https://doi.org/10.22516/25007440.1329

Case report

Gastric Adenosquamous Carcinoma. A Rare Tumor With Aggressive Behavior: Case Report

Felipe Portilla-Arenas,[1] Franz Carlos Basuri-Guzman,[2] Miguel Andrés Lima,[3] Mónica Arcos-Ramírez,[4] Melissa Bastidas,[5] José Darío Portillo-Miño.[6*]

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Citation:
Portilla-Arenas F, Basuri-Guzman FC, Lima MA, Arcos-Ramírez M, Bastidas M, Portillo-Miño JD. Gastric Adenosquamous Carcinoma. A Rare Tumor With Aggressive Behavior: Case Report. Revista. colomb. Gastroenterol. 2025;40(4):512-516. https://doi.org/10.22516/25007440.1329

[1] Medical School, Universidad Libre. Medical Internship Program, Fundación Hospital San Pedro. Pasto, Nariño, Colombia.
[2] Medical School, Fundación Universitaria San Martín. Medical Internship Program, Fundación Hospital San Pedro. Pasto, Nariño, Colombia.
[3] Physician, subspecialist in Surgical Oncology. Surgical Oncologist. Department of Surgical Oncology, Clinical Research Center, Fundación Hospital San Pedro. Pasto, Nariño, Colombia.
[4] Physician, Specialist in Anatomic Pathology. Department of Pathology, Fundación Hospital San Pedro. Pasto, Nariño, Colombia.
[5] Research Group on Infectious Diseases and Cancer (GINFYCA), Clinical Research Center and Digestive Unit of Gastroenterology and Endoscopy, Fundación Hospital San Pedro. Pasto, Nariño, Colombia.
[6] Research Group on Infectious Diseases and Cancer (GINFYCA), Clinical Research Center, Fundación Hospital San Pedro. Pasto, Nariño, Colombia.

***Correspondence:** José Darío Portillo-Miño.
cic.investigaciones@hospitalsanpedro.org

Received: 15/01/2025
Accepted: 31/03/2025

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Abstract

Gastric cancer ranks as the fifth leading cause of cancer-related mortality worldwide. According to the Global Cancer Observatory (GLOBOCAN), approximately one million new cases and 768,000 deaths were reported in 2020. Gastric adenosquamous carcinoma is exceptionally uncommon, accounting for only 0.2% of cases, with roughly 164 cases described in the literature. We report the case of a 62-year-old man who presented to the emergency department with a one-month history of burning epigastric pain, unintentional weight loss, and hematochezia. Upper gastrointestinal endoscopy revealed a Borrmann type II lesion in the gastric body. Histopathological analysis showed diffuse gastric adenocarcinoma involving both the body and the antrum. Subsequent histology and immunohistochemistry confirmed gastric adenosquamous carcinoma, with positive staining for AE1/AE3 pan-cytokeratin, CK7, and p63, supporting the diagnosis.

Keywords

Gastric cancer, *Helicobacter*, survival, carcinoma, adenosquamous, neoplasms.

INTRODUCTION

Gastric cancer (GC) is the fifth most lethal cancer worldwide. According to the Global Cancer Observatory (GLOBOCAN), approximately 1,000,000 new cases were reported, with an estimated mortality of 768,000 individuals in 2020[(1)]. In Colombia, 7,419 cases of GC were reported, of which 5,505 patients died, making it the leading cause of cancer-related mortality in 2018[(2)]. According to the Lauren classification, adenocarcinoma is divided into intestinal and diffuse types and accounts for approximately 90% of GC cases[(3)]. According to the classifications of the World Health Organization (WHO) and the Japanese Gastric Cancer Association (JGCA), several GC subtypes are recognized based on microscopic morphology and topography, including gastric adenosquamous carcinoma (GASC), squamous cell carcinoma, undifferentiated carcinoma, carcinoma with lymphoid stroma, hepatoid carci-

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noma, adenocarcinoma with enteroblastic differentiation, fundic gland-type adenocarcinoma, micropapillary adenocarcinoma, and other rare histologic variants. Among these uncommon subtypes, GASC represents 0.2%, with approximately 164 cases reported in the literature[3].

