ISSN: 2755-0117

Journal of Oncology Research Review & Reports

SCIENTIFIC Research and Community

Case Report

Open Access

Synchronous Multifocal Early Gastric Cancer: How Important is A Meticulous Endoscopic Examination? A Case Report and Literature Review

Flávio Silano*, Vanessa Costa Neves, Ricardo Bandeira de Melo Amaral, Rodolfo Carvalho Santana and Paulo Cezar Galvão do Amaral

Department of Surgery of the Upper Digestive System, Aliança /Rede D'Or São Luiz Hospital Group, Salvador 41920-900, Bahia, Brazil

ABSTRACT

Introduction: The incidence rate of synchronous early gastric cancer is reported to be 5% to 15%, and several risk factors that increase its incidence have already been identified. Synchronous lesions are reported to be neglected in 32.4% of early gastric neoplasia cases.

Method: Case report of a 75-year-old woman, with mucosa atrophy, intestinal metaplasia, with early gastric adenocarcinoma in antrum, CT staging without alterations, underwent surgical treatment using endoscopic submucosal dissection (ESD).

Results: The anatomopathological result demonstrated a lesion of 2 cm, a well-differentiated non-ulcerated adenocarcinoma, without lymphatic-vascular invasion, with a positive deep submucosal margin, eCURE C-2. A D1+ complementary laparoscopic partial gastrectomy was performed. The analyzes of the surgical specimens showed an ESD area of ulcer scar without tumor and another early gastric cancer (T1a) at 2.2 cm distance with normal mucosa between them. Thirty six lymph nodes were free of disease.

Conclusion: In this case, the patient had 3 risk factors for synchronic injury, but it was only discovered during the salvage gastrectomy. Thorough endoscopy should be performed in all patients and even more so in patients with risk factors. Failure to recognize these lesions can result in evolution to advanced cancer.

***Corresponding author**

Flávio Silano, Department of Surgery of the Upper Digestive System, Aliança /Rede D'Or São Luiz Hospital Group, Salvador 41920-900, Bahia, Brazil.

Received: July 21, 2023; **Accepted:** July 24, 2023; **Published:** July 31, 2023

Introduction

Synchronous early gastric cancer is defined by two or more malignant lesions in the stomach, with a normal gastric wall between them and demonstrably one cannot be a tumoral extension of another [1]. The prevalence of synchronous or multifocal early gastric cancer is reported in the literature between 5 and 15% and when compared to solitary early gastric cancer, its prevalence is higher in patients with atrophy of the gastric mucosa, elderly, male and with a family history of stomach cancer [2]. Synchronous lesions tend to be small, flat and increase the risk of gastric remnants not visualized at endoscopy , with some series showing more than 32% of synchronous lesions overlooked during endoscopic examinations [3-4].

Case Report

Female patient, 75 years old, Karnofsky performance status 100, with mild arterial hypertension, complaining of nonspecific epigastric discomfort. She underwent endoscopic examination which showed: Elevated and irregular area in the proximal gastric antrum, on the anterior wall of the lesser curvature, measuring 1.2 cm in diameter, friable to the touch of clamps and suspicious for early gastric cancer (Figures 1 and 2). In addition, there was atrophic pangastritis (Kimura C-2). The biopsy result showed well-differentiated gastric adenocarcinoma. Chest tomographic staging without findings, tomographic staging with protocol for gastric cancer (Figure 3) did not show changes in the gastric wall, with no evidence of lymph node, liver or peritoneal involvement. She underwent endoscopic submucosal dissection (ESD) at another service (Figure 4) and analysis of the specimen showed: Early gastric cancer, 2 cm in size, well differentiated, absence of signet ring cells, absence of lymphovascular invasion, absence of ulcer, free radial margins, vertical margin with compromised submucosa (e-CURE C-2). She was admitted to our upper digestive tract surgery service for surgical complementation through D1+ videolaparoscopic partial gastrectomy, with partial omentectomy (Figure 5,6) and Roux-en-Y reconstruction. Preoperatively, she was submitted to the ERAS protocol: Physical therapy prequalification for muscle tone, during 20 days before surgery and immunomodulatory supplementary diet for 7 days before the procedure. There was no need for iron supplementation. Preoperative fasting was shortened with maltodextrin, 2 hours before surgery and use of epidural catheter and free opioid analgesia. Surgical time of 5 hours, without transfusion of blood products and without use of abdominal drain. Six hours after the

