CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 12 (2015) 75–77

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

# Gastrointestinal stromal tumor of the stomach and hepatocellular carcinoma: An unusual association

H. Ferreira e Mora[a,*], J. Pinto de Sousa[a], V. Devesa[a], J. Barbosa[a], J. Costa[b], R. Portugal[b], J. Costa Maia[a]

[a] Serviço de Cirurgia Geral, Centro Hospitalar de São João, Portugal
[b] Serviço de Anatomia Patológica, Centro Hospitalar de São João, Portugal

ARTICLE INFO

*Article history:*
Received 23 March 2015
Received in revised form 4 May 2015
Accepted 9 May 2015
Available online 14 May 2015

ABSTRACT

*INTRODUCTION:* Gastrointestinal stromal tumors (GIST) are uncommon, potentially malignant tumors, that arise in the wall of the gastrointestinal tract. Up to 50% can develop metastasis, mainly in the liver, but the occurrence of synchronous primary liver tumors is a rare event in these patients.
*PRESENTATION OF CASE:* The authors report a case of the association of gastric GIST and hepatocellular carcinoma (HCC) in a non-cirrhotic liver in a 76 year-old patient.
*DISCUSSION:* The appearance of an hepatic lesion in a GIST patient does not necessarily imply its secondary nature.
*CONCLUSION:* In diagnosed GIST patients, all efforts should be pursued to characterize synchronous hepatic lesions, in order to plan a correct and tailored treatment of the patients.


## 1. Introduction

Gastrointestinal stromal tumors (GIST) are uncommon, potentially malignant tumors that arise in the wall of the gastrointestinal tract. These tumors account for 1% of all gastrointestinal neoplasms [1] and they are the most frequent mesenchymal tumors in that location [2–3]. They can occur in any portion of digestive tract but they are mainly localized in the stomach (40–65%) and small intestine (25–40%). Its occurrence has a unimodal distribution with a mean at-onset age varying between 59 and 79 years [1–6], with a male increased relative risk [4]. GIST typically exhibits immunohistochemical positivity for vimentin in almost all cases, for CD117 (c-Kit) in 95% and for CD34 in 60–70% (80% in gastric location) [7]. The occurrence of simultaneous tumors in patients with GIST has been reported in 13–43% of patients [8–10] and up to 50% can develop metastasis, mainly in the liver [5]. GIST can occur simultaneously with chronic lymphocytic leukemia, lymphoma, renal cell carcinoma or gastric cancer, but the association with hepatocellular carcinoma (HCC) is extremely rare [10]. The incidence of HCC is increasing. This tumor typically arises in an underlying cirrhotic liver, with well known risk factors including alcoholic abuse, hepatitis B and C chronic infections, non-alcoholic steatohepatitis and other causes of cirrhosis. Up to 25% of tumors, however, arise in non-cirrhotic livers [11] and despite their frequent large size when diagnosed, potentially curative treatments can be offered with a better outcome than tumors arising in cirrhotic liver. [12]

Herein, we report a challenging diagnosis and decision making case of a patient admitted to our medical institution with the unusual coexistence of a gastric GIST and HCC developing in a non-cirrhotic liver.

## 2. Presentation of case

A 76 year-old caucasian male was admitted in our emergency department with an upper gastrointestinal bleeding episode associated with mild upper abdominal pain and non quantified weight loss. Three years previously, the patient had been submitted to a distal gastrectomy with a Billroth II reconstruction at another institution in an attempt to remove a gastric GIST; no tumor, however, was identified in the surgical specimen, and the patient deliberately refused any further treatment or follow-up at that institution. Apart from minor depression, no other significant medical history was noticed. He was medicated with dulosepin 75 mg i.d. and pantoprazole 40 mg i.d. He was negative for hepatitis virus B and C infection markers.

The physical exam only identified skin pallor. Blood tests showed haemoglobin of 5.5 g/dL and no other relevant changes. The patient was transfused with 3 red blood cell units. An upper endoscopy was performed and a polypoid bulging segment with a central bleeding ulceration below the cardia was identified. The bleeding was successfully controlled by endoscopic clipping and adrenalin injection.