Regarding demographic, environmental, and host-related conditions, together with other risk factors that influence disease onset and progression, a family history of GC is present in 10% of cases[4]. In diffuse-type GC, familial factors are related to mutations in the CDH1 gene, which encodes E-cadherin; in addition, mutations may occur in germline genes (CTNNA1)[5]. This type of GC is more frequently observed in hereditary conditions such as familial adenomatous polyposis or Lynch syndrome[6]. Conversely, in intestinal-type GC, associated risk factors include age, male sex, smoking, high salt intake, iron deficiency, and obesity[5]. *Helicobacter pylori* infection is a risk factor associated with both diffuse and intestinal types, including proximal GC and a subset of adenocarcinomas of the gastroesophageal junction[7,8]. The role of the different classical risk factors (diffuse and intestinal) and the *H. pylori*-mediated carcinogenesis model in GASC has not been fully elucidated, which in itself contributes to the development and progression of this tumor type.

In this context, we present a rare clinical case of a patient with GASC, highlighting the associated diagnostic and therapeutic challenges, and we explore the different hypotheses regarding GASC carcinogenesis.

CLINICAL CASE

A 62-year-old male patient presented to the emergency department with burning epigastric abdominal pain, accompanied by weight loss and bloody stools for one month. He reported no significant past medical history. Physical examination revealed a patient with mucocutaneous pallor; the abdomen was soft, compressible, non-distended, with pain on deep palpation in the epigastrium, and no other clinical findings. Laboratory tests showed a hemoglobin level within the range of grade I anemia (10.5 g/dL), with no requirement for transfusion. Upper gastrointestinal endoscopy (UGE) was performed and revealed a Borrmann type II lesion in the gastric body. Colonoscopy showed no relevant findings. According to the histopathological report of the biopsy, the lesion was compatible with diffuse gastric adenocarcinoma involving the gastric body and antrum.

Tumor markers were obtained (carcinoembryonic antigen [CEA] 3.3, CA 19-9: 74.7, CA-125: 22.4). Imaging studies, including computed tomography (CT) of the abdomen and chest, revealed no metastatic foci. Staging laparoscopy demonstrated a tumor at the incisura angularis and along the lesser curvature, with no free fluid in the abdominal cavity. The disease was staged as IIIB (T4N2M0) according to the American Joint Committee on Cancer (AJCC).

Neoadjuvant chemotherapy was initiated using the FLOT regimen, of which the patient received two cycles, followed by ten sessions of radiotherapy as a hemostatic boost due to the finding of tumor bleeding. Subsequently, a laparoscopic total gastrectomy with esophagojejunostomy and Roux-en-Y jejunojejunostomy was performed. Intraoperatively, a lesion involving the body and fundus along the greater curvature and posterior wall of the stomach was identified, firmly adherent to the pancreatic body, measuring 7 × 6 cm. No hepatic metastases, ascites, or omental involvement were found.

Histopathological examination of the resected specimen revealed a Borrmann type IV tumor, a high-grade malignant epithelial tumor measuring 8 × 5 cm, composed of cells with large, bizarre nuclei, glandular chromatin, and prominent micronuclei—some bilobulated—with polygonal, clear, and eosinophilic cytoplasm. The cells formed solid masses and tended to form glands involving the mucosa through the serosa (**Figure 1**). Negative resection margins were obtained.

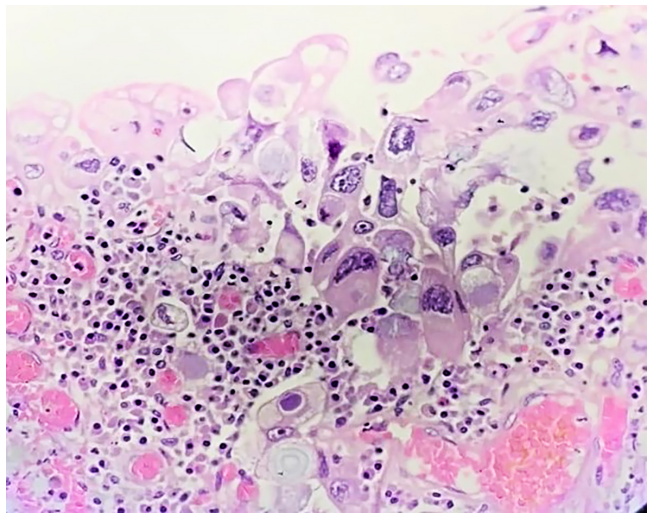


Figure 1. Tumor histopathology. Author's file.

