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Triple primary malignancies in a patient with colorectal adenocarcinoma: A case report

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ABSTRACT

INTRODUCTION: While colorectal carcinoma is one of the most commonly diagnosed malignancies, its synchronous occurrence with other primary malignancies is rare.**PRESENTATION OF CASE:** In this case, we describe the diagnosis and surgical intervention of a 55-year-old male patient who was found to have colonic adenocarcinoma at the hepatic flexure, right renal urothelial carcinoma, and malignant mesothelioma.**DISCUSSION:** None of the previous studies reported these three distinct types of cancer, even in those patients with Lynch Syndrome. To the best of our knowledge, this is the first report of such case. The etiology and pathogenesis of multiple primary malignancies are complex. Common genetic and environmental risk factors that were found in different cancers might increase the risk of multiple primary malignancies.**CONCLUSION:** The use of genetic testing and preoperative imaging studies should be considered to be invaluable tools for detecting synchronous malignancies. Practicing physicians should pay more attention to the risk of simultaneous separate primary malignancies.© 2017 Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Colorectal carcinoma (CRC) is the one of the most common malignancies, affecting 42.4 per 100,000 men and women each year, with the death of 15.5 per 100,000 annually in the United States [1]. The concurrent presence of colorectal cancer and other primary malignancies is relatively rare [2]. Here we report a unique patient with colonic adenocarcinoma at the hepatic flexure, right renal urothelial carcinoma and malignant mesothelioma invading the duodenum and the inferior vena cava and the literature was reviewed.

This report utilized the definition of Warren and Gates to identified those synchronous tumors [3]: each tumor must have definite pathologic evidence and must be distinct that the possibility of cancer metastasis would be excluded. The most possible etiology and pathogenesis of triple primary CRC is that these involved tissues

are simultaneously affected by the same carcinogens, including environmental and hereditary factors [4].

There have been some reports demonstrated that CRC is associated with other primary malignancies, such as pancreatic carcinoma [5,6], prostate cancer [7], and renal carcinoma [4,8,9]. Burgess et al. [10] reported a case that a patient with colonic carcinoma, renal cell carcinoma, and gastrointestinal stromal tumor. Capilna et al. [11] described a female patient presented with primary malignancies of the fallopian tube, endometrium and sigmoid colon synchronously. A patient with Lynch syndrome (LS) diagnosed with triple synchronous primary malignancies of the colon, endometrium and kidney has been reported recently [12]. And we described another patient diagnosed with three distinct malignancies in this article. This work has been reported in line with the SCARE criteria [13].

2. Case presentation

A 55-year-old male presented with intermittent abdominal pain in the right upper quadrant associated with liquid stools in the past 2 months. The patient had no family history of colorectal cancer. He lost 5 kg on his weight. Physical examination revealed an 8*8 cm

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Fig. 1. Abdominal CT scan (A) revealed a severe hydronephrosis of the right kidney and bowel-wall thickening of the ascend colon.

