

due to hyperpressure and subsequent colonisation by infectious agents.²

Meanwhile, GE is defined as the presence of gas in the stomach walls caused by disruption of the mucosa and subsequent dissection of air into the wall. Instrument-related iatrogenic trauma to the mucosa (by intubation or endoscopy) is the predominant cause.² In our case, the precipitating factor was the increase in endoluminal pressure associated with vomiting.

The initial symptoms in both conditions are nonspecific (nausea, vomiting, diarrhoea, etc.), which makes the diagnosis more complex. However, fever and systemic involvement tend to be more common in EG, while GE is generally asymptomatic or causes few symptoms.^{1–3}

The presence of gastric pneumatosis on CT is a typical feature of both disorders, while gastric wall thickening and portal pneumatosis are findings suggestive of EG. Upper gastrointestinal endoscopy enables the gastric mucosa to be viewed and samples to be taken for histological and/or microbiological analysis.³

An accurate differential diagnosis is important due to the differences in treatment approach and outcome. EG has a high mortality rate and requires broad-spectrum antibiotic therapy (with coverage of Gram-negative, Gram-positive and anaerobic germs), fluid therapy, and sometimes emergency surgery (where conservative treatment fails or in cases of suspected complications, such as transmural necrosis or perforation). In our case, surgery was required at the outset due to a suspected complication. GE, in contrast, is generally self-limiting with conservative treatment (nil by mouth, gastric decompression with NG tube, PPI, fluid therapy and analgesia).^{4,5}

Funding

No funding was received for this study.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

1. Szuchmacher M, Bedford T, Sukhramwala P, Nukala M, Parikh N, Devito P, et al. Is surgical intervention avoidable in cases of emphysematous gastritis? A case presentation and literature review. *Int J Surg Case Rep.* 2013;4: 456–9.
2. Matsushima K, Won EJ, Tangel MR, Enomoto LM, Avella DM, Soybel DI. Emphysematous gastritis and gastric emphysema: similar radiographic findings, distinct clinical entities. *World J Surg.* 2015;39:1008–17.
3. Reimunde E, Gutiérrez M, Balboa O, Espinel J, Rodríguez C. Neumatosi gástrica. *Gastroenterol Hepatol.* 2002;25:458–61.
4. Belda González I, Soliva Martínez D, Castro García A, Cantero-Ayllon MJ, De Miguel Ibáñez R. Neumatosi gástrica: cuándo no operar. *Cir Esp.* 2018;96: 122–4.
5. Nasser H, Ivanics T, Leonard-Murali S, Shakaroun D, Woodward A. Emphysematous gastritis: a case series of three patients managed conservatively. *Int J Surg Case Rep.* 2019;64:80–4.

Sonsoles Garrosa-Muñoz, Jaime López-Sánchez, Luis Muñoz-Bellvis*

Complejo Asistencial Universitario de Salamanca, Instituto Biosanitario de Salamanca (IBSAL), Universidad de Salamanca, Salamanca, Spain

* Corresponding author.

E-mail address: luismb@usal.es (L. Muñoz-Bellvis).

2444-3824/ © 2020 Elsevier España, S.L.U. All rights reserved.

Submucosal gland adenocarcinoma of the esophagus. A rare non-Barrett's associated tumor



Adenocarcinoma esofágico originado en glándulas submucosas. Un tumor raro no asociado a Barrett

Esophageal carcinoma is the 7th most frequent type of cancer worldwide, with 572.034 new cases in 2018. The most common histological subtype is the squamous cell carcinoma, although the incidence rate of esophageal adenocarcinoma (EAC) is rapidly increasing.¹ The vast majority of EAC arise from Barrett's esophagus located in the lower esophagus and the esophagogastric junction. Less frequently, EAC can develop from the submucosal gland/duct system or gastric heterotopia.^{2,3}

Adenocarcinoma of the esophagus arising from the submucosal gland/duct system is a rare entity, with to our best knowledge, only seven reported cases of patients ranged between 43 and 74 years-old, presenting equally in both sexes.^{2,3} Tumours were more frequently located in the

middle and lower esophagus. Tumors may be more difficult to diagnose, since there is no visible precursor lesion at endoscopy, as in Barrett's esophagus or gastric heterotopia. Patients have been treated with surgery or endoscopic resection, with or without adjuvant therapy. Two patients died at 10 and 15 months. The rest were alive without disease between 18 months and 5 years follow-up.

