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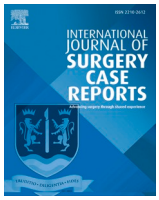

Case report

A case report: Diagnosis of early stage ascending colon adenocarcinoma due to concomitant lymphoma presented by ileocaecal intussusception and literature review

Xiaoli Jin [a], Dongjie Shen [a], Xiaochun Fei [b], Ru Zhou [a,*], Jiankang Shen [a,*]

[a] Department of General Surgery, Ruijin Hospital Lu Wan Branch, Shanghai Jiaotong University, School of Medicine, Shanghai 200020, China
[b] Department of Pathology, Ruijin Hospital, Shanghai Jiaotong University, School of Medicine, Shanghai 200025, China

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ABSTRACT

Introduction and importance: This case report describes a rare occurrence of ileocecal malignant lymphoma combined with adenocarcinoma, due to the low incidence rate of colonic malignant lymphoma.
Case presentation: A 73-year-old female patient presented with abdominal pain and was diagnosed with "acute intussusception with intestinal obstruction" in the emergency department of our hospital. Due to the occurrence of intestinal obstruction the operation was performed, and postoperative pathology revealed a combination of ileocecal DLBCL and ascending colon adenocarcinoma at stage pT1N0M0. One month after the surgery, the patient received an R-CHOP chemotherapy regimen targeting the lymphoma from the hematology department of a local hospital. Upon reexamination after eight cycles of therapy, lymph nodes had enlarged and caused esophageal compression. Unfortunately, the patient contracted COVID-19 and was too weak to undergo any further targeted therapy treatment, and eventually passed away 17 months after the surgery.
Clinical discussion: Synchronous cancers of the colon with malignant lymphoma and adenocarcinoma are rare but still exist. Emphasizing the importance of accurate diagnosis, this report aims to provide clinicians with a broad differential diagnosis, especially in cases where preoperative examination options are limited.
Conclusion: An accurate and comprehensive treatment plan should be tailored to the specific situations of different malignant tumors to improve the survival prognosis of patients.

1. Introduction

Colon carcinoma is a common disease, whereas malignant lymphoma of the colon is relatively rare [1]. The symptoms of malignant lymphoma of the colon are nonspecific. Surgical resection is commonly used for early-stage cases for colon adenocarcinoma, which is uncommon for lymphoma [1]. The occurrence of double primaries is rarer. We present a case of synchronous ileocecal malignant lymphoma and ascending colon adenocarcinoma in one patient; in the hope of broadening differential diagnosis options for clinicians. We present the following case in accordance with the SCARE reporting checklist [2].

2. Case description

A 73-year-old female patient was admitted to the emergency department on September 15th, 2021, complaining of recurrent abdominal pain for one month with worsening symptoms for the past week. The pain was mainly concentrated in the lower right abdomen, and there have been intermittent occurrences of melena and hematochezia over the past week. The patient did not have any fever, chills, nausea, vomiting, constipation, diarrhea, cessation of passing gas and stool or weight loss. (Fig. 1). The patient had a history of hypertension but no other significant medical history. She had no history of cancer and denied any family history of cancer. She was neither a smoker nor an alcohol consumer. Physical examination revealed tenderness in the upper and right lower abdomen. A firm, smooth, well-defined, immobile mass measuring approximately 5*6 cm was palpated in the lower right abdomen, accompanied by mild tenderness upon palpation. No other positive signs were noted. Complete blood count (CBC), biochemical tests, and tumor markers were all normal. No significant abnormalities

* Corresponding authors at: Department of General Surgery, Ruijin Hospital Lu Wan Branch, Shanghai Jiaotong University School of Medicine, Shanghai 200020, China.
E-mail addresses: lw10305zr@rjlwh.com.cn (R. Zhou), mauricesjk@hotmail.com (J. Shen).

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were detected on the chest X-ray examination. Abdominal CT scan revealed an ascending colon mass causing ascending colon and ileocecal intussusception (Fig. 2).

The diagnose of this patient was partial intestinal obstruction caused by Colon neoplasms. With the patient's consent being obtained, the open radical right hemicolectomy was performed on 7th hospital day. A huge mass measuring approximately10*7*8 cm in size was found in the proximal ileocecal region of the ascending colon, accompanied by intussusception. The mass had a hard consistency and limited mobility. The mesenteric lymph nodes were enlarged and fused into a mass, with the largest one measuring approximately 3*3*3 cm and closely adhering to the mesenteric vessels. No tumor was found on the serosal surface of the colon, and no ascites or intra-abdominal metastatic lesions were detected in the surgery. Right hemicolectomy with radical intent was performed, followed by anastomosis of the ileum and transverse colon.