main procedure, the patient walked to the ICU and started using chewing gums for gastro-colic stimulation. Hospital discharge on the 4th postoperative day, with a light diet, without pain and established intestinal rhythm. In the anatomical pathological examination, in addition to extensive intestinal metaplasia and gastric mucosa atrophy, the surgical specimen was divided into three areas: Area 1, distal body / incisura angularis, presence of ulcer (topography of the ESD) (Figure 7), without neoplasia. Area 2, distal third, slightly elevated and without neoplasia. Area 3, the entire upper third, slightly elevated measuring 0.8 x 0.5 cm and 2.2 cm away from area 1, with the presence of normal mucosa between them (Figure 8), presence of gastric adenocarcinoma, well differentiated, restricted to mucosa, without lymphovascular invasion, classified as T1a. The surgical margins of the specimen were free and there was no lymph node metastasis in the 36 lymph nodes studied.

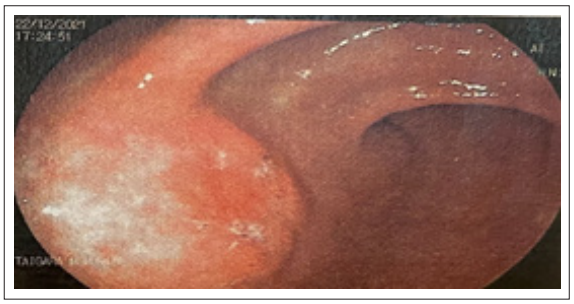

Figure 1: Lesion with slightly raised and friable edges

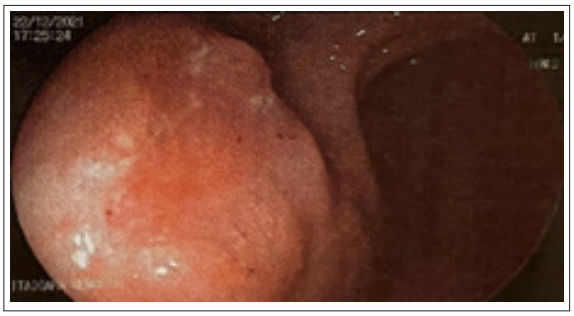

Figure 2: Lesion with irregular surface and 1.2 cm in diameter

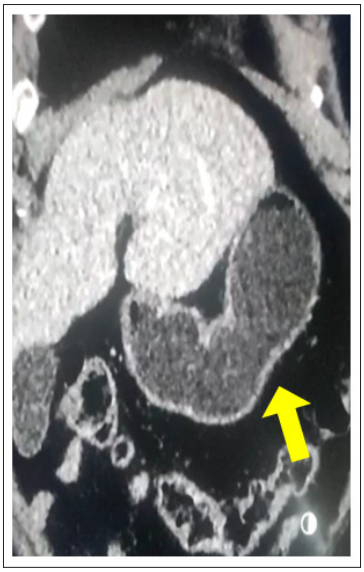

Figure 3: Tomographic staging of the abdomen with protocol for gastric cancer. Stomach distended by liquid (yellow arrow)

