term, unclassified pleomorphic sarcoma (UPS), refers to the unclassifiable sarcomatous component of gastric carcinosarcoma that is immunoreactive to the mesenchymal marker vimentin, but not immunoreactive to any epithelial marker. According to different sarcomatous component, we simply divided gastric carcinosarcomas into 2 subtypes as:

- conventional carcinosarcoma, in which the sarcomatous component shows the conspicuous morphologic features of mesenchymal differentiation, such as chondrosarcoma, osteosarcoma, rhabdomyosarcoma, angiosarcoma, and leiomyosarcoma, etc.;
- carcinosarcoma, not-otherwise-specified (NOS), refers to the tumor demonstrating an obvious carcinomatous component along with an UPS component.

All slides of our 4 cases were reviewed by at least two pathologists for diagnosis verification. Immunohistochemistry would be performed to validate both epithelial and sarcomatous component when it is necessary. Our immunohistochemical panel included pancytokeratin for carcinoma, CK8/18 for AC, P63 for squamous cell differentiation, synaptophysin and CD56 for neuroendocrine differentiation. To detect sarcomatous differentiation we selectively used antibodies of vimentin, S100, desmin, and myogenin.

Statistical analysis

The data were divided into categorical variables, such as proportions and frequencies, which were analyzed with the Chi square test. All statistical analyses were carried out with the GraphPad Prism 6.0 (GraphPad Prism Software Inc, San Diego, CA). A p value of < 0.05 was considered as statistically significant.

Results

Clinicopathologic characteristics of the 4 carcinosarcomas

During 14-year period, 4 cases (3 men and 1 woman) of carcinosarcoma of the stomach were identified among 7966 (0.05%, 4/7966) gastric cancer radical resections performed in two medical centers. As shown in Table I, the median age of patients was 70 years (range: 52 to 71). The symptoms at diagnosis included abdominal pain (n = 3), dysphagia and gastroesophageal reflux disease (n = 1). In 2 patients, the initial biopsy diagnosis was AC. The site of tumors included gastric cardia (n = 3) and antrum (n = 1). The tumors were protruding (n = 1) and ulcerative (n = 3) in appearance. Focal NEC was detected in Case 1. An evident chondrosarcomatous component was revealed in cases 1, 3, and 4. According to the proposed classification, 3 cases (No 1, 3 and 4) were conventional carcinosarcomas and the remaining case (No 2) was carcinosarcoma, NOS. One patient was lost of follow-up, while the other 3 patients were alive.

Immunohistochemical stains with a routine protocol showed that the chondrosarcomatous component in cases 1, 3, and 4 were positive for S100 and negative for cytokeratins (CK8/18, CK20) (Fig. 1). In case 2, the sarcomatous component was positive for vimentin but negative for EMA and CK (Fig. 2). In case 1, neuroendocrine markers (synaptophysin and CD56) were focally positive in the carcinomatous component.

Literature review

Upon review of the literature, 76 cases were identified (Table II) [1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51]. The clinical features of patients with gastric carcinosarcoma appeared to be nonspecific with epigastric pain, weight

Table I. Clinicopathologic features of our 4 gastric carcinosarcomas.

Case	Gender/ Age	Location/ Size (cm)	Appearance	Histological features		Immunohistochemical results	Outcome
				Carcinomatous component	Sarcomatous component		
1	F/52	Antrum/9	Protruding	Mixed AC and NEC	SC with CD	AC: EMA (+), CEA (+), CK20 (–), CK8/18 (+), CK (+); NEC: Syn (+), CD56 (+); SC: Vim (+), S100 (+), CD34 (–), CD117 (–), Desmin (–)	NA
2	M/71	Cardia/7	Ulcerative	Intestinal-type AC	UPS	AC: CK (+); SC: Vim (+), CD34 (–), CD117 (–), DOG-1 (–)	A, 20 mo
3	M/71	Cardia/5	Ulcerative	Intestinal-type AC	SC with CD	AC: CK (+), CK8/18 (+), CK20 (–); SC: Vim (+), S100 (+), CD34 (–), CD117 (–)	A, 15 mo
4	M/69	Cardia/1.5	Ulcerative	Diffuse-type AC	SC with CD	AC: CK8/18 (+), CK20 (–); SC: Vim (+), S100 (+), CD34 (–), CD117 (–)	A, 6 mo

A – alive; AC – adenocarcinoma; CD – chondroid differentiation; F – female; M – male; mo – months; NA – not available; NEC – neuroendocrine carcinoma; SC – sarcoma; UPS – unclassified pleomorphic sarcoma.

