Collision tumor of primary malignant lymphoma and adenocarcinoma in the colon, diagnosed by molecular genetics analyses: case report and review of literature

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Case Report

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Abstract

Purpose We report one collision tumor of the ascending colon adenocarcinoma and primary diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) with molecular genetics analyses.

Methods The present case and twenty-two previous cases with collision tumors of primary colorectal lymphoma and adenocarcinoma were reviewed. Clinicopathological characteristics, molecular genetics analyses, possible pathogenesis, management and prognosis of the tumor were analyzed.

Results A 74-year-old female patient was found to have an invasive adenocarcinoma in the ascending colon, and underwent laparoscopic radical resection of right colon cancer. The mass comprised of two tumors was found incidentally through postoperative pathological sampling. Molecular genetics and immunohistochemical analyses showed collision tumor of DLBCL, NOS with germinal-center B-cell (GCB) subtype and **TP53** mutation, and adenocarcinoma arising in a tubulovillous adenoma in the colon, with **BRAF** mutation and **MLH1** promoter methylation. The mean age of the 23 patients was 73 years. The most cases of the available histopathological staging of adenocarcinoma were stage I (7/16), whereas those of lymphoma components were stage (10/20). The most common histological subtypes of the lymphoma were B-cell lymphomas (22/23). There were 15 cases with follow-up data including 11 alive and 4 dead with a 3-year overall survival rate (OS) of 71.5%.

Conclusions Our report highlights the need for pathologists, radiologists, surgeons and oncologists to be aware of the rare possibility of collision tumors. The accurate molecular genetics analyses and comprehensive treatment including surgery combined with chemotherapy are required for the rare cases.

Background

Colorectal cancer (CRC), a malignant epithelial tumor originating in the large bowel with glandular or mucinous differentiation, is the second most common cancer in women and the third most common cancer in men [1]. Primary lymphoma of the digestive system refers to an extranodal lymphoma arising in a specific site of the digestive system, with the bulk of the disease localized to the site, with or without regional lymph node involvement [2]. Adenocarcinoma is the most common malignant tumor of the colon, while primary malignant lymphoma is relatively rare.

Two or more distinct tumors of different cell lineages that independently occur at the same space or organ and combine to form one mass are defined as collision tumors. Collision tumors of primary malignant lymphoma and adenocarcinoma in the colon are extremely rare. To the best of our knowledge, only 22 cases have been described in the literature [3-24]. Unfortunately, collision tumors of primary malignant lymphoma and adenocarcinoma in the colon remain subjects of uncertainty, especially in molecular genetics analyses. The relative importance of the various lineages of differentiation within these neoplasms remains unknown. It is also uncertain how these neoplasts develop and how they should be treated clinically, such as a therapeutic dilemma in deciding postoperative adjuvant chemotherapy regimen for the collision adenocarcinoma or lymphoma. These issues are a matter of debate because hard evidence is lacking, but improvements in the pathological criteria and classification of these neoplasms should help to standardize the diagnostic approach and facilitate better clinical and genomic research.

Herein, we reported a case of collision tumor of primary diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) with germinal-center B-cell (GCB) subtype and **TP53** mutation, and adenocarcinoma arising in a tubulovillous adenoma in the colon, with **BRAF** mutation and **MLH1** promoter methylation, with reviewed literature. Written informed consent was obtained from her family members to publish this case report and accompanying images.

Case presentation

A 74-year-old female patient with arterial hypertension was referred to Sun Yat-sen Memorial Hospital, in March 2018, with a loss of weight for 6 months and abdominal pain for one month. She mentioned a loss of 8 kg over the past six months and had anemia, while had no history of fever, drenching night sweats and blood in the stools. There was no history of alcohol and tobacco abuse, surgery, trauma and no known family history of gastrointestinal cancers. Upon physical examination, no peripheral lymphadenopathy and hepatosplenomegaly were found. A mass was noted in the right lower quadrant. Colonoscopy revealed a tumor of the ascending colon, which was proven to be an adenocarcinoma on biopsy.

