

REVIEW ARTICLE

Gastric carcinosarcoma: a rare clinical entity looking for an identity

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Summary

Carcinosarcoma of the stomach represents a rare variant of gastric malignancies. It is composed of intimately mixed epithelial and mesenchymal elements. Only few cases of gastric carcinosarcoma have been reported in the literature. Surgical treatment is the only curative modality, but the disease progress is usually aggressive and its prognosis remains poor even after curative treatment. The definitive diagnosis is usu-

ally made by histopathological and immunohistochemical analysis of the resected tumor. This review summarizes the available data concerning epidemiology, pathogenesis, clinical characteristics, diagnosis, histopathology, treatment and prognosis of gastric carcinosarcoma.

Key words: biphasic tumor, carcinosarcoma, gastric cancer

Introduction

Gastric cancer represents the fifth most common malignancy and the third cause of cancer-related death [1]. More than 90% of malignant gastric tumors are classified as adenocarcinomas (AC). Furthermore, gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal (GI) tract with 50-60% of GISTs occurring in the stomach [2]. Carcinosarcoma (CS) of the stomach is a rare, aggressive variant of gastric malignancies, described only in few case reports in the literature. The purpose of this review was to summarize the existing data on epidemiology, pathogenesis, clinical characteristics, diagnosis, histopathology, treatment and prognosis of gastric CS.

Definition and epidemiology

CS of the stomach is a rare, biphasic malignant tumor composed of intimately mixed epithelial and mesenchymal elements. It is defined by WHO as 'a malignant tumor composed of intimately mixed epithelial and mesenchymal elements of a type ordinarily found in malignancies of adults [3]. It is commonly found in other organs such as the uterus, ovary, breast, esophagus, thyroid gland, lung, larynx, and urinary system [4]. The most common site of origin is the uterus. In the alimentary tract, CS appears most commonly in the esophagus. About 60 cases of gastric CS have been reported in the literature. The reported median age of patients affected by gastric CS is 62 years (range 29-80) and males predominate over females (M:F=2.8:1) [3].

Pathogenesis and histological classification

CS is classified into three histological patterns based on its origin. In type I, 'collision' tumors, there is a sharp interface between the two tumor components, with no or with minimal mixing. In type 2, or 'combination' tumors, the two components mix completely without maintaining discrete stromal components. In type 3, or 'composite' tumors, the two components mix but maintain recognizable stromal differentiating features [4]. Some authors propose a biclonal origin of CS, which supports the collision tumor theory [5]. A common stem cell origin having an ability to pursue both epithelial and mesenchymal differentiation, analogous to malignant mixed Mullerian tumours of the uterus, has been also supported for gastric CS [6]. The AJCC/UICC TNM staging system does not have any specific classification for gastric CS; however, it is utilized by some authors based on the disease stage of the carcinoma component [7,8].

Diagnosis

The clinical, endoscopic and radiological presentation of gastric CS does not differ from this of gastric AC. Symptoms are usually not specific and include dysphagia, weight loss, anorexia, fatigue, vomiting, upper GI bleeding, epigastric pain, palpable epigastric mass and anemia. The serum levels of carcinoembryonic antigen (CEA) can be normal or elevated, while increased serum levels of carbohydrate antigen (CA 19-9), CA 125 and alpha-fetoprotein have been reported [8,9]. In the computed tomography (CT) the tumor size varies between small nodular lesions and huge prominent formations; a tumor size of 21x14x18 cm has been described [9]. Moreover, perigastric, paraortic, retroperitoneal and subclavicular lymph nodes may be involved whereas liver metastases have been also reported [3,10-12]. Li et al. published 18F-FDG PET/CT images of a gastric CS, showing a large mass in the stomach with SUVmax of 11.9 [10]. In the upper GI endoscopy the lesion can be exophytic, submucosal, ulcerative, with well-defined or indistinct borders. Since the surfaces are ulcerated and they frequently infiltrate the gastric wall by forming large tumor masses, they are often mistaken for Borrmann III AC [7].