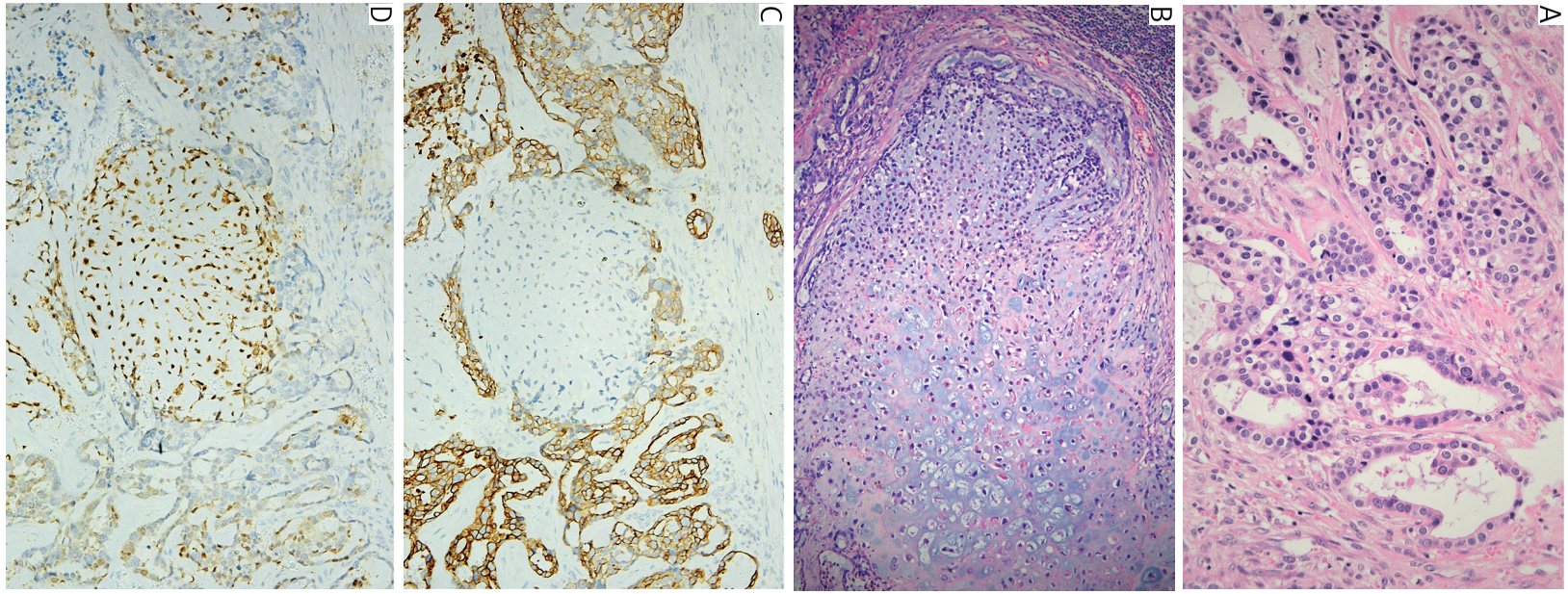

Fig. 1A-D. Representative case of gastric carcinosarcoma in a 71-year old male Chinese patient (case 3). A) A carcinomatous component of the Lauren intestinal-type adenocarcinoma; B) both adenocarcinoma and chondrosarcoma component were detected in a metastatic lymph node; C) the adenocarcinoma was positive for CK8/18; D) the chondrosarcoma was positive for S100 and negative for CK8/18