Blood examination showed an increase in LDH, CA125, CA19-9 level, and a decrease in lymphocyte proportion and count, hemoglobin, and total protein (Table 1). Blood detection of syphilis, hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) was negative. Hypertensive heart disease was diagnosed by color sonography. Chest radiograph showed no evidence of metastasis in the lung and computed tomography scans of the liver and spleen were negative. Contrast-enhanced computed tomography revealed bowel wall thickening with contrast enhancement at the cecum; however, no lymph node or organ metastases were found. As above, the patient received laparoscopic radical resection of right colon cancer with lymph node dissection. Unfortunately, the patient refused postoperative adjuvant chemotherapy. The symptoms of the patient rapidly progressed and the patient succumbed to cancer 3 months subsequent to the initiation of diagnosis of collision tumor of primary malignant lymphoma and adenocarcinoma in the colon.

Pathological findings

Received in formalin was a section of the intestine with omentum (part of the ileum, cecum, and ascending colon). The lengths of the three portions were respectively 6 cm, 11 cm and 22 cm; and the circumferences were 2.5 cm, 8 cm and 6 cm. A circumferential ulcerative mass with a size of 11cm×7.5cm×10cm was seen on the cecal mucosa adjacent to the ileocecal valve (Figure 1). Macroscopically, the mass appeared to be comprised of two tumors. The cut surface of the part of the mass with crater-like was gray, soft, fish-like and necrotic appearing central area, whereas the remaining polyoid part of the mass was hard and grayish-white. A cross-section demonstrated that these two tumors formed a union, and it was impossible to determine the borderline of the two tumors,
grossly. Adjacent to the aforementioned tumor, a 0.6-cm polypoid mass was found in the ascending colon. The appendix was 5 cm long, 0.8 cm in diameter, and the volume of the omentum was 15cm×15cm×1.5cm. Nine lymph nodes varying in size from 0.1 cm to 1.2 cm were isolated from the specimen.

Microscopy showed that the tumor was composed of two components. They were adjacent to each other but relatively independent (Figure 2). One component was a moderately differentiated adenocarcinoma having a mucinous component arising in a tubulovillous adenoma (Figure 3A), which invaded muscularis propria with pushing borders (Figure 3B). The other component was distributed from the mucosal lamina to the subserous layer. The medium-to-large lymphocytes grew diffusely, with relatively uniform morphology, frequent mitosis and obvious cell atypia (Figure 3C). There was no intramural and extramural vascular, lymphatic or perineural invasion. The surgical cut margins and the appendix were free of tumor and all lymph nodes lacked tumor dissemination. Histological examination of the 0.6-cm polypoid mass in the ascending colon showed tubular adenoma.

**Immunohistochemistry**

The adenocarcinoma strongly expressed cytokeratin (CK) (Figure 3D), CK 20, caudal-related homeobox transcription factor 2 (CDX2) and MSH6, while MSH2 and MLH1 were negative. The presence of MLH1 and MSH6 was confirmed by immunohistochemistry of the 0.6-cm polypoid mass in the ascending colon showed tubular adenoma.

In situ hybridization

In situ hybridization showed Epstein-Barr virus (EBV) encoded small RNA (EBER) was negative.

**Gene detection**

Mutational analysis of BRAF was restricted to the V660E alteration. BRAF mutations were detected from fixed formalin paraffin-embedded DNA using the Snapshot mutation detection platform. MLH1 promoter methylation was performed by quantitative real-time polymerase chain reaction. The sample of adenocarcinoma exhibited both a BRAF mutation and MLH1 promoter methylation.

**Discussion and conclusion**

1. **Clinicopathological characteristics of collision tumor of primary malignant lymphoma and adenocarcinoma in the colon**

There are few reports of colonic adenocarcinoma in collision with primary colorectal lymphoma [3-24]. The clinicopathological characteristics of the present case and twenty-two previous cases with collision tumors of primary colorectal lymphoma and adenocarcinoma are summarized in Table 2.

