

Case report of primary gastric adenosquamous carcinoma

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Abstract

Gastric adenosquamous carcinoma is an extremely rare variant of gastric cancer. This type of malignancy is more aggressive and has worse prognosis when compared to gastric adenocarcinoma. Due to the small number of reported cases, the most appropriate management of this kind of tumor is still in debate. We report the case of a 71-year-old woman who underwent subtotal gastrectomy with D2 lymphadenectomy for an ulcerative lesion in the antrum of the stomach that turned out to be a primary gastric adenosquamous cell carcinoma. After curative surgery, patients with primary gastric adenosquamous cell carcinoma must be enrolled in strict follow-up protocols, since the risk for metastasis is high.

Keywords

Adenosquamous carcinoma; Gastric cancer; Stomach cancer.

Introduction

Gastric adenosquamous carcinoma (GASC) is a very rare variant of gastric cancer, accounting for less than 1% of cases [1]. GASC is more aggressive and carries a worse prognosis compared to gastric adenocarcinoma (GAC) [2]. Due to the small number of reported cases, the most appropriate management of this kind of tumor is still in debate. We present a case report of a patient with GASC from our institution in order to provide information for future cases and researches about this histological type.

Case Presentation

We present the case of a 71-year-old woman with no relevant medical history, who presented to emergency department with vomiting and epigastric pain over a 1-month period. She also reported unintentional 7 kg weight loss. She had a benign physical exam. On laboratory evaluation, she had anemia (hemoglobin 9.0 g/dl). Esophagogastroduodenoscopy (EGD) demonstrated an ulcerating lesion in gastric antrum (Figure 1) and biopsies obtained by EGD showed poorly differentiated carcinoma with immuno-

histochemical stains consistent with squamous cell carcinoma. A computed tomography (CT) scan of the thorax, abdomen and pelvis demonstrated irregular thickening of the antrum wall, caused by a stenosing circumferential lesion, which conditions a marked gastric distension (25 X 11 X 9 cm). There were multiple lymph nodes on hepatic hilum with dimensions up to 8mm. There was no evidence of distant metastasis. She was recommended for surgery due to the presence of obstructive symptoms and GI bleeding. The patient underwent an open subtotal gastrectomy accompanied by a D2 lymphadenectomy with Roux-en-Y gastrojejunostomy. Final histopathological examination of the tumor was consistent with GASC, composed of both squamous cell and adenocarcinoma (Figure 2a). The former showed squamous differentiation and areas of keratinization (Figure 2a), with positive p40, a marker of squamous differentiation, on immunohistochemical (Figure 2b). The latter showed foci of mucin production (Figure 2c) as evidenced by periodic acid-Schiff-diastase staining (Figure 2d). Carcinoma cells invaded into the serosa. Seven of 42 lymph nodes were positive. According to the American Joint Committee on Cancer (AJCC, 8th edition) staging, the patient stage was pT4aN3aM0 (stage IIIB). Concerning the rarity of this histologic type, the patient performed an abdominal MRI and PET scan to exclude an extra-gastric origin. PET scan showed a suspect hepatic metastasis in segment 6 and abdominal MRI showed four hepatic lesions. Adjuvant chemotherapy was recommended. She started on cisplatin and 5-fluorouracil (5-FU) regimen. Follow-up CT scan after 6 cycles showed multiple adenopathic retroperitoneal lesions. The patient was started on FOLFIRI, but follow-up CT scan showed an increase in size and number of abdominal metastasis. The patient was switched to palliative chemotherapy with paclitaxel. Unfortunately, disease progressed with biliar obstruction and patient died 21 months after diagnosis.



Figure 1: Endoscopic findings: ulcerating lesion in gastric antrum.

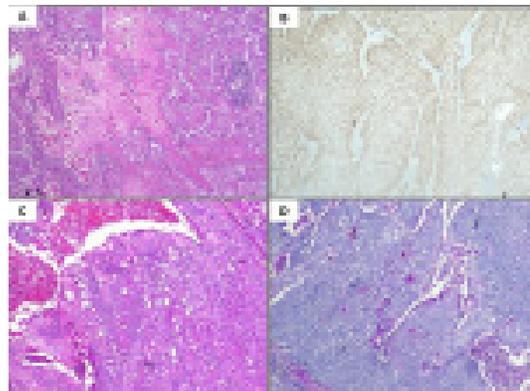


Figure 2: Histopathological findings of subtotal gastrectomy. On hematoxylin and eosin staining (H&E), a transmural malignant epithelial neoplasm with solid or nested architecture was found. The tumour displayed squamous differentiation and areas of keratinization (A – H&E, 20X), which expressed p40 diffusely and heterogeneously (B – p40, 20X). There were foci of mucin production (C – H&E, 20X), as evidenced by periodic acid-Schiff-diastase staining (D – PAS/D, 20X).

Discussion

Gastric cancer has increasingly been recognized as a heterogeneous disease, each histologic subtype of GC differs in its biology, so histology is very important in individualized evaluation of patients with gastric cancer [3]. Due to the rare incidence of GASC, most of the literature is described in case reports.