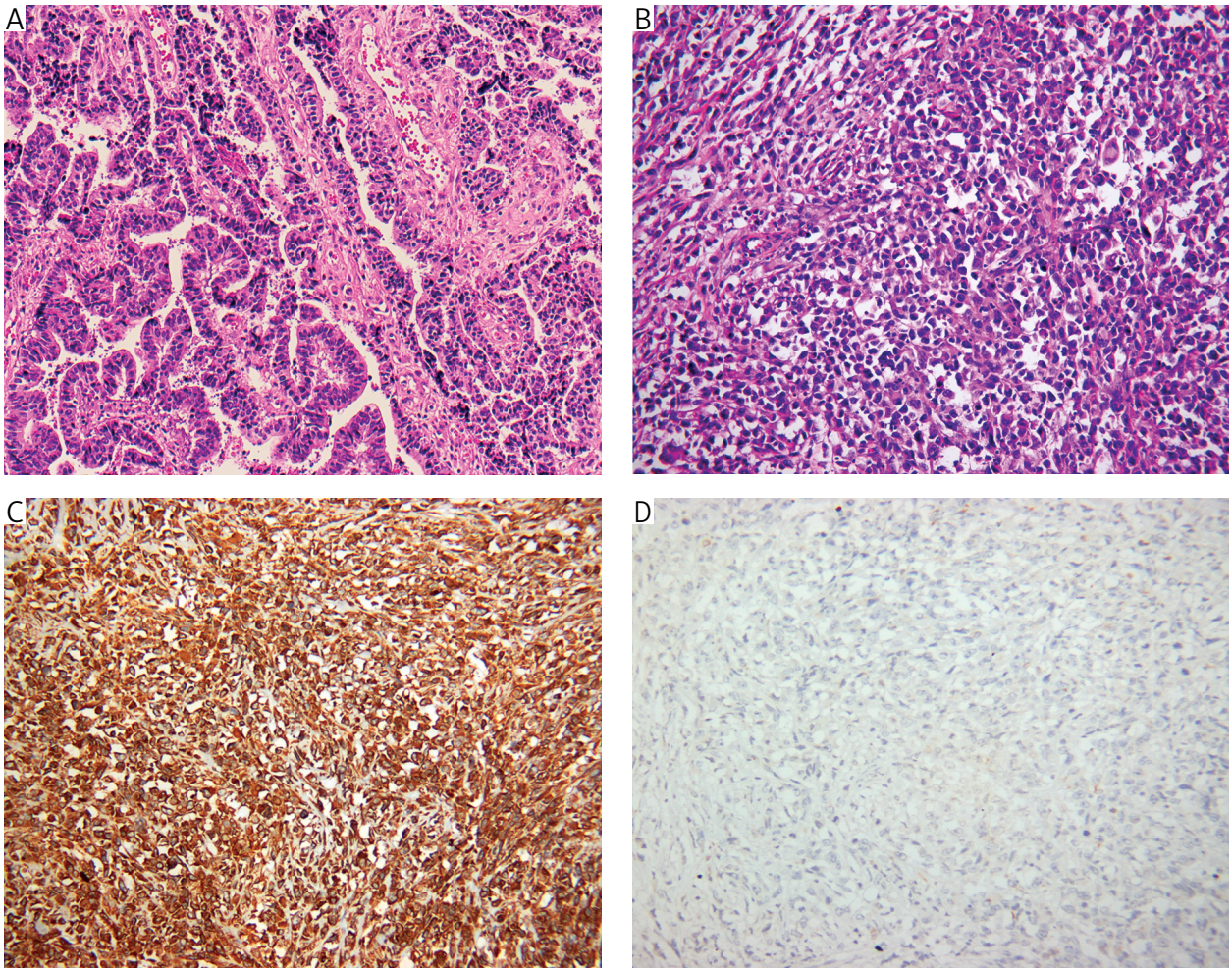

Fig. 2A-D. A case of gastric carcinosarcoma, not otherwise specified, in the gastric cardia of a 71-year old male Chinese patient (case 2). A) A carcinomatous component of the Lauren intestinal-type adenocarcinoma; B) an unclassified pleomorphic sarcoma (UPS) component with spindle or polygonal cells without specific epithelial or mesenchymal differentiation; C) the UPS component was immunoreactive to Vimentin, D) but not to pancytokeratin