* Corresponding author. Tel.: +351 225512100; fax: +351 225096908.
*E-mail address:* henrique_mora@hotmail.com (H. Ferreira e Mora).

http://dx.doi.org/10.1016/j.ijscr.2015.05.020

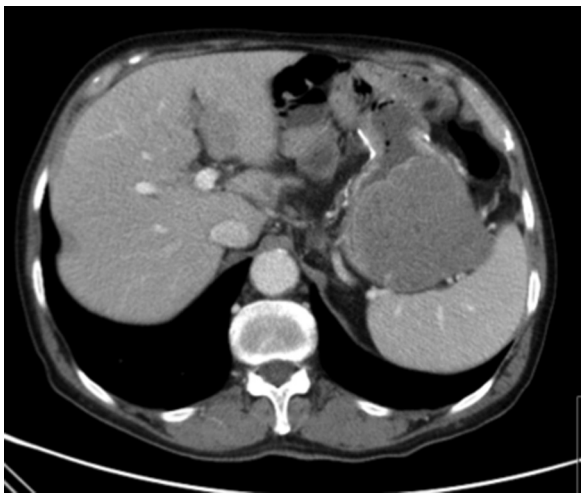

**Fig. 1.** CT-imaging showing the hepatic and gastric masses.

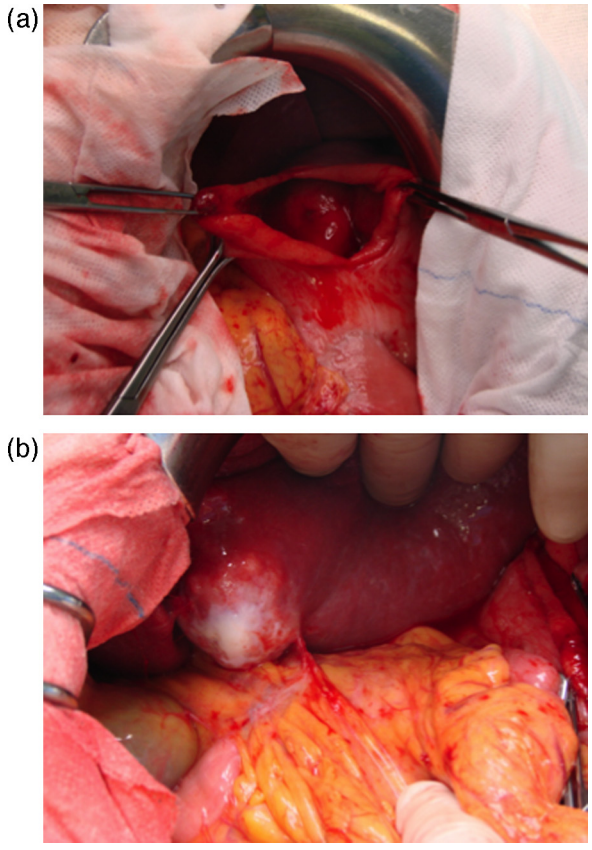


**Fig. 2.** Intra-operative view: (a) performed gastrostomy with gastric lesion; (b) hepatic lesion.

A CT-scan showed a 78 × 86 mm tumor in the stomach remnant and a 34 × 28 mm nodular lesion in the left liver lobe, with associated biliary dilatation (Fig. 1).

Echoendoscopic guided biopsies of the gastric and the hepatic lesions were performed and the pathological results were compatible with GIST (CD117+; vimentin+) in the gastric lesion and HCC (HepPar1+; CK7; HSP-70+; Glutaminsynthetase+ [13–14]) in the liver nodule.

At laparotomy, a posterior gastric wall infra-cardiac pedicled lesion with the same size described in CT-scan and a segment III lesion were observed. An anterior gastrotomy was performed in order to enable an atypical gastrectomy of the posterior wall lesion area (Fig. 2a), preserving the previous Billroth II gastrointestinal continuity, and a left liver ultrasound guided lobectomy was followed (Fig. 2b).