The pathological evaluation was completed with tumor immunohistochemistry, which confirmed gastric adenosquamous carcinoma, with positivity for pancytokeratin AE1–AE3, CK7, and p63; CDX2 expression was observed in the neoplastic cells, with negativity for CK20 and preserved nuclear expression of MSH2, MSH6, MLH1, and PMS2 (**Figures 2–5**). Adjuvant chemotherapy was initiated using the XELOX regimen. The patient remains under follow-up by the Clinical Oncology service.

DISCUSSION

Gastric adenosquamous carcinoma (GASC) is an uncommon type of adenocarcinoma and is therefore rarely reported in the literature, with an incidence rate of approximately 0.2%. GASC is characterized by the formation of keratin pearls, accompanied by intercellular and glandular bridges, with a neoplastic squamous component occupying more than 25% of the tumor[9].

The etiopathogenic process involved in the development of GASC remains unknown. Several hypotheses have been proposed to explain its development and biological behavior; however, to date, there is insufficient evidence to establish a definitive mechanism. In this regard, proposed hypotheses to explain the etiopathogenesis of GASC include the emergence of squamous metaplasia from a pre-existing adenocarcinoma; carcinomatous transformation of non-neoplastic metaplastic squamous cells; malignant

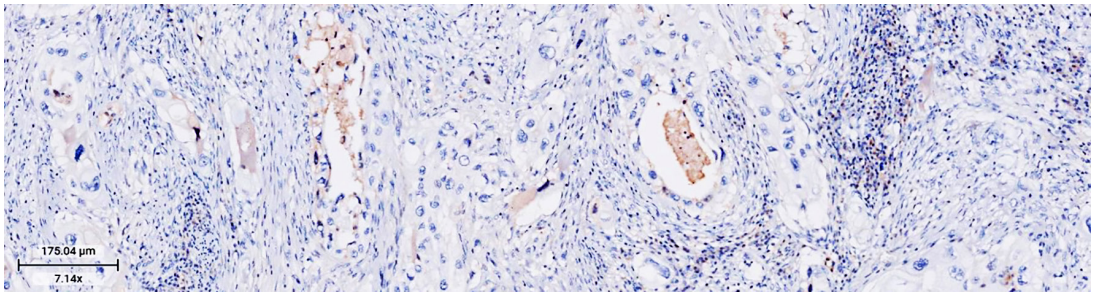


Figure 2.
Immunohistochemistry positive for CDX2.
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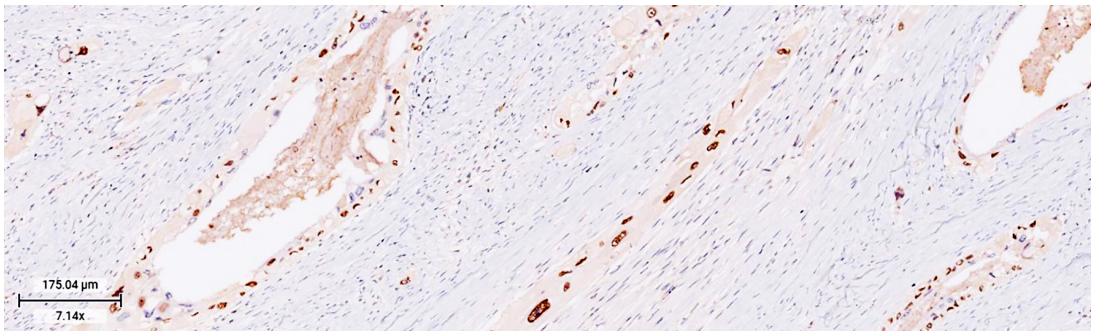