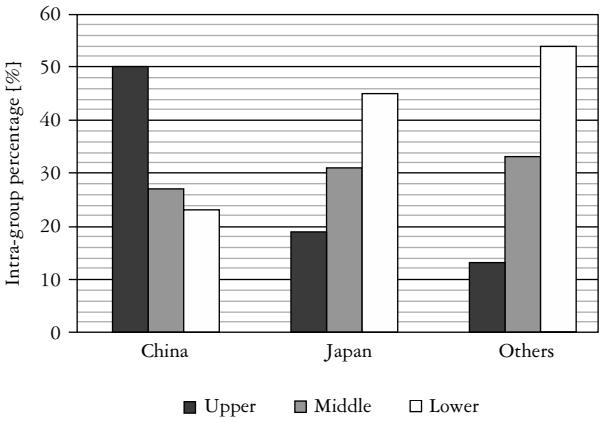

Fig. 3. A high (50%) prevalence of tumors involving gastric cardia was found in Chinese patients, compared to 19% in Japanese, and 13% in other ethnic patient groups

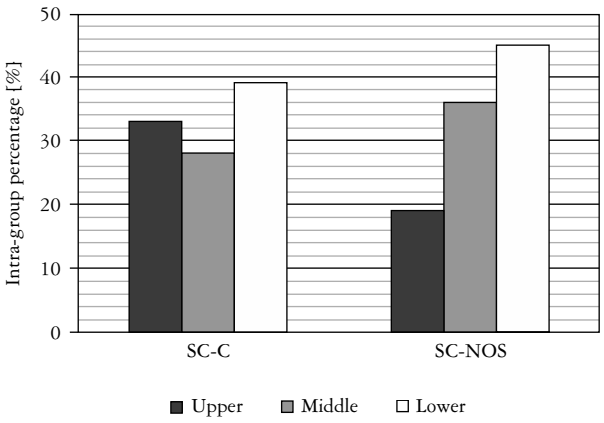

Fig. 4. Conventional carcinosarcoma was prone to involve gastric cardia, but the difference did not reach a statistically significant level ($p = 0.4350$)

Table II. Clinicopathologic features of 76 gastric carcinosarcomas reported in the literature

