

Gallbladder and Rectal Synchronous Adenocarcinoma: Case Report

Geraldo Ishak, Raquel Carvalho Montenegro, Caroline de Fátima Aquino Moreira-Nunes, Leandro Augusto Costa Bahia, Daniel Souza da Costa, Felipe Soares Ribeiro, Sérgio Figueiredo Lima Júnior, Samia Demachki, Paulo Pimentel Assumpção, Rommel Rodriguez Burbano

Geraldo Ishak, Sérgio Figueiredo Lima Júnior, Paulo Pimentel Assumpção, Faculty of Medicine, João de Barros Barreto University Hospital and UNACON (High Oncology complex Unit) Federal University of Pará, Belém, PA, Brazil

Raquel Carvalho Montenegro, Rommel Rodriguez Burbano, Institute of Biological Sciences, and UNACON (High Complexity Oncology Unit) Federal University of Pará, Belém, PA, Brazil

Caroline de Fátima Aquino Moreira-Nunes, Institute of Biological Sciences, University of Pará, Belém, PA, Brazil

Samia Demachki, Medicine University of the Federal University of Pará (UFPA), Belém, PA, Brazil

Leandro Augusto Costa Bahia, Daniel Souza da Costa, Felipe Soares Ribeiro, Faculty of Medicine, João de Barros Barreto University Hospital, Federal University of Pará, Belém, PA, Brazil

Correspondence to: Rommel Rodriguez Burbano, PhD, Human Cytogenetics Laboratory, Institute of Biological Sciences, Federal University of Pará. Av. Augusto Corrêa, no. 01, Guamá, Belém, Pará, Brazil

Email: rommel@ufpa.br

Telephone: +9779396131 Fax: +1752212055

Received: March 21, 2013 Revised: July 11, 2014

Accepted: July 22, 2014

Published online: December 21, 2014

ABSTRACT

Synchronous tumors in both the rectum and the gallbladder are extremely rare. This study reports a case of gallbladder and rectal synchronic tumors, histopathologically confirmed, and discusses the therapeutic strategies in managing multiple primary cancers. Patient files from the Patient Files and Statistical Department of the University Hospital João de Barros Barreto and review of English literature were analyzed. Data from a case of a 69-year-old female patient with compressive vaginal and anal pain, constipation, and hematochezia were reviewed. Rectal touch evidenced a vegetating and infiltrative tumoral lesion, and colonoscopy demonstrated an elevated, vegetating, and infiltrative lesion. The histopathological

analyses confirmed a moderately differentiated adenocarcinoma. A preoperative computer tomography scan was negative for metastasis investigation and, as an incidental finding, demonstrated cholelithiasis. The histological evaluation of the surgical specimens demonstrated rectal cancer, gallbladder cancer, and also hepatic metastasis. Due to the presence of hepatic and rectal cancer metastases, the standard management of the gallbladder cancer was modified according to the general concept that radical treatment of synchronous tumors should be reserved to situations where all tumors can be treated curatively or can improve life expectancy. Primary gallbladder and rectal synchronous neoplasms are rare and the treatment must be specific to each tumor, following the guidelines of each cancer whenever feasible. In case of metastasis or advanced stages of the disease, the treatment strategies must consider the most advanced tumor and/or the worst prognosis, and aggressive procedures must be avoided when it is not possible to radically treat every synchronous tumor.

© 2014 ACT. All rights reserved.

Key words: Synchronous tumors; Rectum and gallbladder; Hepatic nodes and clinical management

Ishak G, Montenegro RC, Moreira-Nunes CFA, Bahia LAC, da Costa DS, Ribeiro FS, Júnior SFL, Demachki S, Assumpção PP, Burbano RR. Gallbladder and Rectal Synchronous Adenocarcinoma: Case Report. *Journal of Gastroenterology and Hepatology Research* 2014; 3(12): 1401-1404 Available from: URL: <http://www.ghrnet.org/index.php/joghr/article/view/981>

INTRODUCTION

Colorectal cancer (CRC) is the third most frequent cancer type among the sporadic malignant cancers and accounts for 11% of cancer deaths. CRC is associated most to multiple primary tumors. Gallbladder cancer is a rare tumor, even though it is the fifth most common cancer in the gastrointestinal tract, showing higher incidence

between the seventh and eighth decades of life^[1,2].

Synchronous tumors are rare and in addition synchronous adenocarcinoma of both the rectum and gallbladder is extremely rare. In recent years more cases of multiple primary tumors are being reported^[1,3,4]. The main associated factors to multiple primary cancers include: genetic, environmental, immunological, and also previous radiotherapy or chemotherapy treatments^[5]. The synchronic tumors are those which cannot be considered metastases, invasion or recurrence of the first tumor, and the ones which are diagnosed at least six months after the diagnosis of the primary tumor^[1,2,6].

