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ABOUT COVER

Peer-Reviewer of *World Journal of Clinical Cases*, Dr. Adonis Protopapas is a gastroenterology Resident at the first Propaedeutic Department of Internal Medicine of the Aristotle University of Thessaloniki (Greece), located at the A.H.E.P.A Hospital. He earned his Bachelor's degree in 2015 from the Democritus University of Thrace, followed by three Master's of Science degrees, with specializations in clinic pharmacology, medical research methodology, and healthcare management. His research interests are mainly focused on the area of hepatology, although he also participates in various projects related to endoscopy and inflammatory bowel disease. He is particularly fascinated by research on cirrhosis and its complications. (L-Editor: Filipodia)

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Synchronous colonic mucosa-associated lymphoid tissue lymphoma found after surgery for adenocarcinoma: A case report and review of literature

Juan-Juan Li, Bing-Chen Chen, Jie Dong, Yuan Chen, You-Wei Chen

ORCID number: Juan-Juan Li 0000-0003-0421-0606; Bing-Chen Chen 0000-0001-8977-6072; Jie Dong 0000-0002-2338-8955; Yuan Chen 0000-0002-9476-8816; You-Wei Chen 0000-0002-5663-6118.

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Juan-Juan Li, Department of Intensive Care Unit and Comprehensive Support, Wang-Jiang-Shan Branch of Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, Hangzhou 310014, Zhejiang Province, China

Bing-Chen Chen, Department of Colorectal Surgery, Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, Hangzhou 310014, Zhejiang Province, China

Jie Dong, You-Wei Chen, Department of Gastroenterology, Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, Hangzhou 310014, Zhejiang Province, China

Yuan Chen, Department of Pathology, Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, Hangzhou 310014, Zhejiang Province, China

Corresponding author: You-Wei Chen, MSc, Chief Doctor, Department of Gastroenterology, Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, No. 158 Shangtang Road, Hangzhou 310014, Zhejiang Province, China. cyw@zju.edu.cn

Abstract

BACKGROUND

Mucosa-associated lymphoid tissue (MALT) lymphoma is a subtype of non-Hodgkin lymphoma that is mainly involved in the gastrointestinal tract. The synchronous occurrence of colonic MALT lymphoma and adenocarcinoma in the same patient is extremely rare. We here report a case of synchronous colonic MALT lymphoma found on surveillance colonoscopy five months after surgery and chemotherapy for sigmoid adenocarcinoma.

CASE SUMMARY

A 67-year-old man was admitted because of hematochezia for two months. Colonoscopy suggested a colonic tumor before hospitalization. Abdominal computed tomography (CT) revealed local thickening of the sigmoid colon. The patient underwent a left hemicolectomy with local lymph node dissection. The histopathology revealed moderately differentiated adenocarcinoma and partially mucinous adenocarcinoma. The pTNM stage was T3N1Mx. The patient received chemotherapy with six cycles of mFOLFOX6 after surgery. Colonoscopy was performed five months later and revealed single, flat, polypoid lesions of the colon 33 cm away from the anus. Subsequently, the patient underwent endoscopic

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mucosal resection for further diagnosis. The pathological diagnosis was MALT lymphoma. Positron emission tomography /CT suggested metastasis. The patient refused further treatment and died ten months later.

CONCLUSION

Colonic MALT lymphoma may occur after surgery and chemotherapy for adenocarcinoma as a synchronous malignancy. Regular surveillance colonoscopy and careful monitoring after surgery are critical.

Key Words: Mucosa-associated lymphoid tissue lymphoma; Adenocarcinoma; Colon; Synchronous malignancy; Surgery; Case report

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Core Tip: The synchronous occurrence of colonic mucosa-associated lymphoid tissue (MALT) lymphoma and adenocarcinoma in the same patient is extremely rare. Few cases have been reported in the literature to date. Colonic MALT lymphoma is often asymptomatic and found on surveillance colonoscopy. When it presents synchronously with colonic adenocarcinoma, MALT lymphoma is easily missed. Regular surveillance colonoscopy and careful monitoring after surgery are critical. We report a case of synchronous colonic MALT lymphoma found on surveillance colonoscopy five months after surgery and chemotherapy for sigmoid adenocarcinoma.