The diagnosis of GASC is based on the presence of both adenocarcinoma and squamous cell carcinoma (SCC) on histopathological examination, with the squamous cell component constituting at least 25% of the tissue [1]. Besides this, the tumor must be outside the cardia, without esophageal involvement and without adenosquamous carcinoma in other organs [4].

The origin of the SCC component remains obscure since the first report of this rare disease in 1905 by Rolleston and Trevor [5]. Several hypotheses have been proposed for pathogenesis of GASC: squamous metaplastic transformation of adenocarcinoma, transformation of ectopic squamous epithelium or transformation of metaplastic squamous cells; fusion of coexisting squamous cell carcinoma and adenocarcinoma [4], or stem cells differentiation toward both glandular and squamous cells [1,5]. The most convincing hypothesis regarding the pathogenesis of the SCC component is squamous metaplasia of a preexisting GAC, which is widely accepted by most authors [6,7].

The highlights of this case report are as follows: (1) atypical presentation in a Caucasian woman and (2) the presence of GASC only at final postoperative diagnosis.

In the case we report the initial biopsy obtained by EGD showed poorly differentiated carcinoma with immunohistochemical stains consistent with squamous cell carcinoma, however final histopathological examination of the tumor was consistent with GASC, composed of both squamous cell and adenocarcinoma.

GASC is more common in men, Asians, and incidence peaks in the 6th decade of life[8]. It is an extremely aggressive tumor, and the majority of these tumors are found in an already advanced stage on initial diagnosis. Hence, GASC is associated with a worse prognosis than conventional adenocarcinoma [2][8], with the 3-year overall survival rate reported to be 15.4% [1].

Feng et al (167 cases of GASC) demonstrated that 25.4% of patients with GASC had distant metastasis, and its most common location was the liver, followed by peritoneal dissemination[2].

Ge et al, in a retrospective cohort study, concluded that patients with GASC had higher rates of poorly differentiated tumors and a higher rate of metastasis, and more than 15% of patients had a tumor that was at T4 stage [9].

Our patient had an advanced stage at diagnosis, with metastization in 7 of the 42 nodes studied, which is consistent with the reports in the literature, that the GASC usually behaves like an aggressive adenocarcinoma and presents with early lymphatic metastization [8]. She had a survival of 21 months which was worse than that of stage IIIB gastric adenocarcinoma (overall survival IIIB = 32,8 months, AJCC, 8th edition).

The role of the SCC component in the survival of patients with gastric cancer is not well construed. Usually, the SCC component is associated with less favorable survival than the conventional gastric adenocarcinoma component [8,2,1,4]. However, it appears that the adenocarcinoma component plays a leading role, even when it is not superior to the SCC component in quantity [10]. Adenocarcinoma components are predominantly found in hematogenous and hepatic metastases. The existence of the adenocarcinoma or SCC component in the metastatic lymph nodes remains controversial in the literature [11]. Some studies

showed only the adenocarcinoma [12] or SCC component [10] and others demonstrated both components. Some authors [11] believe that the ratio of the adenocarcinoma to SCC component in metastatic lymph nodes might influence the prognosis of gastric ASC. The hypothesis is that GASC with major component of adenocarcinoma in metastatic lymph node may be more aggressive than those with major component of SCC in metastatic lymph node.

In our case, metastatic lymph nodes were infiltrated by a carcinoma with same characteristics of the gastric carcinoma. There was no information about the ratio of the adenocarcinoma to SCC component. Hepatic biopsy was not performed, so we do not have information about the component of metastases.

There is no standard of care of GASC. Surgical resection remains the most commonly used treatment modality in the literature despite about half of the patients with GASC present with metastatic disease. There is limited data about the surgery, radiotherapy and chemotherapy use in this rare pathology. Data is limited to institutional case series and varies significantly [1].

Surgical resection was performed in about 77% of the GASC cases in two of the largest case series published in literature. Use of adjuvant therapy in published literature ranges between 15% and 46% [1,2].

In Li et al study, chemotherapy did not prove to be a prognostic factor in the multivariate analysis. Several possible reasons include the following: the high malignancy of this disease and insensitivity to chemotherapy; not enough statistical power due to the limited sample; the statistical effect of chemotherapy for survival is overshadowed by surgery; and the resistance of cytotoxic drugs caused by the multipotential stem cells [13].

After curative surgery, patients with primary GASC must be enrolled in strict follow-up protocols, since the risk for metastasis is high.

Conclusion

GASC is an extremely rare variant of gastric cancer, with poor outcome that could be attributed to the aggressive nature of these tumors with a higher likelihood of serosal invasion, early lymph node involvement or the presence of distant metastasis at the time of diagnosis. Surgical resection remains the gold standard treatment for GASC, although the rate of tumor recurrence/metastasis remains high even after radical resection. Further investigations are needed to determine the prognostic factors and find new therapeutic approaches to achieve better prognosis.

Declarations

Acknowledgments: None to declare.

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Informed Consent: Written Consent was obtained from patient.

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Manuel Oliveira were responsible for the supervision.

Data Availability: The authors declare that data supporting the findings of this study are available within the article.

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