Although very uncommon, almost 40% of multiple primary tumors involving gallbladder cancer are associated to gastric cancer and 30% to colon cancer^[7]. As mentioned, the association of rectal cancer and gallbladder cancer is rare and the management of each one must be tailored according to its clinical settings.

Despite the fact that synchronous colorectal carcinoma has been recognized as a significant clinical entity its clinical and pathological features and its prognosis are still controversial. Herein, we report a case of a female with adenocarcinoma of the rectum and cholelithiasis. The histopathology revealed early primary adenocarcinoma of both the rectum and the gallbladder as well as liver metastasis.

CASE REPORT

A 69-year-old female patient was evaluated at the General and Digestive Surgery Department of João de Barros Barreto's University Hospital, at Amazon region in Brazil, reporting compressive pain in the vagina and in the anus, and painful anal burning during the last 3 months. Constipation and hematochezia were also reported during the last month. Previously, she was medicated with Lactulose, releasing the constipation but not the other symptoms. She also had experienced a weight loss (6 kilograms) during the last six months. She had no nausea, vomiting, jaundice, fever, or urinary symptoms. As for the family cancer history (Figure 1): her mother and grandmother had liver neoplasms, her aunt and brother had colonic neoplasms. She was in good clinical condition but the rectal touch exam evidenced an infiltrative and vegetating tumoral lesion at the lower rectum attached to its epithelium, occupying 75% of its lumen. The colonoscopy evidenced an elevated lesion, vegetative and infiltrative with 3 cm of extension, and slight colonic diverticulum, with no sign of bleeding or inflammation. The histopathological exam concluded it was a moderately differentiated adenocarcinoma of the rectum (Figure 2A). The abdominal-pelvic tomography evidenced cholelithiasis, sigmoid colon dilatation full of gas and fecal content, and circumferential thickening of the rectum, but no signs of metastatic disease. She also presented anemia with serum hemoglobin of 9 g/dL (as 13.5-18 g/dL), the only positive laboratorial finding.

During the surgical procedure, a lower rectum tumor with a hard consistency, 2 cm from the anus and fixed to the sacral region was found. There was no peritoneal involvement or ascitis. However there were two liver nodules smaller than 1cm in each lobe, suggesting metastasis. The gallbladder had many gallstones and adhesions to the transverse colon. The patient underwent Miles surgery in addition to cholecystectomy and liver biopsy of the left lobe nodule (Figure 2B). She recovered very well from the surgery, without any type of complication and with early hospital discharge on the 4th postoperative day. Chemotherapy and radiotherapy were not performed because they were not available and therefore we chose to do these two therapies during the postoperative period. Regarding the postoperative information, these were lost during the patient

follow-up. Histopathological findings of the rectum concluded it was a moderately differentiated adenocarcinoma at the lower rectum, constrictive, and around 5cm of length. The distal and proximal borders were free of neoplasm, showing angiolymphatic invasion and extensive invasion of the pericolic tissue. Examining the visceral peritoneum and the lesion borders showed an infiltrative pattern, with moderate stromal desmoplastic reaction (Figure 2A). No magnetic resonance imaging was performed, although the staging was performed with computed tomography. There were metastases in three of four identified nodes, and the pathological staging for the intestinal specimen was pT4pN1. Histopathology of the gallbladder evidenced moderately differentiated adenocarcinoma (Figure 2C), reaching to the muscular layer with no lymph nodal, angiolymphatic, or perineural invasion, T2N0 (stage IA). The tumor had invaded the perimuscular connective tissue. The liver nodules revealed an adenocarcinoma, with a moderately differentiated pattern showing tumor vessel emboli.

DISCUSSION

Synchronous cancers are defined as those diagnosed at the same time or within six months; cancers are considered metachronous when the second tumor is diagnosed more than six months after the first. Colon and gallbladder primary synchronic adenocarcinomas are rare^[3]. In the literature, only five cases were related worldwide since 2005^[1]. However, in the last years, multiple primary tumors have been more frequently documented due to the increase in life expectancy and the improvement of diagnosis techniques^[1,7]. A Japanese study done by Horii *et al* evidenced that microsatellite instabilities were frequently observed in multiple primary neoplasms rather than in single neoplasms^[2,8].

The Warren and Gates criteria define synchronic tumors and can be applied if a second primary tumor falls into these criteria: (a) each tumor should represent a single form of malignancy; (b) each tumor has to be distinct from each other; and/or (c) the metastatic tumor should be excluded^[1,7].

A review of 659 cases of multiple primary tumors identified by autopsy demonstrated that the colon was the most frequent organ involved in those cases, especially in elder people^[1,9]. Another study evaluated 308 colorectal adenocarcinoma cases where twelve multiple primary cancers were found. Also, fourteen tumors in other organs outside the colon were found. This is unusual considering that colon cancers with second primary tumors in other segments of the colon are a common finding. The standard surgical treatment for multiple primary tumors is the curative resection of each individual tumor, when it is feasible^[2,7].