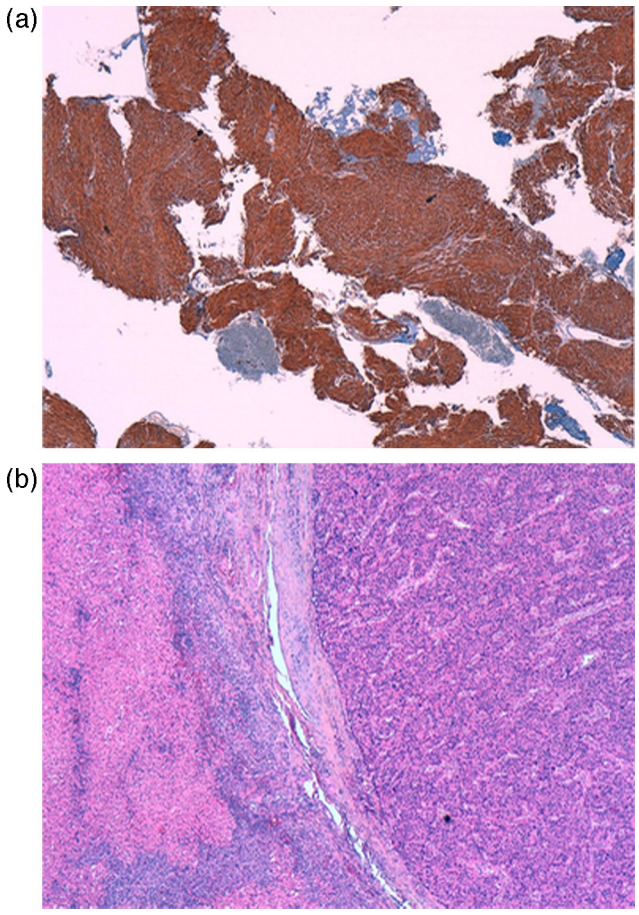


**Fig. 3.** (a) Biopsy specimens of the GIST with immunoexpression of C-kit (40X); (b) hepatocellular carcinoma in a non-cirrhotic liver (H&E; 40X).

Histologically the gastric tumor was compatible with GIST (Fig. 3a). It was 85 mm long, with a mitotic index of 4/50HPF [15]. The hepatic tumor was catalogued as HCC and the underlying liver showed no evidence of cirrhosis (Fig. 3b). The immunohistochemical patterns were similar to those on the previous biopsies. The postoperative period was uneventfully and the patient was discharged on the 7th post-operative day.

The patient was monitored in regular follow-up until 30 months after surgery. No signs of recurrence were found.

## 3. Discussion

A high (13–43%) prevalence of synchronous malignant tumors has been reported in GIST patients [8–9], with no literature consensus as to the role (if any) of genetic and environmental factors [8]. Synchronous primary liver tumors are not common in these patients [6] and the association of GIST and HCC remains an exceptional event, with very few cases published to the best of our knowledge: one case of perivascular epithelioid cell tumor of the liver [16] and 2 cases of HCC (one c-Kit positive and other c-Kit negative) [17,18] have been reported in association with GIST.

In this context, even considering the relatively high potential to metastasize to the liver, the appearance of an hepatic lesion in GIST patients does not warrant its secondary nature. Therefore, if feasible, a biopsy is of utmost importance in planning the correct

treatment of these patients, especially, as in the present case, when both lesions are considered resectable.

In this case, the diagnostic and staging work-up established the two independent diagnoses and led to the R0 resection of both tumors and to a potentially better prognosis than if the liver lesion had been considered a metastasis from the gastric GIST. In that situation the patient would have been driven to a life-long treatment with a TK inhibitor [19].

## 4. Conclusion

Despite few reports has shown GIST and HCC association, considering the multiple different treatment perspectives, in diagnosed GIST patients all efforts should be pursued to characterize synchronous hepatic lesions with independent biopsies, in order to plan a correct and tailored treatment of the patients.

## Conflicts of interest

All authors disclose any financial and personal relationships with other people or organisations that could inappropriately influence (bias) their work.

## Funding

All authors declare they had no source of funding for this study.

## Consent

All authors declare that written and signed consent was obtained to publish this case report. All the patient's privacy rights were respected. The authors also obtained patientís consent for the publication of the accompanying images.

## Ethical approval

All authors declare that this paper was not a research study.

## Author contribution

All authors had equal contribution for this case report.

## Guarantor

The Guarantor of this study is Henrique Miguel Gomes Sebastião Ferreira e Mora.