	Author and year [referene]	Gender /Age	Location/Size (cm)	Gross Appearance	Key Histological Features		Proposed classification	Outcome
					Carcinomatous component	Sarcomatous component		
China	Li *et al.* 2015 [32]	M/70	Corpus/10.8	NA	IAC	SC with RD	SC-C	DOD, 6 mo
	Song *et al.* 1983 [37]	M/62	Antrum/7.0	Fungating	IAC	SC with LD	SC-C	NA
	Song *et al.* 1991 [38]	M/67	Fundus/7.0	Protruding	IAC	UPS	SC-NOS	DOD, 8 mo
	Zhao *et al.* 1994 [39]	M/55	Cardia-fundus/4.0	Protruding	IAC	SC with LD	SC-C	NA
	Su 2001 [40]	M/58	Cardia/2.0	Polypoid	ASC	SC with LD	SC-C	NA
	Guo *et al.* 2003 [41]	M/76	Cardia-corpus/6.0	Ulcerative	IAC	UPS	SC-NOS	NA
	Wang *et al.* 2005 [42]	F/45	Antrum/7.0	Protruding	DAC	UPS	SC-NOS	NA
	Wu *et al.* 2007 [43]	F/75	Antrum/12.0	Protruding	NEC	UPS	SC-NOS	A, 6 mo
	Xue *et al.* 2008 [44]	F/15	Corpus/5.0	Ulcerative	DAC	UPS	SC-NOS	NA
	Zhao *et al.* 2008 [45]	M/59	Corpus/8.0	Protruding	NA	UPS	SC-NOS	NA
	Ding *et al.* 2011 [46]	M/47	Cardia/4.0	Protruding	IAC with ND	SC with LD, CD and OD	SC-C	DOD, 9 mo
	Zheng *et al.* 2011 [47]	M/60	Cardia-fundus/6.0	Ulcerative	DAC	UPS	SC-NOS	NA
	Ge *et al.* 2011 [48]	M/61	Cardia/8.0	Fungating	IAC	UPS	SC-NOS	NA
	Yang *et al.* 2012 [49]	M/69	Cardia/8.0	Protruding	ASC;	SC with FD	SC-C	DOD, 8 days
	Zhang *et al.* 2016 [50]	F/51	Corpus/5.5	NA	IAC	SC with CD	SC-C	NA
	Jiang *et al.* 2016 [51]	M/69, 79, 84	Cardia, corpus, and antrum /5.0-14.0 cm	Protruding (2), ulcerative (1)	IAC (3), ASC (1), NEC (1)	SC with OD (1) and RD (3)	SC-C (3)	DOD; 3, 4 and 7 mo
Japan	Tanimura 1967 [1]	F/65	Cardia-corpus/8.0	Fungating	IAC	SC with LD	SC-C	A, 7 mo
	Tokunaga 1979 [5]	M/66	Antrum/8.0	Fungating	IAC	UPS	SC-NOS	DOD, 3 mo
	Hanada 1985 [7]	F/70	Pylorus/8.0	Fungating	IAC	UPS	SC-NOS	NA
	Kida 1993 [12]	M/65	Corpus/5.5	Ulcerative	IAC	UPS	SC-NOS	A, 20 mo
	Matsukuma 1997 [13]	M/74	Gastric remnant/15	Polypoid	IAC;	SC with RD	SC-C	DOD, 6 mo
	Nakayama 1997 [14]	M/69	Gastric remnant/20	Polypoid	IAC	SC with RD and OD	SC-C	DOD, 1 mo
	Tsuneyama 1999 [15]	M/63	Pylorus/7.0	Polypoid	IAC, NEC	SC with RD	SC-C	A, 10 mo
	Sato 2001 [16]	F/67	Cardia-fundus/8.0	Polypoid	ASC	SC with CD and RD	SC-C	A, 11 mo
	Teramachi 2003 [18]	M/62	Corpus/10.0	Ulcerative	NEC	SC with RD, CD and OD	SC-C	A, 20 mo

Table II. Cont.