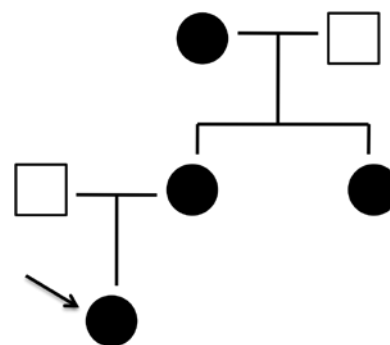


Figure 1 Family Pedigree. The black arrow indicates the case reported.

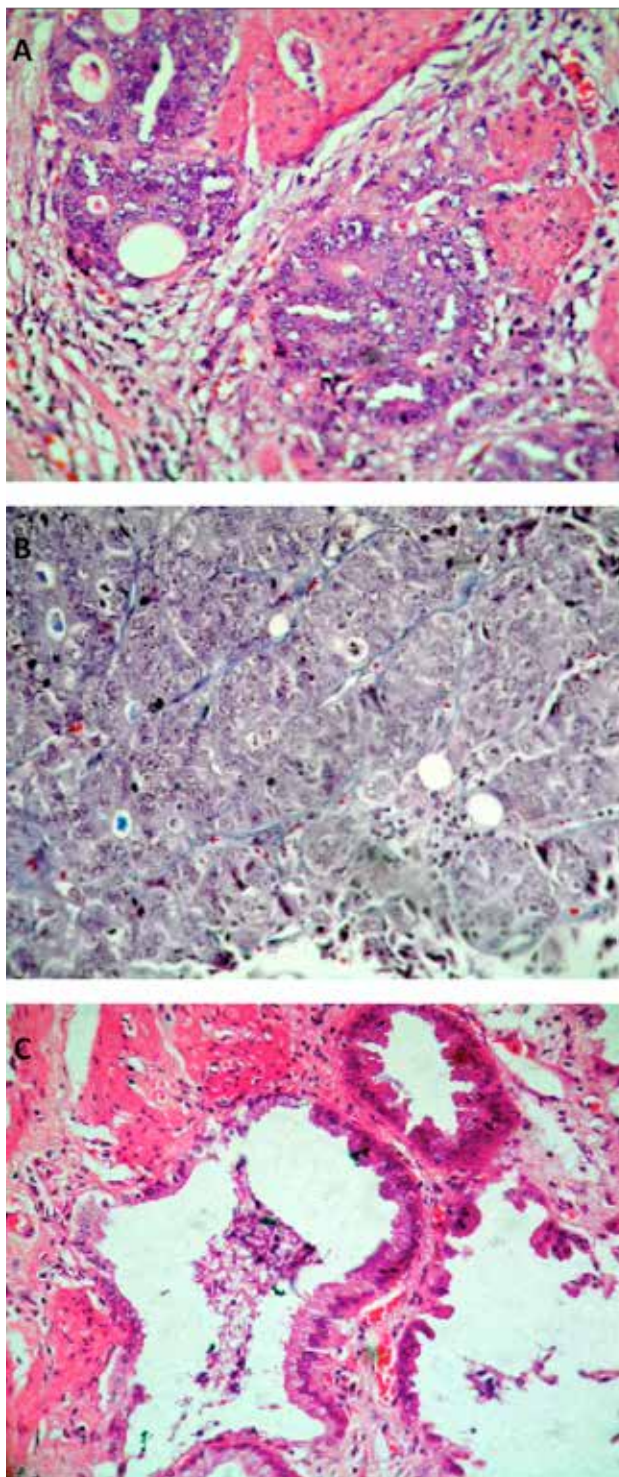


Figure 2 Histopathological analysis by hematoxylin and eosin staining (10×). A. Rectal adenocarcinoma infiltrating into the muscular layer; B. Liver metastatic adenocarcinoma; C. Gallbladder adenocarcinoma infiltrating into the muscular layer.

The prognostic of multiple tumors can be independently defined by the stage of each tumor isolate^[10]. The therapy and the follow-up of these patients must follow the standard guidelines for each tumor. However, it is necessary to keep in mind the procedure's target cost / benefit ratio for each case. Aggressive procedures may not be indicated in the treatment of one tumor if the other primary tumor is

not feasible to treat due to its advanced stage. In those cases, the life expectancy has to be evaluated. Despite the advanced stage of the rectal cancer, neoadjuvant therapy was not performed because the surgery is more effective to address the metastases in the liver and bladder cancer.