It was found that this type of tumor mostly occurs in elderly people. The age of the patients ranged from 43 to 86 years, with a mean age of 73 years. Most of the patients were more than 60 years old (21/22) and the male-to-female ratio was 1.3 to 1. In all cases, anemia, multiple colon polyp, and inflammatory bowel disease were the most common diseases in past medical history, and immunological or virus infection-related diseases were found in 5 patients, hypertension, diabetes and coronary artery disease were confirmed in one case, respectively. Most cases had symptoms associated with colorectal adenocarcinoma (n = 20). The site of lesions varied on the ileocecal portion (n = 1), cecum (n = 7), ascending colon (n = 2), hepatic flexure of the colon (n = 2), sigmoid colon (n = 2), rectosigmoid region (n = 1), rectum (n = 1), cecum and distal ileum (n = 2), hepatic flexure of the colon and the terminal ileum (n = 1), cecum and duodenum (n = 1), cecum and descending colon (n = 1), cecum and rectum (n = 1), rectum and mesorectum (n = 1). Thus, the most common site of lesions was the cecum, which may be due to the rich and active proliferation of lymphoid tissue there. The histologic morphology of tumors could be roughly divided into three types [14]: the most common type was where carcinoma and lymphoma were in the same tumor and the two types of tumor cells are mixed and grow crosswise, such as case 1, 5, 6, 8, 9, 10, 11, 12, 16, 18, 19, 20 and 22. The second was with carcinoma and lymphoma in the same tumor, but the two tumor types were not mixed and grow relatively independently, our case and case 2, 4, 13, 14, 15, 17 and 21 belonged to this type. Third, the two tumor components were in separate tumors respectively, and the two tumors were adjacent or close to each other (whether the latter is a real collision tumor remains to be discussed).
Most of the adenocarcinoma components were moderately differentiated adenocarcinoma (18/21), and well and poorly differentiated adenocarcinoma were two cases (2/21) and one case (1/21), respectively. Among sixteen patients with available histopathological staging of adenocarcinoma, patients in stage A, B, C and D were 7, 4, 3, 1 and 1, respectively. The first, second and sixteenth cases showed adenocarcinoma arising in a villous adenoma. There was a large tubulovillous adenoma containing invasive adenocarcinoma in the fifteenth case and our case. The most common histologic subtypes of the lymphoma were B-cell lymphomas, such as diffuse large B-cell lymphoma (DLBCL, 9 cases), marginal zone B-cell lymphoma (MZL, 2 cases) or extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (EMZL-MALT, 3 cases), follicular lymphoma (FL, 3 cases), low grade B-cell lymphoma (LGBL, 1 case), high-grade B-cell lymphoma (HGBL, 1 case), lymphoplasmablastic lymphoma (LPL, 1 case), mantle cell lymphoma (MCL, 1 case) and simultaneous MZL and FL (1 case). Only one case was peripheral T-cell lymphoma (PTCL). Among twenty patients with an available histopathological staging of lymphoma, patients in stage A, B, C and D were 7, 3 and 10, respectively. 16 cases (16/19) had an intermediate or high-risk IPI score, and three cases (3/19) had a low or intermediate-risk IPI score [28-31].

Regional lymph nodes were identified with no carcinoma metastasis or lymphoma involvement in the third, thirteenth, fourteenth, fifteenth, sixteenth, twentieth cases and our case. Lymph nodes were manifested metastatic lesions of carcinoma without lymphoma involvement in the ninth and eleventh cases. Lymph nodes were identified with lymphoma involvement and without carcinoma metastasis in the second, sixth, twelfth, nineteenth and twenty-first cases. Regional lymph nodes were manifested metastatic adenoarcinoma and lymphoma, while no lymph nodes contained components of both neoplasms in the fourth case [6]. Regional lymph nodes were identified with carcinoma metastasis or lymphoma involvement in the same lymph node in the seventh, tenth and eighteenth cases.

2. Molecular genetics analyses are valuable diagnostic adjuncts for collision tumor of primary malignant lymphoma and adenocarcinoma in the colon

These collision tumors of primary lymphoma and adenocarcinoma in the colon have no unique clinical features and are difficult to diagnose before operation. Although rectal MR imaging could detect different morphology and signal densities in each tumor, pathological identification of the two components is the only way to make the correct diagnosis [4]. Pathologists should be aware of the existence of collision tumors under these two conditions [4, 8]. First, A different appearance from that of the other on gross resection specimen and/or an extensive or monotonous infiltrate should alert the pathologists to carefully assess its morphology, immunophenotype and clonality in order to confirm or exclude a coexisting lymphoma. Second, any effacement of the architecture of lymph nodes from a resection specimen with a known colorectal carcinoma needs a closer look to exclude the possibility of an underlying lymphoma. In order to differentiate this collision tumor from having only adenocarcinoma, it can be also crucial for the radiologist to consider the possibility of collision tumor through detailed MRI analysis and to recommend a biopsy (such as fine needle aspiration biopsy) in each tumor.