We present a case of a 56-years old male who consulted with dysphagia. The upper digestive endoscopy revealed a distal esophageal stenosis covered with normal mucosa. (Fig. 1A), the Endoscopic Ultrasound (EUS) showed a hypoechogenic lesion within the esophageal wall invading the submucosa, the muscularis propria and reaching the adventitia. However, the mucosal layer was normal on EUS examination (Fig. 1B). EUS-FNA was performed and revealed an esophageal adenocarcinoma. Computed tomography scan (CT) showed concentric wall thickening (Fig. 1C). The patient received neoadjuvant chemotherapy with FLOT (docetaxel, oxaliplatin and fluorouracil/leucovorin) and an Ivor Lewis esophagectomy was performed. Gross examination revealed a normal mucosa with superficial erosion and no Barrett's esophagus (Fig. 1D). Transversal sections showed the tumor located within the wall thick-

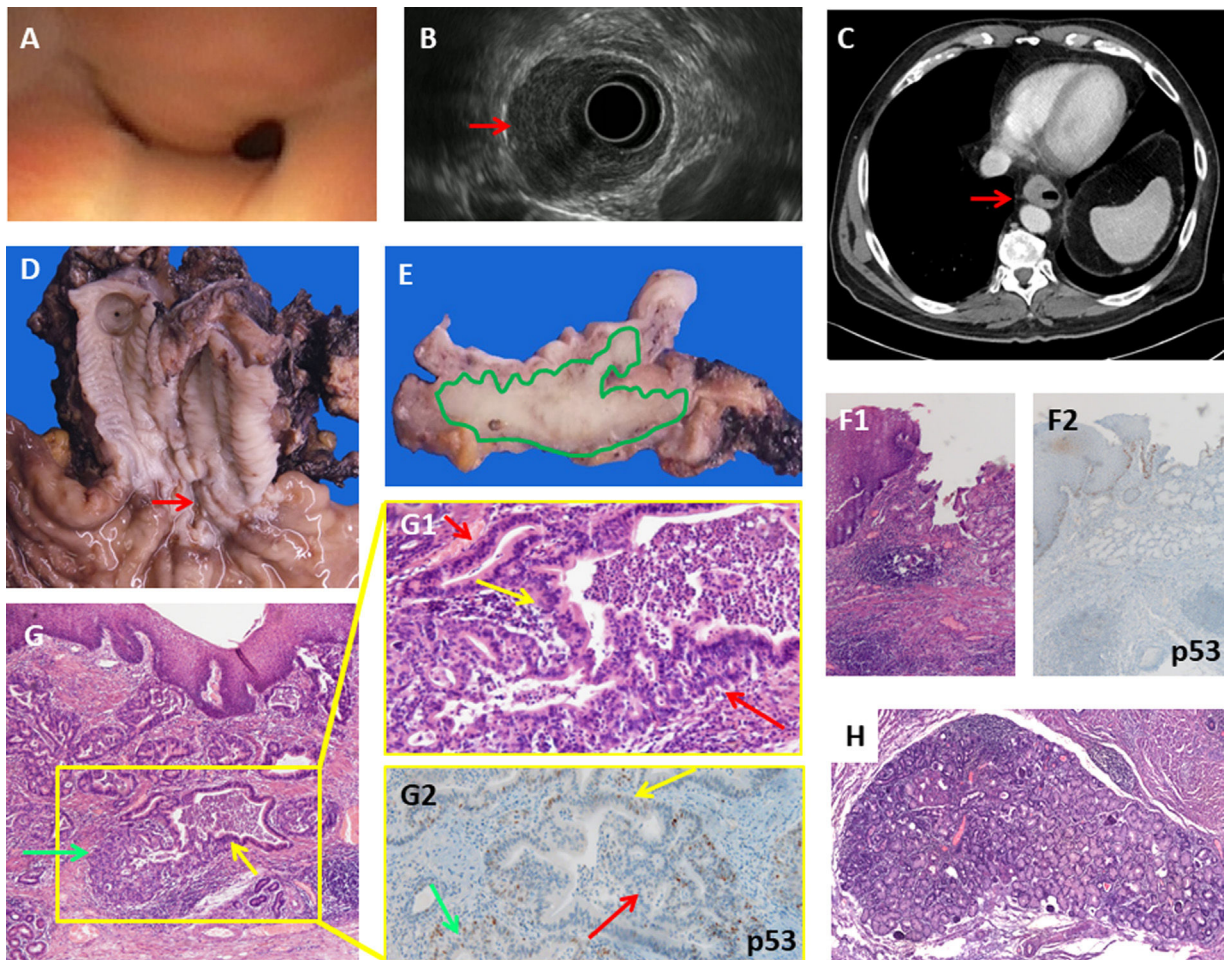


Figure 1 **A:** Endoscopic view of the stenosis of the distal esophagus covered with normal mucosa. **B:** Endoscopic Ultrasound (EUS) showing a tumor in the esophageal wall infiltrating the muscular layer (red arrow), but sparing the mucosal layer, and affecting 50% of the circumference. **C:** CT scan showing mural thickening of the distal esophagus (red arrow). **D:** Gross findings: a longitudinal erosion in the lower esophageal mucosa (red arrow), with no Barrett's esophagus or any lesions in the rest of the esophageal and gastric mucosa. **E:** Transversal section of the esophagus wall showing that the tumor (depicted in green) occupies the full thickness of the wall, reaching the adventitia and sparing the mucosa. **F1:** Microscopic findings: normal esophagogastric junction showing no evidence of Barrett's esophagus (H&E $\times 10$). **F2:** p53 IHC of esophagogastric junction ($\times 10$). **G:** low power view of the esophageal wall lined by hyperplastic-non dysplastic squamous epithelium. The submucosa and muscular propria show a neoplastic glandular proliferation with normal submucosal glands (green arrow) showing a dilated duct with dysplasia (yellow arrow) (H&E $\times 10$). **G1:** Higher power view of the inset showing a transition from normal submucosal gland epithelium to dysplasia (yellow arrow) and adenocarcinoma (red arrows) (H&E $\times 20$). **G2:** "Wild type" p53 staining in a gland showing a transition from normal submucosal gland epithelium (green arrow) to dysplasia (yellow arrow) and adenocarcinoma (red arrow) (p53 IHC $\times 20$). **H:** Peritumoral hyperplastic submucosal gland without dysplasia (H&E $\times 10$).