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INTRODUCTION

Mucosa-associated lymphoid tissue (MALT) lymphoma, also known as extranodal marginal zone lymphoma, is a subtype of non-Hodgkin lymphoma (NHL)^[1,2]. MALT lymphoma is the third most frequent histologic subtype, accounting for approximately 7% - 8% of all NHLs^[3]. MALT lymphoma may arise anywhere outside the lymph nodes, predominantly involving the gastrointestinal (GI) tract and other areas, such as the ocular adnexa, salivary glands, thyroid, skin, lungs, and breast. MALT lymphoma occurring in the GI tract is found mainly in the stomach, accounting for more than half of all cases, followed by MALT lymphomas in the small intestine, cecum, and colorectum^[4]. The synchronous occurrence of colonic MALT lymphoma and adenocarcinoma in the same patient is extremely rare^[5-7]. Only one case of synchronous colonic MALT lymphoma diagnosed after hemicolectomy due to adenocarcinoma within six months has been reported in the literature to date^[8]. We here report a case of synchronous colonic MALT lymphoma found on surveillance colonoscopy five months after surgery and chemotherapy for sigmoid adenocarcinoma.

CASE PRESENTATION

Chief complaints

A previously healthy 67-year-old man presented with hematochezia for two months.

History of present illness

The patient had hematochezia for two months. His stool was dark red and bloody, occasionally pale pink in color, but the blood was not mixed with the stool; thinning of the stool was also observed. He occasionally had abdominal distension but no abdominal pain, nausea, vomiting, diarrhea, or fever. Colonoscopy at a local hospital suggested a sigmoid tumor.

History of past illness

The patient had no history of hypertension, heart disease, diabetes, smoking or drinking. He denied a history of surgery.

Personal and family history

The patient denied a relevant family history.

Physical examination

The physical examination was unremarkable.

Laboratory examinations

His hemoglobin level was 144 g/L. The blood biochemistry and coagulation function results were normal. Anti-human immunodeficiency virus (HIV) and anti-hepatitis C virus testing was negative. The carcinoembryonic antigen level was 6.7 µg/L, while the carbohydrate antigen 19-9 level was 39.0 U/mL. A fecal occult blood test was mildly positive.

Imaging examinations

Abdominal computed tomography (CT) revealed local thickening of the sigmoid colon.

FINAL DIAGNOSIS

The diagnosis was synchronous colonic MALT lymphoma following surgery and chemotherapy for sigmoid adenocarcinoma.

TREATMENT

The patient underwent left hemicolectomy with local lymph node dissection. The histopathology revealed moderately differentiated adenocarcinoma and partially mucinous adenocarcinoma, and the macroscopic classification was the ulcerative type. The size of the mass was 3.3 cm × 3.0 cm × 1.0 cm, and the mass involved the serosal layer. Additionally, vascular and nerve involvement was observed. There was involvement of the pericolic lymph nodes (1/6) but no involvement of the mesenteric lymph nodes (0/6). Metastatic carcinomas were found in the abdominal cavity. The diameters of the three metastatic tumors were 0.2- 1.0 cm. Immunohistochemical staining showed that the tumor cells were positive for Ki67 (80% positive), CD34 (vascular), D2-40 (lymphatic), PMS2, MSH2, MSH6, MLH1, CDX2, E-cadherin, EGFR, CK20, and CK (pan) but negative for CK7 and p53. The final pTNM stage was T3N1Mx.

The patient received chemotherapy with six cycles of mFOLFOX6 (calcium folinate (0.6 g), fluorouracil (0.6 g), and oxaliplatin (130 mg) after surgery.