In addition, cytokeratin (CK) expression is being frequently used for the differential diagnosis of carcinomas originating from different sites. Among the various CKs, the combination of CK7 and CK20 is considered to be the most useful for this purpose^[11]. In the present study we did not perform immunohistochemical analysis for CKs because the very few reports in the literature regarding CK7 and CK20 expression in gallbladder carcinoma indicate that the clinical significance of CK7/CK20 expression still requires further investigation.

In this report, the association of rectal and gallbladder cancer together was a casual case of synchronous tumors because the preoperative diagnosis was cholelithiasis. The adjuvant therapy was indicated for the rectal cancer, as usually done according to standard protocol for rectal cancer treatments. Nevertheless, no aggressive surgical procedure was indicated for the gallbladder cancer. Considering the therapeutic guidelines for exclusive gallbladder tumors at this stage, the treatment should also include liver resection (keeping in mind that the hepatic metastases were due to rectal cancer). The liver resection was performed in addition to a lymphadenectomy (the histopathology report of which did not detect the presence of metastatic lymph nodes). The main determinant for this tailored approach was the initial evaluation results of the adjuvant therapy against liver metastases and also for the biological behavior of the tumors, since the possibility of disease progression in a short period of time should eliminate the need for any additional radical surgical procedure.

CONCLUSION

The existence of primary gallbladder and rectal neoplasms is a rare condition and its treatment must be standardized for each tumor individually. It is important that when tumors are found in advanced stages of the disease or when the metastasis of one of the tumors is found, the treatment should be tailor according to the management of the tumor presenting the worse prognostic scenario, avoiding aggressive procedures when it is not possible to radically and integrally treat both tumors.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

ACKNOWLEDGMENTS

Author contributions: Montenegro RC, Assunção PP, Moreira-Nunes CFA and Burbano RR wrote the paper; Ishak G, Lima Júnior SF and Assunção PP operated on the patient and completed patient follow-ups together with Bahia LAC, Costa DS and Ribeiro FS for data collection; Demachki S analyzed the histopathology data; Montenegro RC, Assunção PP and Burbano RR supervised the writing and organization process. All authors have contributed to the elaboration of this manuscript.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

REFERENCES

1. Sakellaridis T, Mathioulakis S, Antiochos C. Synchronous early primary adenocarcinoma of both rectum and gallbladder. Report of a case. *International Seminars in Surgical Oncology* 2005; **2**: 19
2. Lee TK, Barringer M, Myers RT, Sterchi JM. Multiple primary carcinomas of the colon and associated extracolonic primary malignant tumors. *Ann Surg* 1982; **195**: 501-507.
3. Arai T, Sawabe M, Takubo K, Kanazawa K, Esaki Y. Multiple colorectal cancers in the elderly: a retrospective study of both surgical and autopsy cases. *Gastroenterol* 2001; **36 (suppl 11)**: 748-752
4. Schmid KW, Glaser K, Wykypiel H, Feichtinger H. Synchronous adenocarcinoma of the transverse colon, the gallbladder and the vermiform appendix. *Klin Wochenschr.* 1988; **66**: 1093-1096
5. Howe HL: A Review of the Definition for Multiple Primary Cancers in the United States. In Proceedings of the North American Association of Central Cancer Registries, Springfield (IL) December 4–6 May 2002, Princeton, New Jersey. Edited by Howe HL; 2003.
6. Ribeiro MD, Viana HL, Silva R, Dias LM, Viana RL. Associated primary tumors in patients with gastric cancer. *J Clin gastroenterol* 2002; **34 (suppl 5)**: 533-535
7. Tamura M, Shinagawa M, Funaki Y. Synchronous triple early cancers occurring in the stomach, colon and gallbladder. *Asian J Surg* 2003; **26**: 46-49
8. Horii A, Han H-J, Shimada M, Yanagisawa A, Kato Y, Ohta H, Yasui W, Tahara E, Nakamura Y. Frequent replication errors at microsatellite loci in tumor of patients with multiple primary cancers. *Cancer Res* 1994; **54**: 3373-3375
9. Parkash O. Multiple primary malignancies. A statistical study based on autopsy data from 1943-1972. *Virchow Arch [Pathol Anat]* 1977; **375**: 281-286
10. Jará RL, Santos CHM, Alves LP, Miji LNO. Tumor de Reto e Cár-dia Sincrônicos. Relato de Caso e Revisão da Literatura. *Rev bras Coloproct* 2007; **27 (suppl 1)**: 080-082
11. Kalekou H, Miliaras D. Cytokeratin 7 and 20 expression in gallbladder carcinoma. *Pol J Pathol* 2011; **62**: 25-30

Peer reviewers: Alejandro Serrablo MD PhD, Associate Professor of Surgery, Hepatopancreatic biliary Surgical Unit, Miguel Servet University Hospital, Zaragoza 50009, Spain; Raja Kalayarasan, Senior registrar, Department of Gastrointestinal surgery, GB Pant Hospital & Maulana Azad Medical College, New Delhi -110002, India.