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CASE REPORT

Primary gastric adenosquamous carcinoma: a case report and literature review

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Abstract

Primary gastric adenosquamous carcinoma (GASC) is exceedingly rare. It accounts for less than 1% of all gastric cancers. In this report, we describe our pathological findings along with a review of the literature to improve our understanding of the disease and reduce misdiagnosis, as well as to provide evidence for its treatment and prognosis. A 49-year-old male patient was admitted to our hospital (Dalian Municipal Central Hospital, Dalian, China) with a complaint of epigastric pain that had persisted for half a month. Physical examination, regular laboratory blood tests, and computed tomography revealed no obvious abnormalities. Gastroscopy revealed ulcers in the lower part of the stomach, and pathological assessment revealed adenocarcinoma. Radical gastrectomy was performed, and the folinic acid, fluorouracil, oxaliplatin (FOLFOX) chemotherapy regimen was administered postoperatively. Pathological assessment of the mass revealed a protruding tumor measuring 1.5 × 1.5 × 0.7 cm in the lower part of the stomach. The tumor infiltrated through the full wall of the stomach. This was confirmed by immunohistochemical (IHC) staining for cytokeratin (CK) (+), villin (-), p63 (++), and high-molecular-weight CK (+++). The patient remains alive with no recurrence more than seven years after surgery. Primary GASC is a rare malignant neoplasm. The diagnostic criteria for GASC mainly depend on the clinical, radiographic, and histopathological findings. Pathological assessment and IHC staining can be utilized to confirm the diagnosis. Radical gastrectomy plus postoperative chemotherapy containing the FOLFOX regimen is effective for treating GASC and might contribute to long-term survival.

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Gastric cancer is one of the most common malignant tumors. Gastric adenocarcinoma is most prevalent in patients with gastric cancer, and squamous cell carcinoma is relatively rare with a poor prognosis [1]. Meanwhile, adenosquamous carcinoma is a rarer malignancy than adenocarcinoma and squamous cell carcinoma. Adenosquamous carcinoma contains elements of both squamous cell carcinoma and adenocarcinoma in the same tumor [1]. Primary gastric adenosquamous carcinoma (GASC) is characterized by the squamous cell carcinoma component making up ≥ 25% of the entire tumor mass [1–2]. GASC is an extremely rare entity and accounts for less than 1% of all gastric malignancies [3]; metastasis and recurrence commonly occur in the early stage, so the prognosis is poor. At present, the pathogenesis of GASC is still unclear, and its clinicopathological features and standardized treatment methods have not been established. Most publications regarding its clinicopathological manifestations are primarily in the form of case reports; therefore, there is limited awareness regarding GASC.

Here, we describe a patient with primary GASC with epigastric pain as the initial presentation who remains alive more than seven years after treatment that included

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a combination of surgery and chemotherapy to improve the diagnosis and treatment of GASC.

Case report

A 49-year-old male patient who presented with the chief complaint of epigastric pain that persisted for half a month was admitted to Dalian Municipal Central Hospital, China. The pain was paroxysmal, dull, and more serious after consuming a meal, but did not present with acid regurgitation, belching, nausea, or emesis. As the patient did not experience any relief from the pain after taking omeprazole orally, he visited our hospital on July 7, 2011. Physical examination showed a body temperature of 36.5℃, pulse rate of 60 beats/min, and blood pressure of 130/80 mmHg. His abdomen was soft and nontender, and the liver and spleen were not palpable. Laboratory data showed a hemoglobin level of 163 g/L and a hematocrit level of 43.9%. Chest and abdomen computed tomography did not identify any abnormalities in the liver, lungs, and kidneys. The levels of tumor markers, including carcinoembryonic antigen (CEA), alpha fetoprotein, and carbohydrate antigen 19-9 (CA19-9), were within normal limits.

Gastroscopy revealed an ulcerative lesion in the small curved side of the lower part of the stomach, about 1.2 × 1.2 cm in size, with rough and uneven surface mucosa, dirty coating, irregular surrounding mucosa, and unclear boundaries with surrounding tissues (Fig. 1). The pathological diagnosis of the biopsy specimen indicated adenocarcinoma. Laparoscopy-assisted total gastrectomy was performed successfully on July 11, 2011, and the patient recovered well. His postoperative hemoglobin level was 138 g/L, hematocrit level was 39.7%, and CEA and CA19-9 levels were 1.26 ng/mL and 2.77 U/mL, respectively. Pathological examination of the mass showed a protruding tumor measuring 1.5 × 1.5 × 0.7 cm, which infiltrated the full wall of the stomach, but had not invaded the incised edge. In addition, none of the perigastric lymph nodes showed metastasis, and vascular congestion, interstitial edema, and cancer invasion in the omentum were not detected (Fig. 2). The pathological manifestations under high-power lens confirmed the presence of a mixed-pattern carcinoma (glandular and squamous components). Immunohistochemical (IHC) staining analysis showed cytokeratin (CK) (+), villin (-), C-erbB2 (+), p63 (++), and high-molecular-weight CK (+++) (Fig. 3). Therefore, the pathological diagnosis of the resected specimens was well-differentiated GASC. The patient then received chemotherapy containing the folinic acid, fluorouracil, oxaliplatin (FOLFOX) regimen that included tegafur capsules, calcium folinate, and fluorouracil twice daily for two weeks with a one-week break, for a total of seven courses over five months. The patient recovered well, and his CEA and CA19-9 levels were 3.19 ng/mL and 4.48 U/mL, respectively, after chemotherapy. The patient is currently alive and has had no recurrence.