Colonoscopy was performed five months after surgery. Colonoscopy revealed a single, flat, 1.2 cm × 0.8 cm polypoid lesion of the colon 33 cm from the anus (Figure 1). The size was approximately 1.0 cm in diameter. Subsequently, the patient underwent endoscopic mucosal resection for further diagnosis. Microscopically, hematoxylin and eosin staining showed lymphoid hyperplasia (Figure 2). Immunohistochemical staining showed that the tumor cells were positive for CD19, CD20, CD21 and CD23 (dendritic cells), as well as CD43, CD79a, BCL-2, and Ki67 (10% positive) (Figure 3), but negative for CD3, CD5, CD10, Cyclin D1, Kappa, Lambda, BCL-6, and EBER (Figure 4). Molecular detection of EBER was also negative. The final pathological diagnosis was MALT lymphoma.

To confirm whether distant metastasis occurred, 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) was performed. PET/CT demonstrated subcapsular effusion in the liver with increased FDG metabolism; the upper right area of the peritoneum was slightly thickened and had slightly increased FDG metabolism (Figure 5). These results suggested metastasis.

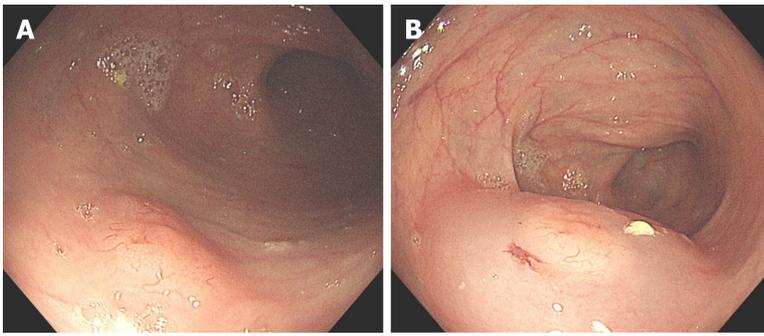


Figure 1 Colonoscopy. A: A 1.2 cm × 0.8 cm flat polypoid lesion in the colon; B: The lesion after submucosal injection of normal saline into the colon.

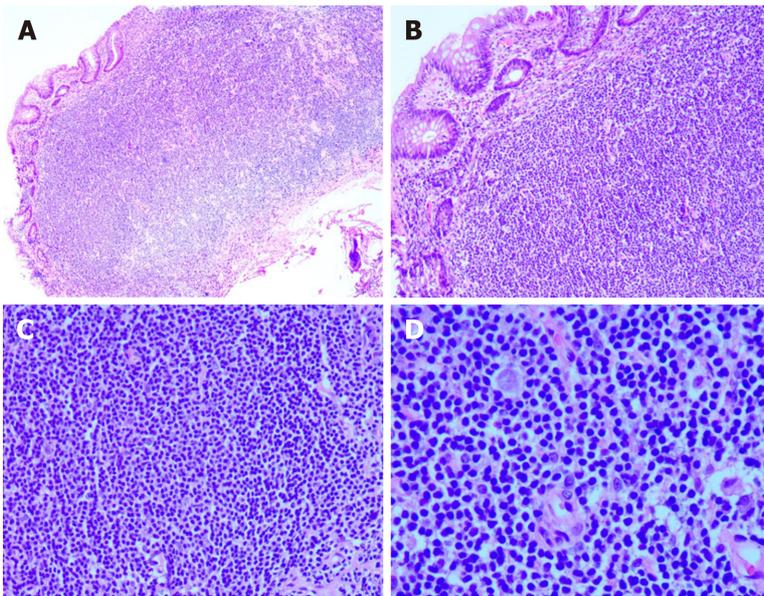


Figure 2 Histopathological findings. A: Hematoxylin and eosin (HE) staining (× 40); B: HE staining (× 100); C: HE staining (× 200); D: HE staining (× 400).

OUTCOME AND FOLLOW-UP

The patient refused further treatment because of the suspicion of metastasis and died ten months later due to tumor metastasis.

DISCUSSION

To the best of our knowledge, our case is the one of the few ever reported concerning synchronous colonic MALT lymphoma found on surveillance colonoscopy after hemicolectomy for colonic adenocarcinoma.