Endoscopic biopsy does not always reveal the definitive diagnosis; due to severe tissue necrosis and hemorrhage no malignant cells may be identified and a specific histologic type may not be determined [7,13]. Furthermore, only an epithelial

or sarcomatous component of the tumor may be observed, falsely suggesting a poorly differentiated AC or a sarcoma [5,12,14]. Because of poor differentiation, conventional H&E staining alone may not be useful for the definitive diagnosis and additional immunohistochemical stains may be required [7]. Histopathological and immunohistochemical analysis of the resected tumor is the gold standard for the diagnosis of the gastric CS. Microscopy reveals carcinoma and sarcoma components, mixed in different patterns, corresponding to the histological classification mentioned above. The most common carcinoma component in gastric CS is tubular or papillary adenocarcinoma [5]. Teramachi et al. reported a case of gastric CS whose carcinoma component consisted entirely of endocrine cell carcinoma [15]. One case of gastric CS with the carcinoma component consisting of AC and squamous cell carcinoma has been also reported [16]. The sarcomatous areas consist typically of spindle cells with elongated oval nuclei and eosinophilic cytoplasm showing frequent mitotic activity and arranged irregularly or in an interlacing bundle pattern. Rhabdomyo-, chondro- or osteosarcomatous, osteoblastic, leiomyosarcomatous and myofibroblastic differentiation have been reported [14,15,17-19].

Immunohistochemically, the cells of the sarcomatous component show affinity for vimentin, desmin and smooth muscle/sarcomeric actin [20,21]. The epithelial components may show positive reaction for epithelial membrane antigen (EMA), CEA, cytokeratin, AFP and negativity for the mesenchymal markers [5,13]. Positivity of the epithelial component for chromogranin A and synaptophysin implies neuroendocrine differentiation [14,15]. Moreover, positive nuclear staining with p53 and Ki-67 in both components has been reported [12,22].

Treatment

Treatment of gastric CS depends on the disease stage and the patient's general condition, but surgical treatment is mostly performed. The most common surgical procedure carried out is total gastrectomy. Curative treatment includes resection of perigastric lymph nodes [8,15,23]. A case of laparoscopic distal gastrectomy with D2 lymph node dissection has been reported [18]. Gohongi et al. reported a case of a 70-year-old man with a CS occupying the upper anterior wall of the stomach with enlarged hepatogastric and paraaortic lymph nodes, to whom one course of neoadjuvant chemotherapy consisting of tegafur, gimestat, otastat potassium and cisplatin was initially applied without

radiological signs of tumor downstaging before he was submitted to a total gastrectomy [8]. Because of tumor invasion in the surrounding structures, splenectomy, distal pancreatectomy and left adrenalectomy has also been reported [3,13]. Wedge resection as well as radiofrequency ablation have been performed to treat liver metastases, when feasible, at the time of gastrectomy [3,12].

Palliative gastrectomy or subtotal gastrectomy is also considered as an option in order to control a gastric CS when bleeding [7,22]. Palliative systemic chemotherapy with S-1 and cisplatin followed by second-line irinotecan and mitomycin has been also used [22].

Best supportive care is considered in case of rapid tumor growth in patients with poor general status to undergo a surgical operation [9].

Prognosis

The prognosis of gastric CS is poor because of its aggressive biological behavior and its usual

delayed clinical presentation at an advanced stage. The mean survival period is estimated to be 10-15 months, while more than 50% of tumor recurrences occur in the first postoperative year in peritoneal surface or liver [7,17,24]. Ashida et al. reported a patient with gastric CS who survived 7 years post-operatively [25].

Conclusion

Gastric CS represents a rare entity of biphasic tumors of the stomach. Carcinoma and sarcoma components coexist in different histologic patterns. The definitive diagnosis is usually made by immunohistochemical analysis of the biopsy specimen or even postoperatively. Surgical treatment represents the only curative option, but the overall prognosis is poor.

Conflict of interests

The authors declare no conflict of interests.

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