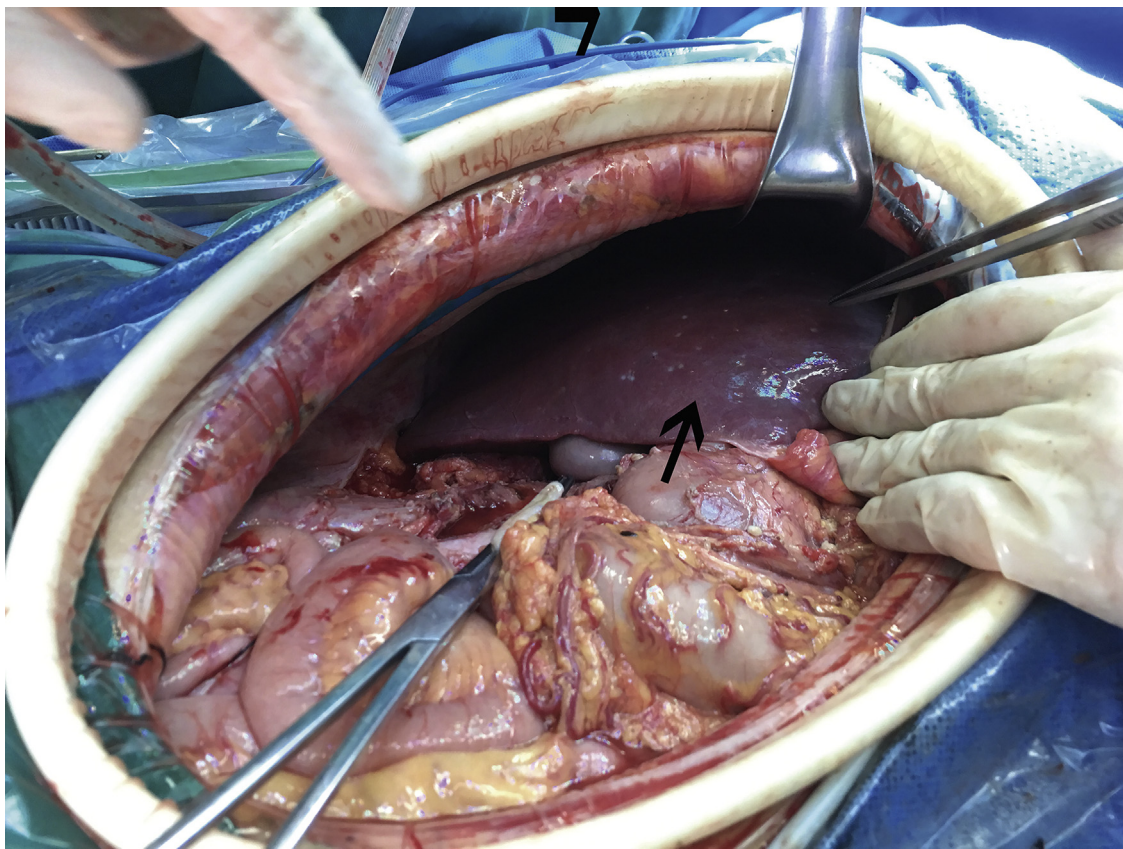


Fig. 2. Multiple diminutive ill-defined hepatic lesions (arrow) were visualized during the surgery.

mass palpable in the right upper abdomen and pain on percussion the right costovertebral angle. Colonoscopy and biopsy demonstrated that a well-differentiated adenocarcinoma in the hepatic flexure, multiple tubular adenomas in the transverse and sigmoid colon and hyperplastic polyps in the rectum. Initial computed tomography (CT) scan showed a 6.5*6.5 cm mass in the hepatic flexure (Fig. 1B and C), multiple low-density foci in the left lobe of liver, multiple small mesenteric nodules, and hydronephrosis of the right kidney. A large lymph node was also revealed on CT scan with a size of 5*5 cm, causing obstruction of the right ureter and hydronephrosis of the right kidney (Fig. 1A). The patient developed a severe flank pain during hospitalization and a percutaneous nephrostomy was performed under the guidance of Color Doppler Ultrasound.

After multidisciplinary discussion with the oncology department, an exploratory laparotomy was performed due to imminent bowel obstruction. During the surgical exploration, an 8*7*6 cm

irregular globular clear-edged mass was identified in the ascending colon and multiple diminutive ill-defined hepatic lesions were visualized (Fig. 2), leading to right hemicolectomy (Fig. 3A) without hepatic resection. A 5*5 cm solid nodule was found posterior to the ascending colon, invading the right ureter, the second portion of the duodenum, the inferior vena cava, and the lumbar vertebra. The patient then underwent right nephrectomy (Fig. 3B). Wedge resection of the duodenum and nodules detaching before the inferior vena cava were performed including the invading mass.

Postoperative examination of the specimen (hematoxylin-eosin staining, HE staining) revealed a moderately or poorly differentiated adenocarcinoma (Fig. 4D) (T4b), positive for Ki-67 (70%), MLH1, MSH6, PMS2, CDX2, human epidermal growth factor receptor-2 (HER2), cyokeratin (CK) 20, carcinoembryonic antigen (CEA) and negative for MSH2, CK5/6, MC, CK7. Interestingly metastasis was found in none of the 54 lymph nodes (T4bN0M1).