Any second malignancy in a patient with an existing malignancy is classified as either synchronous or metachronous. According to the definition of Gluckman^[9], synchronous malignancies include malignancies that are present either simultaneously or within six months of the original tumor diagnosis. Malignancies diagnosed beyond the six-month interval are referred to as metachronous. Our case met the definition of a synchronous malignancy.

MALT lymphoma, first described in 1983^[10], was classified as an extranodal marginal zone B cell lymphoma by the World Health Organization in 2008^[2]. MALT lymphoma may arise anywhere outside the lymph node and has cellular immunophenotypic features that are similar to those of lymphomas in other areas, predominantly affecting the GI tract as well as the ocular adnexa, salivary gland, thyroid, skin, lung, and breast^[4,11]. The stomach is the most common site of MALT lymphoma in the GI tract, accounting for 60% - 75% of all cases, followed by MALT lymphomas of the small intestine, ileum, cecum, and colorectum^[4]. Although the

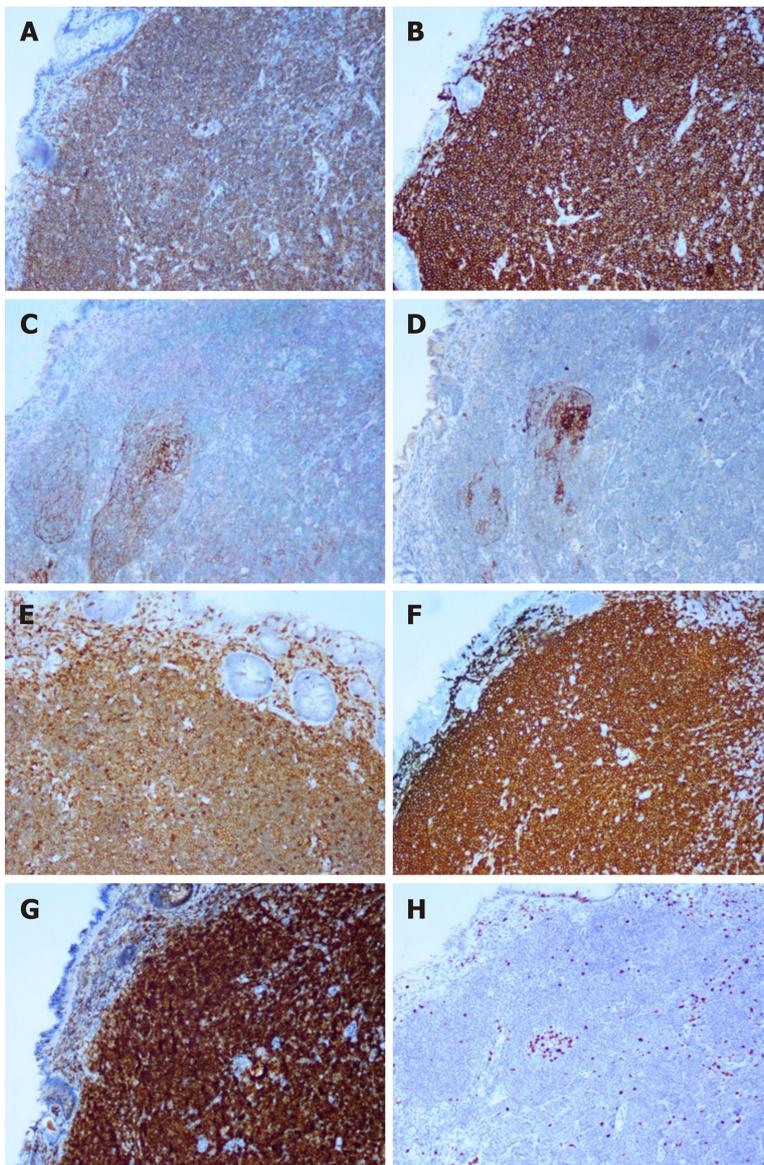


Figure 3 Immunohistochemical staining (× 100). A: Immunostaining for CD19; B: Immunostaining for CD20; C: Immunostaining for CD21 (dendritic cells); D: Immunostaining for CD23 (dendritic cells); E: Immunostaining for CD43; F: Immunostaining for CD79a; G: Immunostaining for BCL-2; H: Immunostaining for Ki67 (10% positive).

incidence of gastrointestinal lymphoma is increasing^[12], primary colonic MALT lymphoma remains a rare disease, accounting for less than 5% of GI lymphomas^[13] and less than 1% of all colorectal malignancies^[14].