Since the first collision tumor of primary marginal zone B-cell lymphoma and adenocarcinoma in the cecum was reported in 1995 [20], molecular genetics analyses were becoming increasingly important for individualized treatment. Gene detection, in situ hybridization and immunohistochemical were used to identify subtypes of lymphoma and gene mutation sites in colon adenocarcinoma in order to provide guidance for the selection of targeted drugs. Most of the DLBCL components were not further classification in the fourth, eleventh, twelfth and fourteenth cases due to the lack of molecular genetics analyses, while the thirteenth case was diffuse large B-cell lymphoma (DLBCL) with non-germinal-center B-cell (non-GCB) subtype and the sixteenth case and our case were primary DLBCL with GCB subtype [15,18].

In our case, the morphological, immunohistochemical and molecular pathological findings confirmed the diagnosis of collision tumor of primary diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) with germinal-center B-cell (GCB) subtype and TP53 mutation, and adenocarcinoma arising in a tubulovillous adenoma in the colon, with BRAF mutation and MLH1 promoter methylation, which all indicated sporadic cancer and no Lynch syndrome.

Expression of DNA mismatch repair proteins in the adenocarcinoma components of the fifteenth, seventeenth, and twenty-second cases was found to be intact. In situ hybridization showed EBER was positive in the twenty-second case, while negative in the thirteenth case and the present case. Immunohistochemical analyses showed that the atypical lymphocytes in the fourteenth case were negative for Epstein Barr virus nuclear antigen 2.

3. Possible pathogenesis of the collision tumor of primary malignant lymphoma and adenocarcinoma in the colon

The formation mechanism of collision is still controversial. There have been some hypotheses suggesting the eternity of collision tumors of primary malignant lymphoma and adenocarcinoma in the colon [6]. To date, there are no known common etiologic factors for the occurrence of both cancer and lymphoma in the colon. One hypothesis is that the two primary tumors occur by a chance of accidental “meeting” in colon where the microenvironment is altered by the same carcinogenic signal. Another hypothesis is that the presence of the first malignant tumor compromises the patient’s immune system in advance, which is conducive to the development of the second adjacent tumor. Primary colonic lymphoma and adenocarcinoma might be attributed to the advanced age of the patient [8]. This may explain this type of tumor mostly occurs in elderly people. The association between the immune system and cancer development has been previously well described [32]. Due to the severe immunosuppression of the seventeenth patient, lymphoid-type neoplasm was present to a greater degree and with greater severity [20]. Synchronous colonic adenocarcinoma and lymphoma with tuberculosis were found in the seventh and the ninth cases. The inflammatory condition has facilitated malignancy and the impaired immune mechanism has further facilitated the development of second malignancy [11]. Infectious diseases including tuberculosis [9,11], ulcerative colitis [13], esophageal candidiasis [19], rheumatoid arthritis [24] were involving in collision tumor of primary malignant lymphoma and adenocarcinoma in the colon. In the eleventh case, ulcerative colitis could have been the precipitating factor that led to dysplastic changes evolving into malignancy [13], and the development of DLBCL in the twenty-second patient with a medical history of rheumatoid arthritis was determined to be driven by EBV, with immunosuppression being the underlying cause [24]. Preceding lymphoma leading to defects in the antitumor immunity may induce adenocarcinoma through inactivation of tumor-suppressor genes or activation of oncogenes [14]. Some inflammatory diseases, such as ulcerative colitis and Crohn’s disease, are known to increase the risk of malignancy, but the causal relationship between malignant tumors and tuberculosis in the colon is still unclear [9].
Cancers may show underlying molecular changes associated with three main mechanisms of genetic instability in colon cancer: (1) chromosomal instability; (2) microsatellite instability (MSI) or (3) defective proofreading polymerase with a very high mutation rate (ultramutant) affecting very large numbers of genes. MSI results from the defective mismatch repair mechanism leading to predisposition to mutations. MSI drives one of the key mechanisms of oncogenesis in CRC. The presence of MSI is important in the context of cancer immunotherapy with PD1 inhibitors in patients who failed conventional therapy [33-35].