	Author and year [referene]	Gender /Age	Location/Size (cm)	Gross Appearance	Key Histological Features		Proposed classification	Outcome
					Carcinomatous component	Sarcomatous component		
Japan	Yamazaki 2003 [19]	M/56	Corpus/9.0	Ulcerative	IAC, NEC	UPS	SC-NOS	DOD, 2 mo
	Kuroda 2006 [21]	M/59	Corpus/9.2	NA	IAC with ND	SC with LD	SC-C	NA
	Kikuyama 2009 [24]	F/83	Antrum/ND	Ulcerative	IAC	UPS	SC-NOS	NA
	Cirocchi 2012 [26]	F/62	Corpus-fundus/13.0	Polypoid	IAC	UPS	SC-NOS	DOD, 4 mo
	Selcukbiricik 2012 [27]	M/73	Cardia/12.0	Fungating	Mixed AC	SC with OD	SC-C	DOD, 14 mo
	Yoshida 2012 [28]	M/59	Cardia/11.5	Protruding	IAC	SC with OD	SC-C	DOD, 7 mo
	Maeda 2014 [3]	F/61	Antrum/NA	Protruding	IAC	SC with FD and CD	SC-C	DOD, 9 mo
	Gohongi 2015 [33]	M/70	Cardia-corpus/7.5	Ulcerative	IAC	UPS	SC-NOS	DOD, 22 mo
	Fujiie 2016 [34]	F/71	Corpus/2.0	Fungating	NEC	SC with RD	SC-C	A, 3years
	Watanabe 1975 [22, 29]	F/69	Antrum/9.2	Polypoid	IAC	NA	Not determined	DOD, 6 mo
	Tominaga 1976 [22,29]	M/63	Antrum/6.0	Ulcerative	DAC	UPS	SC-NOS	A, 5 years
	Machida 1981 [22, 29]	F/39	Cardia/7.0	Ulcerative	IAC	SC with CD, LD and RD	SC-C	DOD, 5 mo
	Ooi 1982 [22, 29]	M/80	Antrum/4.5	Polypoid	Mixed AC	UPS	SC-NOS	A, 1 mo
	Yamagiwa 1983 [22, 29]	M/61	Antrum/NA	Ulcerative	IAC	SC with FD	SC-C	NA
		M/69	Antrum/NA	Polypoid	IAC	SC with FD	SC-C	NA
		F/73	Cardia/NA	Polypoid	IAC	SC with FD	SC-C	NA
	Minarnoto 1984 [22, 29]	M/70	Antrum/5.6	Ulcerative	Mixed AC	UPS	SC-NOS	DOD, 51 days
	Kumagai 1984 [22, 29]	M/47	Corpus/4.0	Polypoid	Mixed AC	UPS	SC-NOS	DOD, 2 years
	Sugai 1991 [22, 29]	M/78	Antrum/9.0	Polypoid	IAC	UPS	SC-NOS	DOD, 6 mo
	Ito 1991 [22, 29]	M/72	Antrum/12.7	Polypoid	NA	NA	Not determined	NA
	Muroya 1992 [22, 29]	F/70	Antrum/8.0	Ulcerative	NA	NA	Not determined	A, 10 years
		M/68	Antrum/NA	Ulcerative	NA	NA	Not determined	DOD, 4 mo
	Kawabata 1993 [22, 29]	M/72	Antrum/12.7	Polypoid	NA	NA	Not determined	DOD, 5 mo
	Miyauchi 1994 [22, 29]	M/65	Corpus/5.5	Ulcerative	IAC	UPS	SC-NOS	A, 1 year
	Ashida 1995 [22, 29]	M/74	Antrum/12.0	Ulcerative	IAC	UPS	SC-NOS	A, 7 year
	Inoue 1998 [22, 29]	F/74	Corpus-fundus/7.8	Ulcerative	DAC	SC with LD and CD	SC-C	DOD, 10 mo

Table II. Cont.

	Author and year [referene]	Gender /Age	Location/Size (cm)	Gross Appearance	Key Histological Features		Proposed classification	Outcome
					Carcinomatous component	Sarcomatous component		
Japan	Numoto 1998 [3]	M/65	Corpus-pylorus/8.0	Protruding	IAC	SC with CD and RD	SC-C	DOD, 3 mo
	Fujii 2002 [3]	M/72	Corpus/2.0	Protruding	IAC	SC with RD	SC-C	DOD, 4 mo
	Mori 2004 [3]	M/67	Corpus/6.8	Protruding	IAC	SC with RD	SC-C	A, 30 mo
	Takase 2006 [3]	M/74	Corpus/12	Polypoid	IAC	SC with CD	SC-C	DOD, 5 mo
	Oomori 2007 [3]	M/62	Corpus/3	Ulcerative	DAC	SC with RD	SC-C	DOD, 7 mo
	Fujikuni 2010 [3]	F/69	Corpus-pylorus/6.0	Protruding	IAC	SC with LD	SC-C	A, 26 mo
	Miyagwa 2014 [3]	M/59	Cardia/11.5	Protruding	IAC	SC with OD	SC-C	DOD, 7 mo
Others	Arganaras 1963 [4]	M/70	Pylorus/5.5	Ulcerative	IAC	UPS	SC-NOS	DOD, 7 mo
	Bansal 1982 [6]	M/71	Cardia-corpus/11.5	Fungating	IAC	UPS	SC-NOS	DOD, 6 mo
	Dundas 1988 [8]	M/50	Fundus/7.0	Polypoid	IAC	SC with LD	SC-C	A, 6 mo
	Siegal 1988 [9]	M/72	Corpus/10.0	Polypoid	Mixed AC	SC with CD	SC-C	DOD, 6 mo
	Cho1990 [10]	M/66	Corpus-antrum/4.0	Fungating	IAC	SC with CD	SC-C	A, 6 mo
	Cruz 1991 [11]	M/67	Corpus/10.0	Protruding	IAC, NEC	UPS	SC-NOS	D, NA
	Kayaselçuk 2002 [17]	M/53	Antrum/3.5	Polypoid	IAC	UPS	SC-NOS	A, 8 mo
	Villanacci 2006 [20]	M/45	Antrum/NA	Ulcerative	DAC	SC with CD	SC-C	A, 8 mo
	Randjelovic 2007 [23]	M/62	Cardia-antrum/12.0	Protruding	IAC	UPS	SC-NOS	DOD, 12 mo
	Jang 2010 [25]	M/47	Antrum/9.0	Polypoid	IAC with ND	SC with LD	SC-C	A, 6 mo
	Cirocchi 2012 [26]	F/62	Corpus-fundus/13.0	Polypoid	IAC	UPS	SC-NOS	DOD, 4 mo
	Selcukbiricik 2012 [27]	M/73	Cardia/12.0	Fungating	Mixed AC	SC with OD	SC-C	DOD, 14 mo
	Choi 2013 [30]	F/51	Antrum-corpus/12.0	Ulcerative	DAC	UPS	SC-NOS	A, 9 mo
	Shin 2014 [31]	F/62	Antrum/4.5	Fungating	IAC with ND	UPS	SC-NOS	NA
	Maqsood 2016 [35]	F/52	Corpus-pylorus/ ND	Polypoid	IAC	SC with RD	SC-C	D, NA
	Park 2016 [36]	M/59	Fundus/5.5	Fungating	IAC	UPS	SC-NOS	A, 6 mo