The causative factor of colonic MALT lymphoma remains unclear. An important causative factor is antigen-specific lymphoproliferation. Chronic antigenic stimulation by either microbial pathogens (*e.g.*, *Helicobacter pylori*, *Chlamydia psittaci*, and *Borrelia burgdorferi*) or autoantigens (*e.g.*, the antigens found in Hashimoto's thyroiditis and Sjögren's syndrome) indirectly determines the risk of involvement of specific mucosal sites in primary MALT lymphoma^[15].

Colonic MALT lymphoma affects mainly adults in their fifth to seventh decades of life^[4,16]. The mean age at presentation is 60 years^[16]. The sex bias ranges from almost nonexistent to a 2:1 female predominance^[16-18]. Approximately half of the patients are asymptomatic, with the disease discovered on surveillance colonoscopy^[16,19]. Moreover, the cancer can present with diarrhea, constipation, mucoid stool, hematochezia, abdominal or epigastric pain, weight loss^[19,20], GI bleeding^[21], a palpable mass^[19], intussusception^[22], or acute intestinal obstruction^[23].

MALT lymphoma of the colorectum may show variable presentations on endoscopy. Subepithelial tumors, polyposis, epithelial masses, and ileitis are the four distinct types of endoscopic appearances^[16]. Single or multiple lesions may be flat, elevated, polypoid or semipedunculated, with the surface smooth, eroded, granular or