In the large intestine, the most common type of lymphoma is DLBCL (>50%), followed by extranodal marginal zone lymphoma, follicular lymphoma, mantle cell lymphoma and Burkitt lymphoma. The incidence of large intestinal lymphoma has increased over the years, attributable to acquired or iatrogenic immunodeficiency [36]. Patients with immunodeficiency are more prone to develop lymphoma. Although the influence of one cancer on the other is largely unknown, certain pro-neoplastic cytokines that are released by tumor cells have paracrine activities [18]. One could envision a situation whereby one tumor type is secreting TGF-β, not only cloaking the source tumors but also any adjacent disparate tumors. One tumor type might benefit from its collision counterpart via the stimulation of angiogenesis [18]. The presence of lymphoma may help developing adenocarcinoma evade the immune system[20]. EBV is also an established risk factor for lymphoma and may also increase the risk of adenocarcinoma [7, 24].

4. Management and prognosis of collision tumor of primary malignant lymphoma and adenocarcinoma in the colon

Once a diagnosis of a collision tumor is made, proper treatment should be dictated by clinical pathological and molecular diagnosis for the more aggressive of the two lesions. 12 patients were offered no further treatment after colectomy, 8 cases were administered surgery and adjuvant chemotherapy, two cases received chemoradiotherapy and operation, and one patient only received chemotherapy after biopsy.

The fourth and twenty-third patients died 5 or 3 months after surgery because of recurrence of malignant lymphoma. The nineteenth patient died of ruptured abdominal aneurysm, electrolyte imbalance and myocardial infarction one month after discharge. The tenth patient received FOLFOX-4 for colon carcinoma in 6 cycles, while the lymphoma had progressed, consequently. Chemotherapy was administered to the patient consisting of R-CHOP. However, the symptoms of the patient rapidly progressed and succumbed to the cancer 2 months subsequent to the initiation of treatment [12].

According to survival analysis for 15 cases of collision tumors of primary colorectal lymphoma and adenocarcinoma, the survival outcomes of the surgery in combination with chemotherapy or chemoradiotherapy were better than those of the surgery alone group, which suggested adjuvant radiotherapy or chemotherapy combined with surgery had survival benefits. 7 patients underwent surgery alone and 6 received surgery in combination with chemotherapy (4 R-CHOP; 1 FOLFOX to R-CHOP; 1 FOLFOX), 2 received surgery in combination with chemotherapy and radiotherapy (1 R-CHOP; 1 R-CHOP to FOLFOX). 5 (5/8) patients received R-CHOP chemotherapy regimen only among 8 patients received chemotherapy. Among 3 patients who died due to malignant lymphoma progression, 2 underwent surgery alone and 1 received surgery combined with chemotherapy comprising of FOLOFX and R-CHOP. Whether lymphoma was a preference factor in the patient's prognosis remains unclear, due to the lack of large sample data [6].

A therapeutic dilemma exists in deciding the course of treatment in patients with collision adenocarcinoma and lymphoma [5]. There is a general agreement that surgical treatment alone is effective for localized disease, while combined chemotherapy is the mainstay for disseminated disease. However, it is possible that receiving chemotherapy for the treatment of one type of tumor may trigger the progression of the other type of cancer in collision tumors [12]. Therefore, the choice of treatment invariably depends on the patient's age, performance status, clinical scenario, histological subtype and extent of disease [13]. The treatment of collision tumors requires simultaneous treatment of the two tumor components, mainly surgical resection combined with chemotherapy and radiotherapy [15]. For the adenocarcinoma component, most of adenocarcinoma components of collision tumor of primary malignant lymphoma and adenocarcinoma in the colon were stage I and well-differentiated, there is no need to perform radiotherapy and chemotherapy for cancer after resection. Immunotherapy such as Paberizumab for dMMR/MSI-H can be recommended, which was also benefits lymphoma [37]. If it is a cancer with lymph node metastasis or even distant metastasis, adjuvant radiotherapy and chemotherapy can be carried out after surgery in good physical condition.