## References

[1] M.P. Ridolfini, A. Cassano, R. Ricci, F. Rotondi, S. Berardi, G. Cusumano, F. Pacelli, G.B. Doglietto, Gastrointestinal stromal tumors, Ann. Ital. Chir. 82 (March–April (2)) (2011) 97–109.
[2] Thomas Tran Jessica A. Davila, B. Hashem, The epidemiology of malignant gastrointestinal stromal tumors: an analysis of 1458 cases from 1992 to 2000, Am. J. Gastroenterol. 100 (2005) 162–168.
[3] A.M. Gouveia, J.M. Lopes, Surgical treatment of gastrointestinal stromal tumours, in: R. Lunevicius (Ed.), Gastrointestinal Stromal Tumor, Intech, Rijeka, 2012, pp. 61–73.
[4] G.L. Ma, J.D. Murphy, M.E. Martinez, J.K. Sicklick, Epidemiology of gastrointestinal stromal tumors in the era of histology codes: results of a population-based study, Cancer Epidemiol. Biomarkers Prev. 24 (1) (2015) 298–302.
[5] R.P. DeMatteo, J.J. Lewis, D. Leung, S.S. Mudan, J.M. Woodruff, M.F. Brennan, Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival, Ann. Surg. 231 (1) (2000 Jan) 51–58.
[6] G. Biasco, D. Velo, I. Angriman, et al., Gastrointestinal stromal tumors: report of an audit and review of the literature, Eur. J. Cancer Prev. 18 (2) (2009 Apr) 106–116.
[7] M. Boşoteanu, C. Boşoteanu, M. Deacu, M. Aşchie, Differential diagnosis of a gastric stromal tumor: case report and literature review, Rom. J. Morphol. Embryol. 52 (4) (2011) 1361–1368.
[8] R. Gonçalves, E. Linhares, R. Albagli, M. Valadão, B. Vilhena, S. Romano, C.G. Ferreira, Occurrence of other tumors in patients with GIST, Surg. Oncol. 19 (December (4)) (2010) e140–e143, Epub 2010 August 2.
[9] N. Vassos, A. Agaimy, W. Hohenberger, R.S. Croner, Coexistence of gastrointestinal stromal tumours (GIST) and malignant neoplasms of different origin: prognostic implications, Int. J. Surg. 12 (5) (2014) 371–377.
[10] A. Agaimy, P.H. Wünsch, L.H. Sobin, J. Lasota, M. Miettinen, Occurrence of other malignancies in patients with gastrointestinal stromal tumors, Semin. Diagn. Pathol. 23 (2) (2006 May) 120–129.
[11] D.B. Thomas, A.B. Hall, M. Michel, Non-cirrhotic hepatocellular carcinoma in a young active duty male, Mil. Med. 176 (4) (2011 Apr) 475–476.
[12] A.L. Young, R. Adair, K.R. Prasad, G.J. Toogood, J.P. Lodge, Hepatocellular carcinoma within a noncirrhotic, nonfibrotic, seronegative liver: surgical approaches and outcomes, J. Am. Coll. Surg. 214 (2) (2012 Feb) 174–183.
[13] M. Joo, J.G. Chi, H. Lee, Expressions of HSP70 and HSP27 in hepatocellular carcinoma, J. Kor. Med. Sci. 20 (5) (2005 Oct) 829–834.
[14] J. Long, Z.W. Lang, H.G. Wang, T.L. Wang, B.E. Wang, S.Q. Liu, Glutamine synthetase as anearly marker for hepatocellular carcinoma based on proteomic analysis of resected small hepatocellular carcinomas, Hepatobiliary Pancreat. Dis. Int. 9 (3) (2010) 296–305.
[15] A. Agaimy, Gastrointestinal stromal tumors (GIST) from risk stratification systems to the new TNM proposal: more questions than answers? A review emphasizing the need for a standardized GIST reporting, Int. J. Clin. Exp. Pathol. 3 (5) (2010) 461–471.
[16] C.E. Paiva, F.A. Moraes Neto, A. Agaimy, M.A. Custodio Domingues, S.R. Rogatto, Perivascular epithelioid cell tumor of the liver coexisting with agastrointestinal stromal tumor, World J. Gastroenterol. 14 (5) (2008) 800–802.
[17] E. Felekouras, P. Athanasios, S. Vgenopoulou, I. Papaconstantinou, E. Prassas, A. Giannopoulos, J. Griniatsos, Coexistence of hepatocellular carcinoma (HCC) and c-Kit negative gastrointestinal stromal tumor (GIST): a case report, South Med. J. 101 (9) (2008) 948–951.
[18] R. Jaworski, T. Jastrzebski, M. Swierblewski, K. Drucis, G. Kobierska-Gulida, Coexistence of hepatocellular carcinoma and gastrointestinal stromal tumor: a case report, World J. Gastroenterol. 12 (4) (2006) 665–667.
[19] The ESMO/European Sarcoma Network Working Group, Gastrointestinal stromal tumours: ESMO clinical practice guidelines for diagnosis, treatment and follow-up†, Ann. Oncol. 25 (Suppl. 3) (2014) iii21–iii26.