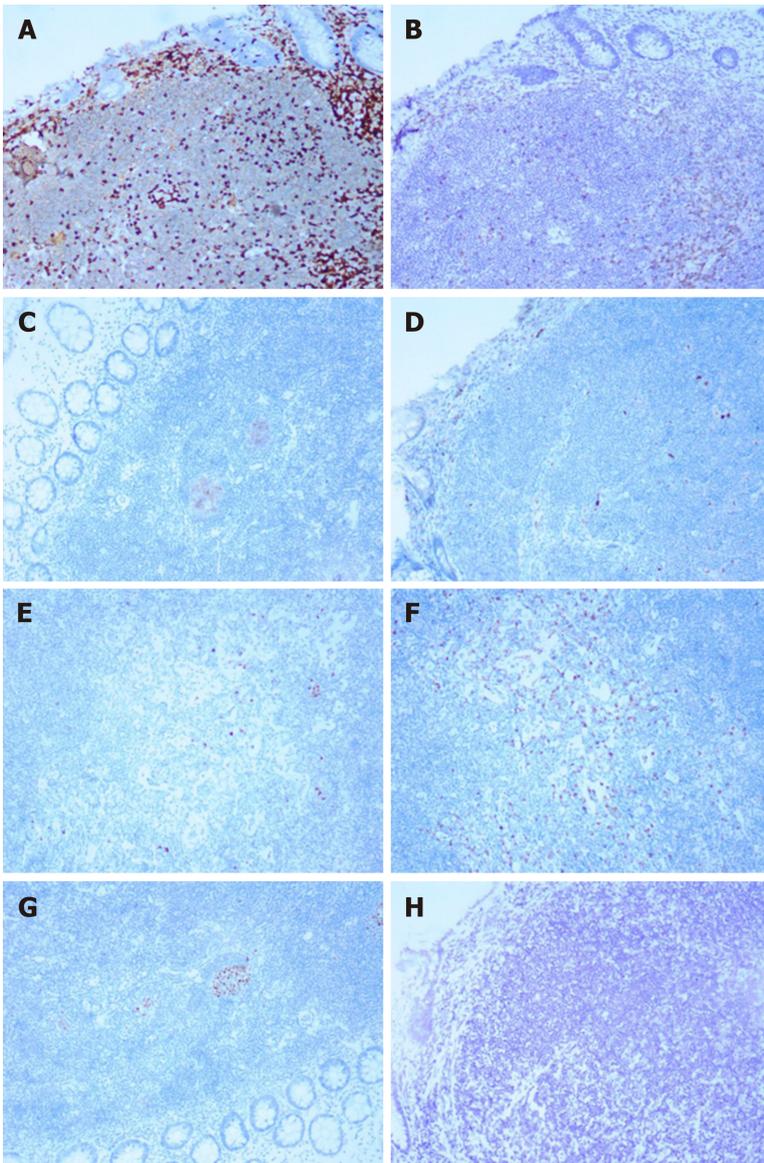


Figure 4 Immunohistochemical staining ($\times 100$). A: Immunostaining for CD3; B: Immunostaining for CD5; C: Immunostaining for CD10; D: Immunostaining for Cyclin D1; E: Immunostaining for kappa; F: Immunostaining for lambda; G: Immunostaining for BCL-6; H: Immunostaining for EBER.

nodular^[17]. The size varies from millimeters to 4-5 centimeters^[4,20,24]. Chromoendoscopy and narrow-band imaging may improve the detection and border delineation of colorectal MALT lymphoma^[25].

Monocytoid B cells, centrocyte-like cells and small lymphocytes are the main cell types in MALT lymphoma, sometimes accompanied by cells with plasmacytoid differentiation, scattered immunoblasts and transformed centroblast-like cells^[17]. The atypical cell population may exist in the mucosa or submucosa and even the muscularis propria of the colon^[17]. Immunophenotypically, colonic MALT lymphomas coexpress B-cell markers, such as CD19, CD20 and CD79a, but are typically negative for CD5, CD10, CD23, and Cyclin D1^[26]. Some also show CD5 reactivity^[17], and the Ki67 proliferation rate is usually low^[19]. Recurrent cytogenetic abnormalities in MALT lymphomas include mainly the t(1;14)(p22;q32), t(11;18)(q21;q21) and t(14;18)(q32;q21) translocations, which may affect the nuclear factor kappa light chain-enhancer of activated B cells (NF- κ B) pathway, and trisomies of chromosomes 3 and 18^[2,17,27].

To date, standardized treatments for colonic MALT lymphoma are lacking since the disease is relatively rare. The common therapies include surgical resection (partial colectomy), endoscopic resection, radiotherapy, chemotherapy, immune therapy (such as rituximab) and antibiotics in varying combinations^[16,18,19,28,29]. The relationship between colonic MALT lymphoma and *Helicobacter pylori* (*H. pylori*) infection remains unclear^[30]. However, the tumor may regress after *H. pylori* eradication^[31]. Because of the indolence of colorectal MALT lymphoma, a "watch and wait" approach may be