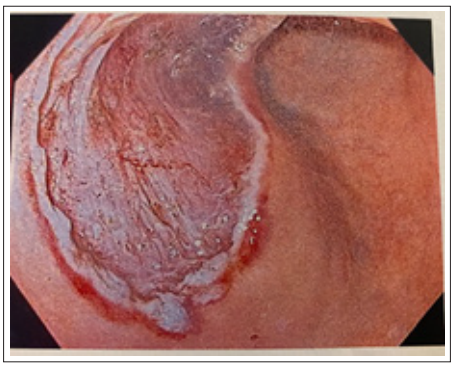

Figure 4: Endoscopic submucosal dissection (ESD) in the lesser gastric curvature

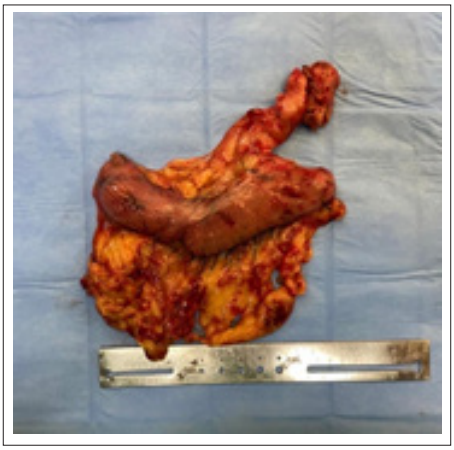

Figure 5: Surgical specimen. Gastrectomy product with en bloc lymph nodes

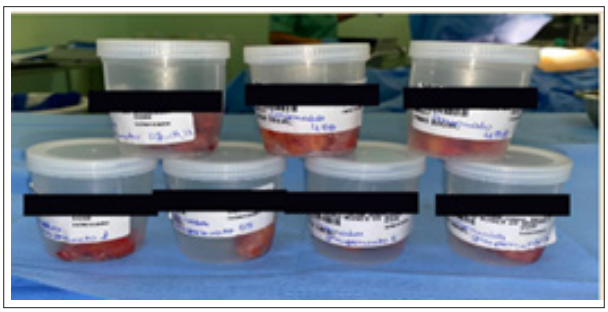

Figure 6: Dissected and isolated lymph node groups

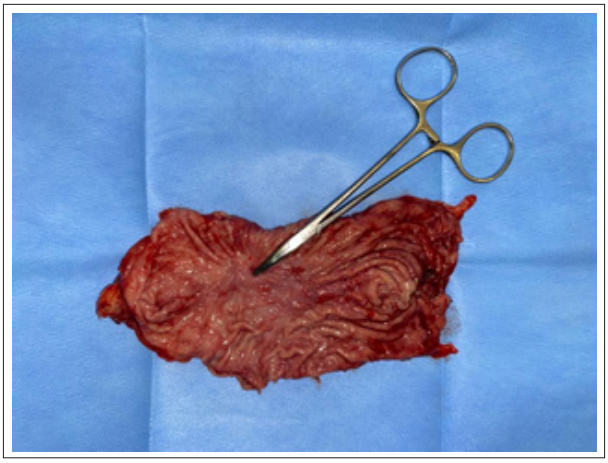

Figure 7: Presence of ulcer in the topograhy of the endoscopic submucosal dissection (ESD) scar

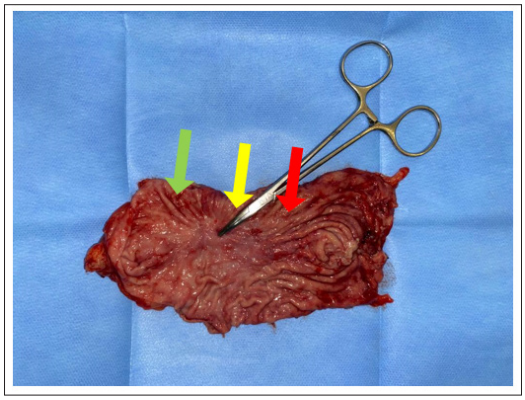

Figure 8: Findings of the anatomopathological study of the surgical specimen. Area 1 (yellow arrow) presence of ulcer measuring 2.3 cm without neoplasm. Area 2 (green arrow) corresponding to the gastric antrum, with the presence of an elevated region without neoplasia. Area 3 (red arrow) corresponding to the upper third of the gastric body, presence of adenocarcinoma in the gastric mucosa measuring 0.8 cm, 2.2 cm away from the ulcerated area (scar from the previous ESD) and with a normal gastric wall between them