The anatomical specimen revealed a raised mass in the ileocecal region. The cross-section was tender and appeared gray, with the intestinal lumen surrounding the tumor overlapping with each other. Additionally, a broadly-based polypoid measuring 1.5 cm × 1.0 cm × 1.0 cm was identified in the colon, approximately 5.5 cm away from the mass. The paraffin section revealed the following:1.A highly aggressive B-cell lymphoma (Figs. 3,4) measuring 5.5 cm × 5.0 cm × 2.5 cm was identified in the ileocecal region, involving the entirety of the intestinal wall and mesentery. 2. A malignant villous tubular adenoma of the ascending colon was detected, characterized by a well-differentiated adenocarcinoma that had infiltrated the submucosa (Fig. 5). No vascular tumor thrombus or nerve invasion was observed, and there was no tumor involvement in the ileum, colon, or appendix. Moreover, lymphomas were present in 12 out of 25 paraintestinal lymph nodes.

To determine the lymphoma type, immunohistochemistry (IHC) and Fluorescence in situ hybridization (FISH) tests were performed. The IHC results were: CD20(+), CD79a(+), CD19(+), CD22(+), BCL-2(+), Bcl-6 (+), C-myc(60 %+), MUM-1(+), Ki67(80 %+), CD23(+), P53(strong +), CD30(−), CD4(−), CD8(−), CD2(−), CD3(−), CD5(−), CD7(−), CyclinD1(−), CD21(−), CD56(−), TIA-1(−), GranzymeB(−), Perforin (−), and EBER(−). The FISH test results revealed that 2 % of tumor cells demonstrated IGH/BCL2 red-green fusion, 2 % showed BCL6 red-green split, 2 % showed C-MYC red-green split (with 3.3 yellow signal copies), and 22 % showed TP53 deletion. It is important to note that all testing showed negative results for the IGH/BCL2 fusion probe, BCL6 break-apart probe, C-MYC break-apart probe, and TP53 probe deletion assay. Based on the IHC and FISH test results, the pathological diagnosis of highly aggressive diffuse large B-cell lymphoma (DLBCL), non-germinal center subtype, was confirmed.

The patient recovered well and was discharged on 12th post-operation day. Since her colon adenocarcinoma stage was early (pT1N0M0), she continued her treatment at hematology department of one local hospital. Following the completion of eight cycles of therapy (6 cycles of CHOP plus 2 cycles of Rituximab), an examination revealed the enlargement of mediastinum lymph nodes accompanied by esophageal compression. As a result, another round of targeted therapy with Rituximab was planned. However, the patient contracted COVID-19 unfortunately. Due to the severity of the infection and the resulting weakened immune system, the patient was unable to tolerate the targeted therapy. The patient died on February 18th, 2023.

Fig. 2. CT scan of the patient*.
*White arrow showed the mass in the ileocecal region with evidence of intussusception.

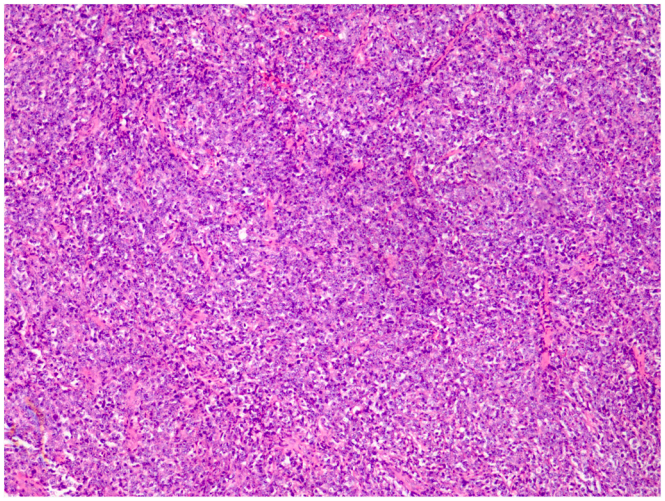

Fig. 3. HE staining for lymphoma (100× magnification).