For lymphoma component, the corresponding radiotherapy and chemotherapy regimen is added according to the different subtypes of lymphoma, owing to lymphoma being a systemic disease. The majority of the patients in this group were over 60 years old, and their IPI score was also at high risk. In addition, most cases of the available histopathological staging of lymphoma components were stage . According to NCCN guidelines, R-CHOP chemotherapy regimen was the first choice for DLBCL [38]. For elderly and frail patients, dose reduction R-CHOP, or mild second-line chemotherapy regimens can also be considered, such as Bendamustine plus rituximab[38]. Dose reduction of Vincristine (VCR) due to toxicity in older patients with aggressive B-cell lymphoma treated with CHOP-14 seems to have no impact on survival outcomes (OS). No survival differences were observed for patients who received only 1 mg VCR by institutional standards as compared to patients who received 2 mg of VCR in every cycle [39].

It is inferred that the prognosis of patients with collision tumor depends on the more aggressive histological grade and stage of the two collision components, and is also closely related to appropriate treatment [15].

Conclusion

In our case, the collision tumor comprising a primary DLBCL and an adenocarcinoma in the ascending colon was found incidentally through postoperative molecular genetics and immunohistochemical analyses, thus highlighting the importance of these techniques in detecting collision tumors that can be
challenging to diagnose. Due to the rarity of collision tumors and challenges in deciding the optimal therapy, the epidemiology and pathogenesis of these collision tumors and their clinical presentation and response to treatment still need further exploration. Our report highlights the need for histopathologists, surgeons and oncologists to be aware of the rare possibility of collision tumors, in order to avoid missed diagnosis and misdiagnosis. The accurate molecular genetics analyses and appropriate comprehensive treatment including surgery combined with chemotherapy are required for the rare cases.

**Abbreviations**

DLBCL, NOS  Diffuse large B-cell lymphoma, not otherwise specified  
IPI  International prognostic index  
TP53  Tumor protein p53  
MLH1  MutL Homolog 1  
EMZL-MALT  Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue  
PET-CT  Postoperative positron emission tomography-computed tomography  
FOLFOX  Folinic acid, fluorouracil, and oxaliplatin  
R-CHOP  Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone  
VCR  Vincristine

**Declarations**

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

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

**Availability of data and materials**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

**Funding**

None

**Authors’ contributions**

All the authors contributed substantially to discussions of the article content. Y.M.L and S.N.Z conceived of the idea. M.J. performed statistical analysis and drafted the manuscript. Y.M.L and S.N.Z revised the manuscript. All authors read and approved the final version for submission.