Discussion

The high rates of gastric cancer in Japan and Korea resulted in population screening programs emphasizing the early detection of the disease and the possibility of endoscopic treatment [5-7]. For this reason, 50% of gastric neoplasms in these countries are discovered early [4, 9, 10]. On the other hand, the West does not have screening programs due to the lower incidence of stomach cancer compared to Asia, a fact attributed to the treatment of Helicobacter Pylori, lifestyle, environmental and genetic factors [8]. In the East and West, a deserved emphasis goes to synchronous early gastric neoplasms, whose incidence varies from 3.2% to 15% and the high number of neglected lesions during the endoscopic examination [1, 2, 11, 12]. Hyeong Seok Nam et al conducted a retrospective study with 488 patients with early gastric cancer who underwent endoscopic resection (ESD) and defined synchronous early gastric lesions as those diagnosed before ESD or up to 1 year after this procedure [4]. Among 77 synchronous early gastric lesions, 25 (32.4%) were diagnosed only after the initial ESD and therefore neglected. Twenty-two of them were not photographed and even those whose images were registered, were not recognized by the endoscopists. In our case report, the synchronous lesion was endoscopically neglected, inadvertently discovered after the complementary surgical treatment to the non-curative ESD (e-CURA C-2 – compromised vertical margin) Otherwise, in our environment, where there is difficulty in following up these patients, the opportunity for early treatment of the disease would possibly have been lost. Unlike the East, which actively searches for early lesions, we do not focus on screening, but we routinely perform endoscopic examinations in populations with characteristics conducive to the development of synchronous early gastric neoplasia, such as: Age over 65, patients with gastric mucosal atrophy and intestinal metaplasia [5]. Therefore, the importance of a thorough endoscopic examination regardless of the country is evident. Furthermore, the presence of two or more malignant neoplasms in the stomach is defined as multiple synchronous lesions, an event more associated with early gastric cancer than locally advanced cancer [14]. Therefore, the suspicion of an early lesion during endoscopy, in itself, is already a sufficient risk factor for the immediate screening of other lesions. Seok Hoo Jeong et al retrospectively observed 68 patients with multiple synchronous early gastric cancer and the multivariate analysis showed male gender and submucosal invasion as independent risk factors in the association with synchronous lesions, $P = 0.01$ (Odd radio - OR 2475; 95% confidence interval, 1234–4965) and $P = 0.03$ (OR 1850; 95% confidence interval, 1051–3256.) respectively [13]. Hyeong Seok Nam et al retrospectively showed in multivariate analysis that the following are independent risk factors associated with synchronous early gastric cancer: Age ≥ 65 years old ($P = 0.042$, OR 1.030–4.666; 95% confidence interval), moderate to severe endoscopic atrophic gastritis ($P = 0.047$, OR 1012–4926; 95% confidence interval) and increased morphology of primary lesions ($P = 0.012$, OR 1191–4060; 95% confidence interval) [4]. Our patient was female, 75 years old, lesion with raised and irregular borders, Kimura C-2 atrophic pangastritis and submucosal invasion with 200μ, that is, 3 important risk factors requiring detailed endoscopy to actively search for synchronous injuries. The non-standardization of the endoscopic examination, the lack of endoscopic equipment necessary for the detection of small lesions, insufficient training, in addition to the lack of knowledge of the risk factors associated with synchronous early gastric cancer, are associated with the neglect of synchronous early lesions (14-17). Whenever there is macroscopic suspicion of early gastric cancer during endoscopy, multiple synchronous lesions should be considered and examination of this should be more thorough in male patients, ≥ 65 years old, presence of moderate to severe endoscopic atrophic gastritis and morphology elevation of the primary lesion [4]. The well-differentiated histological type compared to the undifferentiated and submucosal invasion compared to the mucosa, is more associated with synchronous lesion $P = 0.003$ and $P < 0.001$ respectively [4,17] , however, this information is not available in the initial endoscopy. It will depend on the biopsy and staging results. Kim JH et al in a retrospective study with 963 patients treated for early gastric cancer, 37 (3.8%) had multiple synchronous early gastric cancer [17]. The authors correlated characteristics between the main early lesion and the synchronous lesion and observed that both were located more in the lower third of the stomach, 64.9% and 46%, respectively. Furthermore, when the main lesion was in the upper third of the stomach, it was followed by 83.3% of the synchronous lesions also in this topography. This trend was seen in the middle third of the stomach with 85.7% of the synchronous neoplasms present there, as well as in the greater and lesser curvature. In other words, there is a perspective of proximity between the main lesion and the synchronic one; information that should be used during endoscopic screening. Another piece of data that helps to identify synchronous neoplasia is the macroscopic aspect. The same authors showed that the macroscopy was similar in 67.6% for both lesions, main and synchronous ($P < 0.001$). In our case report, the main lesion measured 2 cm, was located in the lower third of the stomach and had raised borders, and the synchronous neoplasm measured 0.8 cm, was 2.2 cm away, slightly elevated (Figure 8); it was not identified in the initial endoscopy, being seen only in the surgical specimen. Another important point to be discussed is the involvement of the lymph nodes in multifocal synchronous early gastric cancer. Choi et al retrospectively analyzed 1717 patients with early gastric cancer, 1561 (91%) with solitary lesions and 156 (9%) with multiple synchronous early lesions and showed a similar risk of lymphatic metastasis for both groups [17]. The controversy in the literature was that among the main factors associated with lymph node metastasis such as, tumor size, presence of ulcer, depth of lesion, histological type and lymphovascular invasion, the authors observed in multivariate analysis that in the group of multiple synchronous early lesions, only tumors $P < 0,001 \geq$ 3cm and lymphovascular invasion were independent risk factors for lymph node metastasis with $p = 0.001$ (OR 8876; 95% CI

1871-42097) and p = 0.001 (OR 33456; 95% CI 7893-141803) respectively. In our case report, the multiple synchronous lesion was staged as T1a, well differentiated, 0.8 cm, without ulcer, without lymphovascular invasion and there was no lymph node metastasis in the 36 lymph nodes studied.