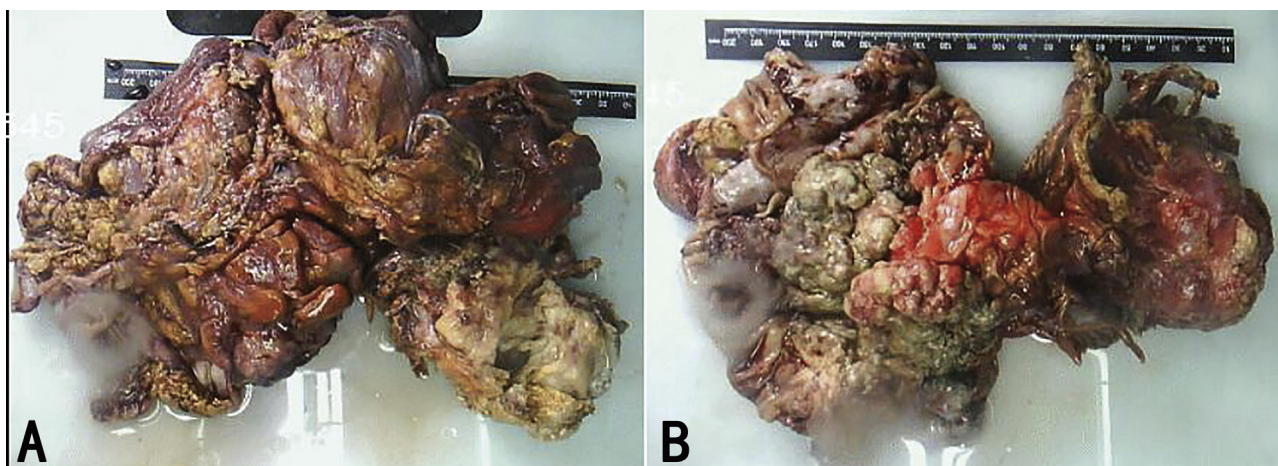


Fig. 3. The resected specimen of hepatic flexure of the colon (A) and right kidney (B).