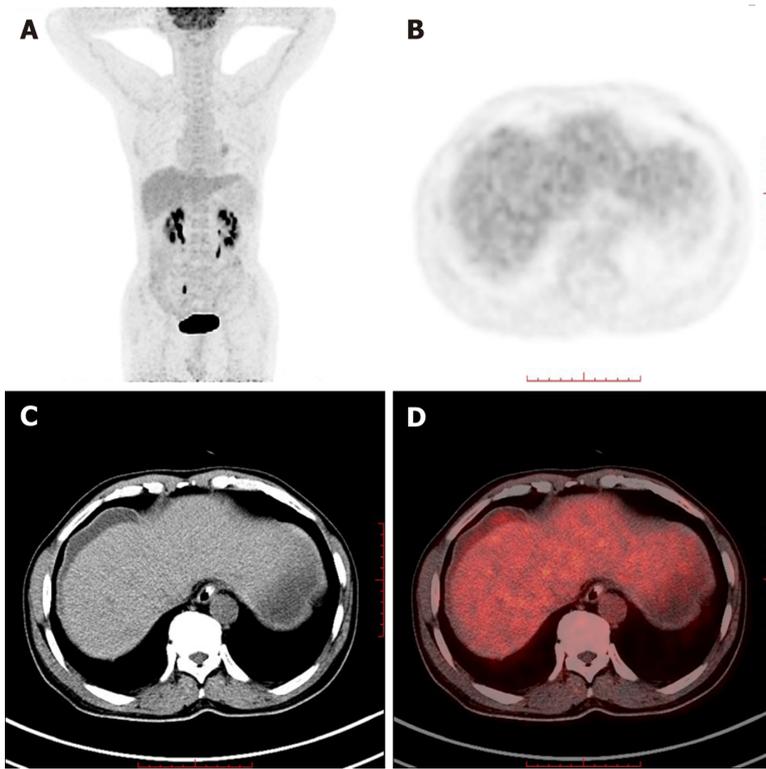


Figure 5 Whole-body maximum intensity projection ^{18}F -fluorodeoxyglucose and positron emission tomography. A: Slightly increased fluorodeoxyglucose metabolism in the subcapsular effusion of the liver, as well as in the right upper area of the peritoneum; B: Positron emission tomography; C: Computed tomography; D: Positron emission tomography/computed tomography in axial projection showing lesions in the subcapsular effusion of the liver.

suggested in patients who are asymptomatic or who have minimally apparent disease on colonoscopy^[29]. Colonic MALT lymphoma has a good prognosis with low recurrence^[17]. The 5-year progression-free survival is 92%, while the overall survival is 94%. The disease-specific survival is 98% at five years^[16].

The relationship between colonic MALT lymphoma and adenocarcinoma is unknown. Colonic MALT lymphoma was found to be a metachronous malignancy in a patient who had undergone hemicolectomy for a prior colon adenocarcinoma^[32]. Very few cases have been reported on synchronous colonic MALT lymphoma and adenocarcinoma simultaneously present in the same patient^[5-7]. Synchronous adenocarcinoma and MALT lymphomas may exist in the same tumor^[5-7], which is also called a collision tumor. Some synchronous colonic adenocarcinomas are accompanied by MALT lymphoma in the lymph nodes and omentum^[6]. Only one case has been reported in which a diagnosis of synchronous MALT lymphoma was made at the second surgery one month after the diagnosis of colonic adenocarcinoma, which was treated with right hemicolectomy^[8]. In our case, the MALT lymphoma found on surveillance colonoscopy five months after surgery and chemotherapy for sigmoid adenocarcinoma occurred neither at the same time nor in the same segment of the colon. Immune-mediated diseases, such as Hashimoto's thyroiditis, Sjögren's syndrome, and inflammatory bowel disease, might be risk factors for colonic MALT lymphoma^[15,33,34], as well as immunodeficiency factors, such as HIV, steroid use, and tuberculosis^[5,33]. Therefore, colonic MALT lymphoma found after surgery and chemotherapy for adenocarcinoma may result from immunosuppression. However, additional research is needed to confirm this hypothesis.

There were limitations in this report. When colonic MALT lymphoma is diagnosed, synchronous malignancy should be excluded. Gastroscopy, bone marrow biopsy, and CT of the thorax and abdomen should be included for tumor staging^[18]. In this case, the patient refused further examination and treatment because of the coexistence of advanced-stage colonic adenocarcinoma. Thus, he did not undergo gastroscopy or bone marrow biopsy.

CONCLUSION

We report an extremely rare case of synchronous colonic MALT lymphoma found on surveillance colonoscopy five months after surgery and chemotherapy for sigmoid adenocarcinoma. Colonic MALT lymphoma is often asymptomatic and found on surveillance colonoscopy. When presenting synchronously with colonic adenocarcinoma, MALT lymphoma is easily missed. Regular surveillance colonoscopy and careful monitoring after surgery are critical.

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