A – alive; AC – adenocarcinoma; ASC – Adenosquamous carcinoma; CD – chondroid differentiation; D – dead; DAC – diffuse-type adenocarcinoma; DOD – dead of disease; F – female; FD – fibrous differentiation; IAC – intestinal-type adenocarcinoma; LD – leiomyomatous differentiation; M – male; mo–months; NA – not available; ND – neuroendocrine differentiation; NEC – neuroendocrine carcinoma; OD – osteoid differentiation; RD – rhabdoid differentiation; SC – sarcoma; UPS – unclassified pleomorphic sarcoma.

Table III. Gross and microscopic features of 80 gastric carcinosarcomas

Gross and microscopic features	Number of cases
Gross appearance	
Protruding	19
Polypoid	21
Fungating	12
Ulcerative	25
Not determined	3
Microscopic features	
Carcinomatous component	
Adenocarcinoma	
Lauren intestinal type	53
Lauren diffuse type	9
Mixed type	7
Neuroendocrine carcinoma	9
Adenosquamous carcinoma	4
Not available	5
Sarcomatous component	
Chondroid	14
Osteoid	8
Leiomyomatous	11
Rhabdoid	16
Fibrous	5
Unclassified pleomorphic sarcoma	32
Not available	5

loss, and melena, as the most common complaints. The median age of patients was 66.5 years (range: 39 to 84). The male-to-female ratio was about 3 : 1. The tumor gross appearance was predominantly protruding or ulcerative with a median tumor size of 8 cm (range: 2 to 21). Histologically, the two components of malignancy varied widely. In the carcinomatous component, the histology type was commonly the Lauren intestinal-type AC, and rarely SCC, NEC. The sarcomatous component was usually UPS (31 cases), while heterogeneous chondroid, osteoid, leiomyomatous, fibrous, and rhabdoid differentiations were also observed (Table II). Metastatic neoplastic cells exhibited histopathologic features of pure carcinoma, pure sarcoma, or a mixture of both components. The prognosis of patients with carcinosarcoma of the stomach was dismal, and the median survival time was 6 months. There was no significant survival difference between patients with conventional carcinosarcoma and carcinosarcoma, NOS.