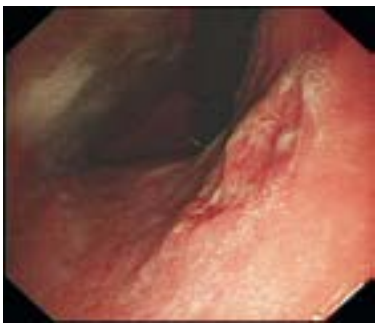

Fig. 1 Gastroscopy showing a sunken ulcerative lesion (1.2 × 1.2 cm) in the small curved side of the lower part of the stomach

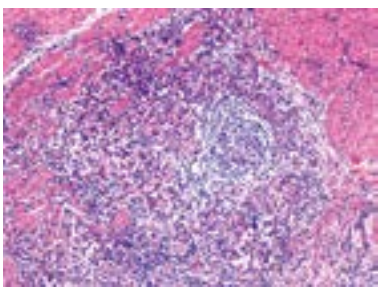

Fig. 2 There was infiltration of poorly differentiated squamous cell carcinoma with slight adenocarcinoma components (hematoxylin and eosin staining, × 100)

Discussion

Adenosquamous carcinoma has been reported to develop in various sites in the digestive tract, such as the esophagus, esophagogastric junction, colon, and hepatobiliary tract; it has aggressive clinicopathological features and a poor prognosis. GASC is a rare cell type of gastric cancer compared with the predominant adenocarcinoma type that has an incidence of more than 90% [4]. Differences in etiology, pathogenesis, and survival also exist between gastric adenocarcinoma and GASC. Some authors have reported that GASC is a mixed neoplasia (gland-like and squamous) and has a male:female ratio of approximately 4:1 [5-8]. The histogenesis of GASC is still unclear. Several hypotheses have been postulated on the origin and metaplastic transformation of GASC [5, 7, 9–10], such as squamous metaplastic transformation of adenocarcinoma, cancerization of ectopic squamous epithelium [6–7], collision of adenocarcinoma and squamous cell carcinoma [7], cancerization of metaplastic squamous cells [9], and stem cell differentiation toward

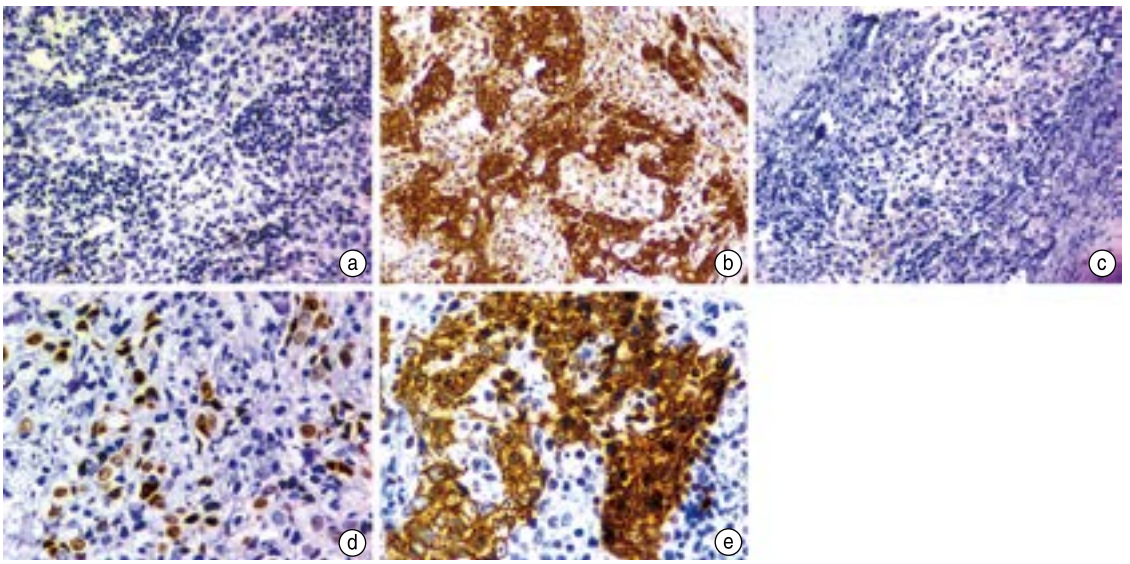

Fig. 3 IHC analysis. The neoplastic cells tested negative for villin (a) and positive for CK (b), C-erB2 (c), P63 (d), and high-molecular-weight cytokeratin (e)

two cell lines: glandular and squamous [8, 10].