ness (Fig. 1E). At histological examination the esophagus was lined with normal stratified squamous epithelium, without intestinal metaplasia at the gastroesophageal junction or heterotopic gastric mucosa (Fig. 1F1 and F2). The tumor was formed by a proliferation of glands invading throughout the esophagus wall, arranged in delimited nests with a tubulo-papillary architectural pattern (Fig. 1G). One definite proof of the submucosal gland origin was the presence of a transition from normal-appearing submucosal glands to cytological atypia and high-grade dysplasia to adenocarcinoma (Fig. 1G1). The tumor was positive for cytokeratin-7 (CK7), CKCAM5.2, CK34 β E12, CDX2, carcinoembryonic antigen (CEA), and BerEp4, being negative for

CK20 and p53 staining, the latter showing a "wild type"-pattern (Fig. 1G2).

The Cancer Genome Atlas (TCGA) characterized EAC finding it more similar to gastric adenocarcinoma than to squamous cell carcinoma of the esophagus, thus, EAC and gastric adenocarcinoma were analyzed jointly.⁴ Most EAC correspond to the chromosomal instability (CIN) group with mutations in *TP53*, *CDKN2A*, *CDKN1B*, *APC* (71%) and *ERBB2* (13%) genes.⁴ Little is known about the molecular characterization of EAC arising from submucosal glands, since the cases reported have not been tested. In the present case no mutations were found in any of the 42 genes included in two Next Generation Sequencing (NGS) panels: *AKT1*, *ALK*, *AR*,

BRAF, *CTNNB1*, *DDR2*, *EGFR*, *ERBB2*, *ERBB3*, *ERBB4*, *ESR1*, *FBXW7*, *FGFR1*, *FGFR2*, *FGFR3*, *GNA11*, *GNAQ*, *HRAS*, *IDH1*, *IDH2*, *JAK1*, *JAK2*, *JAK3*, *KIT*, *KRAS*, *MAP2K1*, *MAP2K2*, *MET*, *MTOR*, *NOTCH1*, *NRAS*, *PDGFRA*, *PIK3CA*, *PTEN*, *RAF1*, *RET*, *ROS1*, *SMAD4*, *SMO*, *STK11*, and *TP53*. Furthermore, no copy number alterations were detected in *AKT1*, *ALK*, *AR*, *BRAF*, *CCND1*, *CDK4*, *CDK6*, *EGFR*, *ERBB2*, *FGFR1*, *FGFR2*, *FGFR3*, *FGFR4*, *KIT*, *KRAS*, *MET*, *MYC*, *MYCN*, *PDGFRA*, and *PIK3CA*.

The other non-Barrett's associated EAC derive from heterotopic gastric mucosa and is more frequent in males. A third actor to consider is the esophageal gland duct adenoma, located in the lower esophagus, with most published cases being in males between 40 and 60 years old, treated with endoscopic resection and with no recurrence or malignancy during follow up.⁵ It is uncertain whether esophageal gland duct adenoma can be a precursor lesion of adenocarcinoma. Our case had some hyperplastic benign submucosal glands, larger than normally seen, but it is difficult to state if the tumour was originated in such a lesion, although it cannot be completely excluded (Fig. 1H).