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**References**

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Tables

Table 1 Laboratory data on admission
<table>
<thead>
<tr>
<th>Item</th>
<th>Detection value</th>
<th>Unit</th>
<th>Normal range</th>
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<tr>
<td>White blood cell count (WBC)</td>
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<td>×10⁹/L</td>
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<td>Red cell count (RBC)</td>
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<td>×10¹²/L</td>
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<td>Hemoglobin (HGB)</td>
<td>98</td>
<td>g/L</td>
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<td>Platelet count (PLT)</td>
<td>163</td>
<td>×10⁹/L</td>
<td>125-350</td>
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<td>%</td>
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<td>0.43</td>
<td>×10⁹/L</td>
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<td>Alanine aminotransferase (ALT)</td>
<td>5</td>
<td>U/L</td>
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<td>30.8</td>
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<td>Direct bilirubin (DBIL)</td>
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<td>Serum calcium (Ca)</td>
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<td>mmol/L</td>
<td>0.02-0.30</td>
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<td>High-density lipoprotein cholesterol (HDL-C)</td>
<td>0.65</td>
<td>mmol/L</td>
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<td>Apolipoprotein A1( ApoA1)</td>
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<td>Apolipoprotein E (ApoE)</td>
<td>51.7</td>
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<td>Prealbumin (PA)</td>
<td>0.06</td>
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<td>Total protein (TP)</td>
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<td>Albumin (ALB)</td>
<td>23.8</td>
<td>g/L</td>
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<td>1.0</td>
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<td>Phosphocreatine kinase (CK)</td>
<td>20</td>
<td>U/L</td>
<td>26-174</td>
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<td>Lactate dehydrogenase (LDH)</td>
<td>538</td>
<td>U/L</td>
<td>108-252</td>
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<td>Hypersensitive CRP (hsCRP)</td>
<td>104.30</td>
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<td>0.00-3.00</td>
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<td>Cholinesterase (CHE)</td>
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<td>Leucylaminopeptidase (LAP)</td>
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<td>U/L</td>
<td>20.0-60.0</td>
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<td>Retinol binding protein (RBP)</td>
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<td>25.0-70.0</td>
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<td>Serum iron (Fe)</td>
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<td>7.0-32.0</td>
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<td>Total iron binding capacity (TIBC)</td>
<td>23.0</td>
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<td>Unsaturated iron binding capacity (UIBC)</td>
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<td>µmol/L</td>
<td>31.0-51.0</td>
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<td>Transferrin (Tf)</td>
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<td>g/L</td>
<td>1.90-3.80</td>
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<td>Adenosine deaminase (ADA)</td>
<td>21.1</td>
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<tr>
<td>Superoxide dismutase (SOD)</td>
<td>94</td>
<td>U/ml</td>
<td>129-216</td>
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<td>1.5</td>
<td>ng/ml</td>
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<td>Alpha-fetoprotein (AFP)</td>
<td>1.6</td>
<td>ng/ml</td>
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<td>Carbohydrate antigen 72-4 (CA72-4)</td>
<td>2.8</td>
<td>U/ml</td>
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<td>Carbohydrate antigen 125 (CA125)</td>
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<td>U/ml</td>
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<td>Carbohydrate antigen 19-9 (CA19-9)</td>
<td>40.5</td>
<td>U/ml</td>
<td>≤34</td>
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*Table 2* Summary of 23 collision tumors of primary colorectal lymphoma and adenocarcinoma.
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<thead>
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<th>NO.</th>
<th>Reference</th>
<th>Age (years)/ Gender</th>
<th>Past medical history</th>
<th>Adenocarcinoma</th>
<th>Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Site</td>
<td>Grade</td>
</tr>
<tr>
<td>2</td>
<td>Sahasrabudhe N 2009 [4]</td>
<td>77/female</td>
<td>Hysterectomy for benign disease, cholecystectomy, ischemic heart disease, anemia</td>
<td>Ascending colon</td>
<td>M</td>
</tr>
<tr>
<td>3</td>
<td>Devi P 2011 [5]</td>
<td>68/female</td>
<td>Not significant</td>
<td>Hepatic flexure of the colon</td>
<td>M</td>
</tr>
<tr>
<td>4</td>
<td>Shigeno T 2011 [6]</td>
<td>76/female</td>
<td>Hepatitis C-related liver cirrhosis, cerebral infarction and dysarthria, anemia</td>
<td>Ileocecal portion</td>
<td>M</td>
</tr>
<tr>
<td>5</td>
<td>Chang H 2011 [7]</td>
<td>86/male</td>
<td>Not significant</td>
<td>Cecum</td>
<td>M</td>
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<tr>
<td>6</td>
<td>Arygropoulos T 2012 [8]</td>
<td>71/female</td>
<td>Anemia</td>
<td>Ascending colon</td>
<td>M</td>
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<tr>
<td>7</td>
<td>Lin HH 2014 [9]</td>
<td>81/male</td>
<td>Tuberculosis</td>
<td>Sigmoid colon</td>
<td>M</td>
</tr>
<tr>
<td>8</td>
<td>Sathya G 2014 [10]</td>
<td>77/male</td>
<td>Tobacco and alcohol abuse, no family history of gastrointestinal cancers</td>
<td>Sigmoid colon</td>
<td>Poorly NC</td>
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<tr>
<td>10</td>
<td>Kus T 2016 [12]</td>
<td>73/male</td>
<td>Not significant</td>
<td>Cecum</td>
<td>NC</td>
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<tr>
<td>11</td>
<td>Soto AR 2018 [13]</td>
<td>79/male</td>
<td>Hypertension, anemia, ulcerative colitis</td>
<td>Rectosigmoid region</td>
<td>M</td>
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<tr>
<td>12</td>
<td>Kim SH 2019 [14]</td>
<td>62/male</td>
<td>Diabetes</td>
<td>Rectum</td>
<td>M</td>
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<tr>
<td>13</td>
<td>Bao L 2020 [15]</td>
<td>77/male</td>
<td>Anemia, cholelithiasis, acute appendicitis, abdominal aortic aneurysm</td>
<td>Cecum</td>
<td>M</td>
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<tr>
<td>14</td>
<td>Kataoka J 2021 [16]</td>
<td>78/male</td>
<td>Anemia, malnutrition, positive for HIV, esophageal candidiasis</td>
<td>Cecum</td>
<td>M</td>
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<tr>
<td>15</td>
<td>Lin YS 2021 [17]</td>
<td>74/female</td>
<td>Iron deficiency, multiple colon polyps, mild and asymptomatic leukocytosis and thrombocytosis</td>
<td>Hepatic flexure of the colon</td>
<td>Well NC</td>
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<tr>
<td>16</td>
<td>Schep D 2022 [18]</td>
<td>NC/male</td>
<td>Cutaneous basal cell carcinoma, chronic peptic stricture</td>
<td>Cecum</td>
<td>M</td>
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<tr>
<td>17</td>
<td>Zapata Palomino M 2022 [19]</td>
<td>72/female</td>
<td>Anemia, malnutrition, positive for HIV, esophageal candidiasis</td>
<td>Cecum, distal ileum</td>
<td>M</td>
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<tr>
<td>18</td>
<td>Hopster D 1995 [20]</td>
<td>74/female</td>
<td>No known risk factors</td>
<td>Cecum, rectum</td>
<td>NC</td>
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<tr>
<td>19</td>
<td>Padmanabhan V 2003 [21]</td>
<td>85/male</td>
<td>Coronary artery disease, Paget disease of the right hemipelvis, small bowel obstruction</td>
<td>Cecum</td>
<td>Well NC</td>
</tr>
</tbody>
</table>
IPI, international prognostic index; M, moderately; NC, not clear; PTCL, peripheral T-cell lymphoma; MZL, marginal zone B-cell lymphoma; EMZL-MALT, extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue; DLBCL, diffuse large B-cell lymphoma; DOD, died of disease; PD, progression disease; LGBL, low grade B-cell lymphoma; HGBL, high grade B-cell lymphoma; FL, follicular lymphoma; CR, complete remission; HIV, human immunodeficiency virus; LPL, lymphoplasmablastic lymphoma; MCL, mantle cell lymphoma.