Conclusion

In this case, the patient had 3 risk factors for synchronic injury, but it was only discovered during the salvage gastrectomy. Thorough endoscopy should be performed in all patients and even more so in patients with risk factors. Failure to recognize these lesions can result in evolution to advanced cancer.

References

1. Hee Man Kim, Hyun Ki Kim, Sang Kil Lee, Jae Hee Cho, Kyung Ho Pak, et al. (2012) Multifocality in Early Gastric Cancer Does not Increase the Risk of Lymph Node Metastasis in a Single-Center Study. Ann Surg Oncol 19: 1251-1256.
2. En Amada, Hirofumi Kawakubo, Satoru Matsuda, Shuhei Mayanagi, Rieko Nakamura, et al. (2021) A case of synchronous intramucosal gastric carcinoma with multiple lymph node metastases. surg case rep 7: 80.
3. In Seob Lee , Young Soo Park, Kab Choong Kim, Tae Hwan Kim, Hee Sung Kim, et al. (2012) Multiple synchro- nous early gastric cancers: high-risk group and proper management. Surg Oncol 21: 269-273.
4. In Seob Lee , Young Soo Park, Kab Choong Kim, Tae Hwan Kim, Hee Sung Kim, et al. (2012) Multiple synchro- nous early gastric cancers: high-risk group and proper management. Surg Oncol 21: 269-273.
5. Huang HL, Leung CY, Saito E, Kota Katanoda, Chin Hur, et al. (2020) Effect and cost-effectiveness of national gastric cancer screening in Japan: a microsimulation modeling study. BMC Med 18: 257.
6. Suh YS, Lee J, Woo H, Shin D, Seong-Ho Kong, et al. (2020) National cancer screening program for gastric cancer in Korea: Nationwide treatment benefit and cost. Cancer 126: 1929-1939.
7. Mohsen Naghavi, Reza Malekzadeh (2020) GBD 2017 Stomach Cancer Collaborators. The global, regional, and national burden of stomach cancer in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease study 2017. Lancet Gastroenterol Hepatol 5: 42-54.
8. Edward Young, Hamish Philpott, Rajvinder Singh (2021) Endoscopic diagnosis and treatment of gastric dysplasia and early cancer: Current evidence and what the future may hold 27: 5126-5151.
9. Daisuke Kakinuma, Hiroki Arai, Tomohiko Yasuda, Yoshikazu Kanazawa, Kunihiko Matsuno, et al. (2021) Treatment of Gastric Cancer in Japan. J Nippon Med Sch 88: 156-162.
10. M Inoue, S Tsugane (2005) Epidemiology of gastric cancer in Japan Postgrad Med 81: 419-424.
11. Jung Ho Kim, Seok Hoo Jeong, Jina Yeo. Woon Kee Lee, Dong Hae Chung, et al. (2016) Clinicopathologic Similarities of the Main and Minor Lesions of Synchronous Multiple Early Gastric Cancer 31: 873-878.
12. Seok Hoo Jeong, Jungsuk An, Kwang An Kwon, Woon Kee Lee, Kyoung Oh Kim, et al. (2017) Predictive risk factors associated with synchronous multiple early gastric cancer. Medicine 96: e7088.
13. Tsutomu Nishida, Masahiko Tsujii, Motohiko Kato, Yoshito Hayashi, Tomofumi Akasaka, et al. (2014) Endoscopic surveillance strategy after endoscopic resection for early gastric cancer 5: 100-106.
14. Evelien Dekker, Britt B S L Houwen, Ignasi Puig, Marco Bustamante-Balén, Emmanuel Coron, et al. (2020) Curriculum for optical diagnosis training in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy Oct 52: 899-923.
15. Andrej Wagner, Stephan Zandanell , Tobias Kiesslich (2021) Systematic Review on Optical Diagnosis of Early Gastrointestinal Neoplasia. Med 10: 2794.
16. Jung Ho Kim, Seok Hoo Jeong, Jina Yeo (2016) Clinicopathologic Similarities of the Main and Minor Lesions of Synchronous Multiple Early Gastric Cancer. J Korean Med Sci 31: 873-878.
17. Jeongmin Choi, Sang Gyun Kim, Jong Pil Im, Seung Joo Kang, Hyuk-Joon Lee, et al. (2011) Lymph node metastasis in multiple synchronous early gastric cancer. Gastrointest Endosc 74: 276-84.