The clinical manifestations of GASC are not consistent and similar with those of gastric adenocarcinoma; it is mainly manifested as abdominal pain, and a few patients manifest acid regurgitation, abdominal distension, and black stool. In the present case, the patient was a middle-aged man; the first clinical manifestation was epigastric pain; there were no other positive pathological manifestations; and laboratory blood tests, tumor markers, and computed tomography showed no obvious abnormalities. Gastroscopy revealed ulcer lesions in the lower part of the stomach.

In the diagnosis of GASC, endoscopic biopsies are superficial and limited in scope, whereas the differentiation, distribution, and composition of squamous cell carcinoma and adenocarcinoma are usually diversified. Preoperative diagnosis of GASC is particularly difficult, and most patients can only be diagnosed by relying on postoperative pathology and IHC analysis. The IHC features of GASC are squamous epithelial CK5/6 expression, CK macromolecule, obvious p63 positivity, focal CK8/18 expression, glandular epithelial low-molecular-weight CK expression, and obvious CK8/18 expression [11]. Chen *et al* have pointed out that poorly differentiated squamous cell carcinoma in gastric adenosquamous carcinoma is not easy to distinguish from neuroendocrine carcinoma, which could be examined by positive expression of chromogranin and synaptophysin [12]. In our case, there was CK macromolecule and obvious p63 positivity in squamous cell carcinoma components but negativity in adenocarcinoma components. CK was weakly positive in adenocarcinoma components, supporting the diagnosis of GASC. Therefore, to improve the accuracy of diagnosis, when GASC is morphologically suspected, additional IHC staining of CK, CK5/6, P63, CK8/18, and CK macromolecule should be performed.

A standard treatment approach for GASC has yet to be established. Radical surgery is extremely crucial when feasible. Similarly, adjuvant therapy such as chemotherapy, immunotherapy, and radiotherapy are also important in prolonging survival and improving the quality of life of patients postoperatively. Ebi *et al* [7] reported that postoperative S-1 chemotherapy may therefore be very useful for treating patients with GASC and that peritoneal metastasis is one of the main factors for the dismal prognosis. The 5-year survival rate is approximately 10%, and the median survival time is only 12 months. A case of palliative gastrectomy for a GASC with peritoneal dissemination in a patient who underwent a course of systemic chemotherapy containing S-1 plus paclitaxel (PTX) after surgery was reported by Hirano *et al* [13]. No serious adverse events were observed, and treatment with S-1 plus PTX was continued for 1 year before being switched to adjuvant chemotherapy containing S-1 alone for another year. The patient remained in clinical remission and survived for over 8 years. In our case, the patient underwent radical total gastrectomy, was followed up for seven courses of chemotherapy containing the FOLFOX regimen, and survived without recurrence after seven years of follow-up.

GASC is characterized by more aggressive clinicopathological features and has a poor prognosis despite its major biological determinant being the adenocarcinoma component [14–15]. Feng *et al* reported that most patients with GASC developed lymph node

metastasis and that most patients were diagnosed in the middle and late stages [16]. Li *et al* summarized the clinical data of 42 cases of primary GASC. They found that all patients had an average survival time of 36.4 months; median survival time of 28.0 months; and overall 1-, 3-, and 5-year survival rates of 82.2%, 42.3%, and 18.2%, respectively [17]. Univariate analysis revealed that tumor size, Borrmann type, tumor differentiation, radical gastrectomy, lymph node metastasis, and clinical stage were associated with postoperative survival. Multivariate analysis revealed that tumor differentiation, radical gastrectomy, and clinical stage were independent prognosis factors. In our case, the patient underwent radical total gastrectomy, was followed up with chemotherapy containing FOLFOX, and survived for more than seven years.

In conclusion, a rare case of GASC that was successfully controlled with surgery and chemotherapy was herein described. Postoperative FOLFOX chemotherapy may therefore be very useful for treating patients with GASC. Due to the limited number of cases we collected, the long-term therapeutic effects need to be further studied.

Conflicts of interest

The authors indicate no potential conflicts of interest.

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