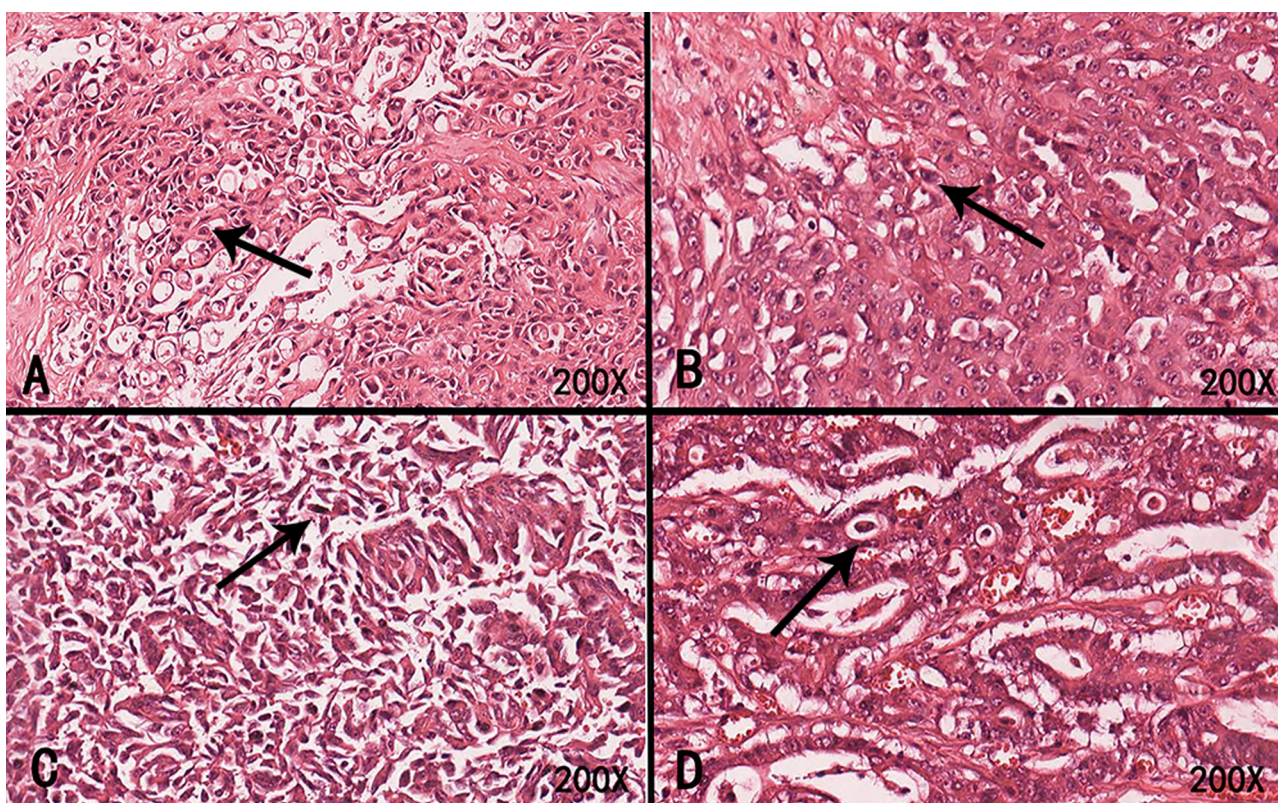


Fig. 4. Histological finding (HE staining) showed that malignant mesothelioma invading the inferior vena cava (A) and duodenum (B) (black arrows). Evaluation of the nephrectomy and hemicolectomy specimen (HE staining) confirmed a non-invasive low-grade urothelial carcinoma (C) in the kidney and a moderately or poorly differentiated adenocarcinoma (D) in the hepatic flexure (black arrows).

Histological findings (HE staining) of the ureter and adjacent tissue confirmed a non-invasive low-grade urothelial carcinoma (Fig. 4C) positive for CD10, Epithelial membrane antigen (EMA), CK20, Ki-67 (5%) and negative for Vimentin, CK7. Moreover, the resected tissue before the inferior vena cava (Fig. 4A) and the involved duodenal segment (Fig. 4B) (HE staining) were demonstrated to be malignant mesothelioma. The genetic testing revealed that the patient harbored KRAS gene mutation but his NRAS, BRAF and PIK3CA genes were wild type.

The patient had an uneventful recovery after surgery and received chemotherapy regularly for his liver metastasis. MSI testing and further genetic testing was suggested for him to detect

defective mismatch repair (MMR) gene, in order to identify suspected LS.

3. Discussion

In the present case report, the patient was diagnosed synchronously with three distinct primary malignancies, which much rarer than those two primary cancers. MSH2 was negative in our patient, suggestive for LS. The incidence of primary extracolonic cancer would increase significantly in those patients with LS, including gynecological cancers, gastric cancer, small bowel cancer and urinary tract cancers [14]. Peritoneal mesothelioma has also been reported in a patient with Lynch syndrome in 2012 [15].

However, none of the previous studies reported these three distinct types of cancer in patients, even in those patients with LS. To the best of our knowledge, this is the first report of such case.

The incidence of multiple primary malignancies varied widely in the literature. A 12-year 7516 cancer patients retrospective study showed 32 patients developed two primary malignancies and only 7 diagnosed with three different cancers [16]. The reported incidence of multiple primary cancers in extracolonic sites among colorectal carcinoma patients ranged from 2.4% to 8.7% [2]. Halak M et al. [8] found that the rate of colorectal carcinoma associated with renal cell carcinoma was 4.85% in their study and the risk of multiple primary malignancies was increased in the elderly.

The etiology and pathogenesis of multiple primary malignancies are complex. Possible etiology include genetic, environmental, hormonal, medical treatment-related, and gender specific factors [10]. Moreover, the common genetic and environmental risk factors that were found in different cancers might increase the risk of multiple primary malignancies. Common risk factors include tobacco, pollution, ultraviolet light, therapeutic chemotherapy and radiotherapy, and endocrinological factors [17].

The use of genetic testing and preoperative imaging studies should be considered to be invaluable tools for detecting synchronous malignancies, especially for the elderly CRC patients. Based on this clinical case and the literature considered, in patients with CRC, we believed practicing physicians should pay more attention to the risk of simultaneous separate primary malignancies.

Conflicts of interest

The authors declare that there is no conflict of interest.

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Ethical approval

Ethics approval has been exempted from your institution for this case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Qunsheng Huang: Data collection, editing the manuscript, and literature review.

Xin He: Searching for the related references and polishing the article.

Huabo Qin: Editing the manuscript, and literature review.

Xinjuan Fan: Took the photographs, data collection.

Minghao Xie: Editing the manuscript, and literature review.

Lei Lian: Concept and design of study, revision, approval of final manuscript.

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