Figure 3.
Immunohistochemistry positive for p63.
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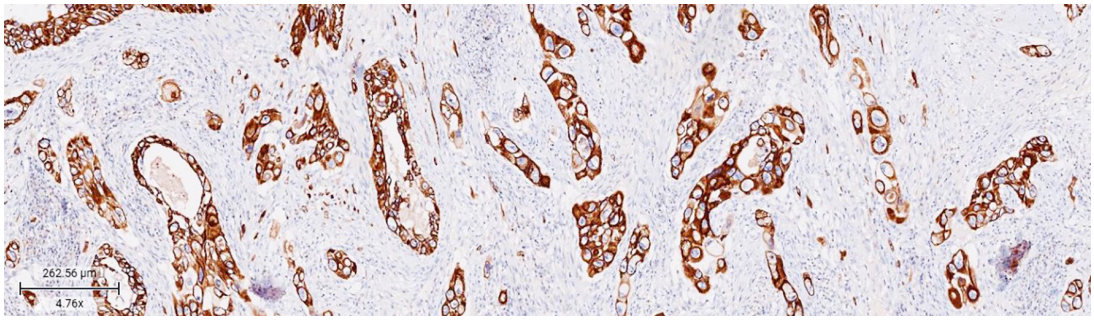


Figure 4.
Immunohistochemistry positive for CK7.
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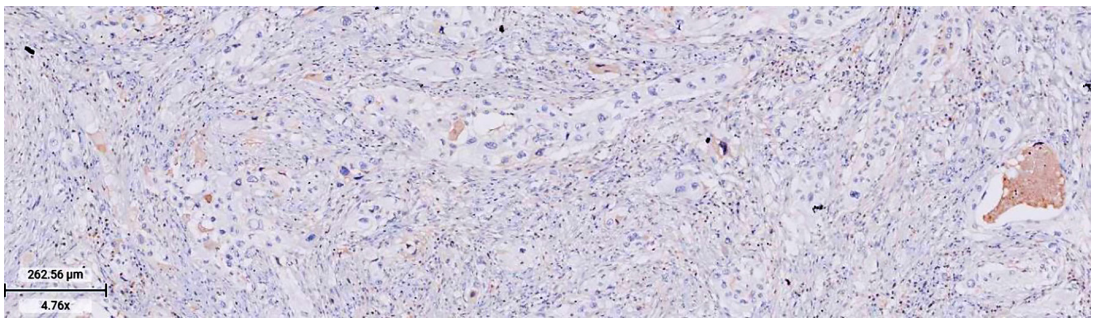


Figure 5.
Immunohistochemistry positive for CK20.
Author's file.

transformation of ectopic squamous tissue; differentiation of squamous and glandular cells from the same stem cell; and collision tumors composed of concurrent adenocarcinoma and GASC[10]. It should also be noted that the appearance of squamous cells may occur from the same stem cell together with cells consistent with adenocarcinoma. In addition, squamous differentiation of preexisting metaplastic cells has been proposed[11]; however, the cellular and molecular mechanisms by which this process culminates in GASC remain unknown. Finally, these theories are supported by reported cases in the literature; nevertheless, discrepancies exist among the findings. Some authors have ruled out squamous metaplasia arising from a preexisting adenocarcinoma, as histologically it represents tissue without a mucin-secreting component[12]. Based on the above, further research is required to elucidate a more precise mechanism underlying the development of this rare type of GC[13–15].

With respect to the immunohistochemical profile identified in the patient, the findings were consistent with gastric cancer with a squamous component, PD-L1 positive with a combined positive score (CPS) of 29, and negative expression of HER2, p63, CK7, and CK2. In the study conducted by Du and colleagues[16], immunohistochemistry showed that 31 patients were positive for p63, CK5, and CK6 in squamous cells, and positive for CK7, CK20, and CK8/18 in adenocarcinoma cells[16]. Owing to its low frequency, very little has been described in the literature regarding the immunohistochemical profile of patients with GASC[17].

Furthermore, due to the limited understanding of this disease, its treatment has yet to be defined in clinical practice guidelines. Surgical resection is widely used; however, given the low incidence of this tumor, approximately half of patients present with metastases at the time of diagnosis. Moreover, there is no consensus regarding the management of GASC, and few studies have described the use of radiotherapy, chemotherapy, and their respective treatment regimens[3,16]. Therefore, as this tumor exhibits aggressive biological behavior and there is no expert consensus on its management, with limited therapeutic options, a poor survival rate has been reported, with a median survival of approximately 17 months[16].

CONCLUSIONS

In conclusion, GASC is an unusual tumor with aggressive behavior and poor survival. Further research is urgently needed to improve understanding of its etiopathogenesis, enabling the identification of new therapeutic targets and the development of standardized, targeted therapies to improve clinical outcomes for affected patients.

Acknowledgments

None.

Conflict of Interest

None.

Funding Sources

None.

Author Contributions

All authors contributed equally to this manuscript.

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