Distributional difference

Although the overall proportion of tumor location was similar among the upper, middle, and lower portion of the stomach, a high (50%) prevalence of cardia involvement was found in Chinese patients, compared to 19% in Japanese, and 13% in other ethnic patient group (Fig. 3). Conventional carcinosarcoma was prone to involve gastric cardia (Fig. 4). But, all these differences did not reach a statistically significant level ($p = 0.0641$ and $p = 0.4350$, respectively).

Discussion

Based on 80 carcinosarcomas of the stomach (4 acquired from our databases and 76 from the literature) we demonstrated heterogeneous histopathologic characteristics and dismal prognosis of this fatal malignancy. Our analysis showed a complex profile of this tumor with intimately admixed carcinomatous and sarcomatous components. The carcinomatous component was mostly of Lauren intestinal-type AC. The sarcomatous component was variable. Sarcomas with discernable differentiation included, in a descending order of frequency, rhabdomyosarcoma, chondrosarcoma, leiomyosarcocma, and osteosarcoma. Sarcomas with a dual differentiation were found in 9 cases. UPSs were diagnosed in 41% (31/75) of carcinosarcomas and frequently imposed diagnostic challenges. Therefore, a complete workup with immunohistochemistry and occasionally selected genetic tests is necessary in daily diagnostic practice. Because of the extreme rarity, a thorough investigation of tumors in other organs seems to be critically important before a definitive diagnosis of carcinosarcoma is made. In addition, such a diagnosis should not be provided on small biopsies and cytology specimens.

Although gastric carcinosarcomas may arise from any region of the stomach, gastric cardia appears to be the predominant site in Chinese patients. This observation is consistent with that of gastric cancer epidemiologic studies. According to the 2012 WHO statistical data [52], over 42% of world-wide gastric cancers occurred in Chinese patients and gastric cardiac cancer accounted for over 23% of gastric cancer resections in one large single center study, which is over 10-times higher than that in other ethnic patient populations [53, 54]. Unlike cancer in the non-cardiac region, gastric cardiac cancer demonstrates a much broader spectrum of histopathologic growth features in Chinese patients [55, 56, 57]. In addition, the gastric cardia is more likely to be involved by conventional carcinosarcoma that shows various sarcomatous differentiation. These findings may support the concept of the critical role of pluripotent/residual

embryonic stem cells in carcinogenesis of gastric cardiac cancer [58].

It has been believed that a primary carcinoma could stimulate excessive stromal growth resulting in a carcinosarcoma [5, 59]. others have claimed that stromal proliferation may be monoclonal and derive from the carcinoma or from a stem cell that undergoes divergent differentiation [19, 60]. The monoclonal origin has been demonstrated in other organs, such as the uterus and breast [61, 62, 63, 64, 65]. In one case report, an ulcerative gastric adenocarcinoma at initial diagnosis, rapidly, within two months, changed its shape into an exophytic mass, in which over 90% of the tumor mass showed the spindle cell and osteoid morphology in the tumor epicenter of the radical resection specimen [28]. The sarcomatous component appears to be responsible for the rapid progression of carcinosarcomas.

At present, there are no guidelines on therapy of this cancer. The reported outcome after radical resection stays poor. For unresectable cases, S-1 plus cisplatin has been proven to be transiently effective [3]. Current terminology does not take into account possible future targeted therapy of sarcomatous component of this rare tumor. Therefore, we proposed a simple new classification scheme covers almost all reported cases of gastric carcinosarcoma and may provide useful information for targeted treatment of various sarcomatous components of this tumor. In order to reveal various types of sarcomatous differentiation, adequate sampling of the tumor is necessary. Our proposal somewhat parallels that used for breast metaplastic carcinoma [65].

In summary, we showed that carcinosarcomas of the stomach comprise a heterogeneous group of tumors with various histopathologic features. We propose that depending on presence or absence of detectable sarcomatous differentiation, carcinosarcomas could be classified as conventional or NOS, based on the results of immunohistochemical assessment. Such distinction may provide useful information for targeted treatment of various sarcomatous components of this tumor. Analysis of the literature suggests that carcinosarcomas in the gastric cardia are prevalent in the Chinese patient population as compared with patients of other ethnicities.

The authors declare no conflict of interest.

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