In conclusion, it is important to identify these rare EAC arising in the submucosal gland/duct system, since they could have a different etiopathogenesis and carcinogenic pathway. Little is known about their genetic profile as no genetic study has been performed in the few reported cases. Our case had a poor response to neoadjuvant therapy, and we did not find any mutation in any of the most frequent genes involved in gastric, esophageal or other frequent human adenocarcinomas.

Acknowledgements

We are indebted to the Molecular Biology Core from the Biomedical Diagnostic Center (CDB) of Hospital Clínic for technical support. We also acknowledge the support of the Xarxa Catalana de Bancs de Tumors-XBTC, the Banc de Tumors of the Hospital-Clínic-IDIBAPS, and the support of CERCA Programme/Generalitat de Catalunya.

References

1. Then EO, Lopez M, Saleem S, Gayam V, Sunkara T, Culliford A, et al. Esophageal cancer: an updated surveillance epidemiology

and end results database analysis. *World J Oncol*. 2020;11:55–64, <http://dx.doi.org/10.14740/wjon1254>.

2. Wang S-W, Chang C-S, Wang J, Yeh H-Z. Early adenocarcinoma originating in submucosal gland of thoracic esophagus presenting as submucosal tumor. *Endoscopy*. 2008;40 Suppl. 2:E237–8, <http://dx.doi.org/10.1055/s-2008-1077680>.
3. Tamura H, Saiki H, Amano T, Yamamoto M, Hayashi S, Ando H, et al. Esophageal carcinoma originating in the surface epithelium with immunohistochemically proven esophageal gland duct differentiation: A case report. *World J Gastroenterol*. 2017;23:3928–33, <http://dx.doi.org/10.3748/wjg.v23.i21.3928>.
4. Kim J, Bowlby R, Mungall AJ, Robertson AG, Odze RD, Cherniack AD, et al. Integrated genomic characterization of oesophageal carcinoma. *Nature*. 2017;541:169–75, <http://dx.doi.org/10.1038/nature20805>.
5. Nie L, Wu HY, Shen YH, Fan XS, Sun Q, Huang Q, et al. Esophageal submucosal gland duct adenoma: a clinicopathological and immunohistochemical study with a review of the literature. *Dis Esophagus*. 2017;30:1–6, <http://dx.doi.org/10.1111/dote.12442>.

Karme Saez de Gordo^a, Jose Guerrero^a, Rosanna Bishop^a, Ivan Archilla^a, Maite Rodrigo^a, Oriol Sendino^{b,e,f,g}, Dulce Momblan^c, Tamara Sauri^{d,e,f}, Pedro Jares^{a,e,f}, Miriam Cuatrecasas^{a,e,f,g,*}

^a Department of Pathology, Hospital Clínic, University of Barcelona, IDIBAPS, Barcelona, Spain

^b Gastroenterology Department, Hospital Clínic, Barcelona, Spain

^c Surgery Department, Hospital Clínic, Barcelona, Spain

^d Oncology Department, Hospital Clínic, Barcelona, Spain

^e Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

^f Universitat de Barcelona (UB), Barcelona, Catalonia, Spain

^g Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Spain

* Corresponding author.

E-mail address: mcuatrec@clinic.cat (M. Cuatrecasas).

0210-5705/ © 2020 Elsevier España, S.L.U. All rights reserved.

Splenosis: An underappreciated cause of gastrointestinal bleeding in splenectomized patients. Case report and literature review



Esplenosis: una causa subestimada de hemorragia gastrointestinal en el esplenectomizado. Caso clínico y revisión literaria

Splenosis is the ectopic splenic tissue autotransplanted following splenectomy or splenic trauma.¹ This tissue may

give rise to a mass or masses located in the peritoneum or extraperitoneally, which may present a difficult differential diagnosis. Occasionally, splenosis may produce abdominal pain, obstruction, and gastrointestinal bleeding.^{1,2}

A 55-year-old male attended the emergency room (ER) for a new episode of melena in July 2018. Previous medical history included a necrotizing pancreatitis in 2003 with a splenic vein thrombosis with collateral circulation as a sign of prehepatic portal hypertension (PPH). In 2007 spleen rupture occurred. Since then, the patient presented several episodes of upper gastrointestinal bleeding (UGIB). They were thought to be secondary to this PPH because on endoscopy an enlarged mucosal fold on the gastric fundus was found to be the source of bleeding recurrently