Figures

**Figure 1**

Macroscopically examination

Macroscopically, the resected specimen presented a circumferential ulcerative mass on the cecal mucosa adjacent to ileocecal valve. The mass appeared to be comprised of two tumors. The upper-right portion of the mass had a crater-like appearance with necrotic appearing central area, whereas the remaining part of the mass had a polypoid, hard and grayish-white aspect.
Microscopic examination disclosed that the tumor was composed of two components, adjacent to each other but relatively independent and showing infiltrative glands with underlying lymphoid proliferation (Hematoxylin and Eosin (HE), original magnification × 20).

Figure 2

Low power view of the mass
Microscopic examination and immunohistochemistry

A. Histopathology of one component of the mass was a moderately differentiated adenocarcinoma having a mucinous component arising from a tubulovillous adenoma (top) (HE, original magnification × 20).

B. Adenocarcinoma invaded muscularis propria (HE, original magnification × 100).

C. The other component was diffusely medium-to-large lymphocytes, with relatively uniform morphology, frequent mitosis and obvious cell atypia (HE, original magnification × 400).

D. Immunohistochemistry of adenocarcinoma was showed strongly positive for cytokeratin, while the atypical lymphocytes were negative (EnVision method, original magnification × 20).

E. Immunohistochemistry of the atypical lymphocytes were strongly and diffusely positive for CD20 (EnVision method, original magnification × 200).

F. Immunohistochemistry of the atypical lymphocytes were negative for CD3 (EnVision method, original magnification × 200).
Figure 4

Survival curve of collision tumors of primary colorectal lymphoma and adenocarcinoma.

A. Overall survival curve.

B. Comparison of survival curves of lymphoma subtypes (Log Rank Test, $X^2=21.114$, $P=0.000$).