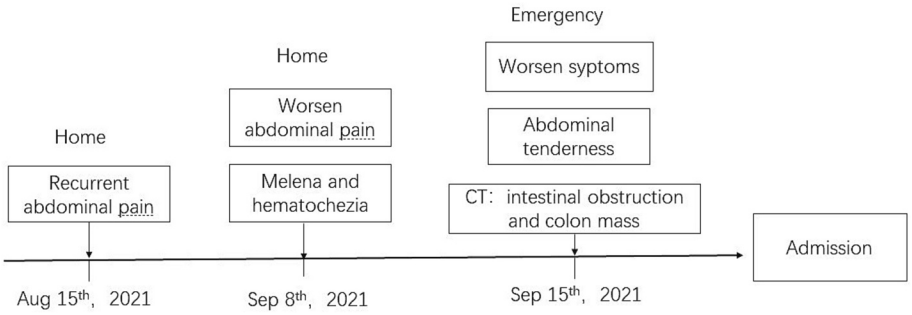

Fig. 1. patient's complete medical history.

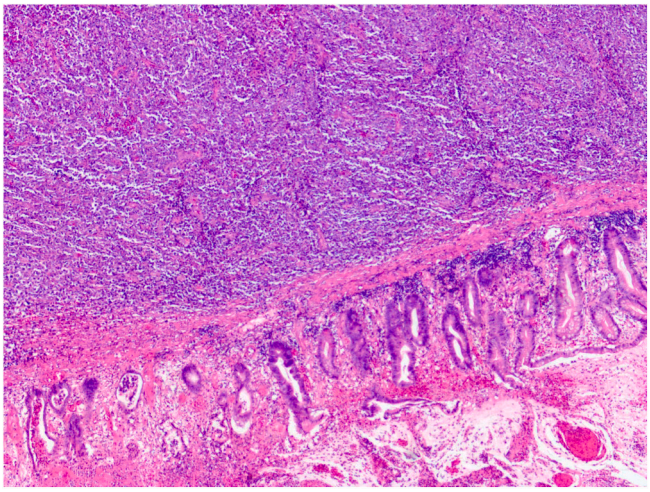

Fig. 4. HE staining for lymphoma (50× magnification).

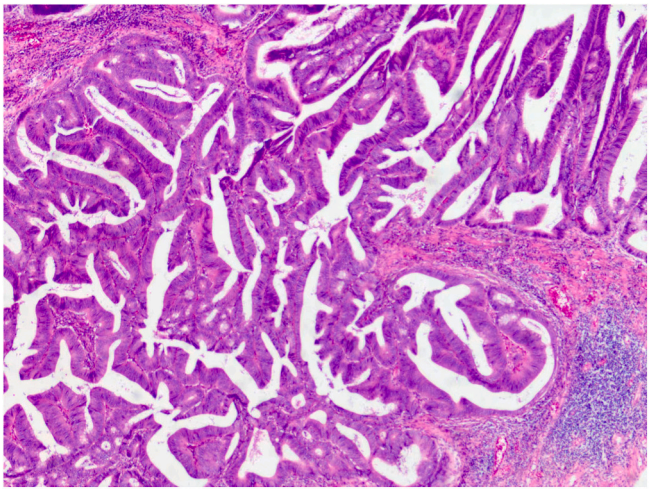

Fig. 5. HE staining for adenocarcinoma (50× magnification).

3. Discussion

Primary malignant lymphoma is classified as a type of hematological malignancy. While the gastrointestinal tract is the most common site of extranodal lymphoma, primary colon lymphoma is a relatively uncommon subtype and accounts for less than 10 % of gastrointestinal lymphomas. Adenocarcinoma is the most frequently type of colorectal malignancy, with the incidence of primary colon lymphoma being less than 1 % [1,3]. Primary colon lymphoma is more common in males, with the most frequently involved site being the ileocecal region (about 60 %), followed by the right colon and sigmoid colon [4].There are many pathological types of primary lymphomas of the gastrointestinal tract and colon, among which DLBCL are the most common. They are composed of many rapidly proliferating cells and are more aggressive than other B-cell lymphomas [3].

Primary colonic lymphoma is a rare condition. The patient reported here has been diagnosed with primary colonic lymphoma and colonic adenocarcinoma, which is a rarer occurrence. We searched the PubMed database for literature related to synchronous colorectal adenocarcinoma and colon malignant lymphoma from 2010 until now, only eight case reports were found (Table 1). All patients were diagnosed with adenocarcinoma and malignant lymphoma. The most common type of lymphoma was DLBCL (3 cases). All patients underwent surgical operation or endoscopic submucosal dissection (ESD) treatment to remove the lesion. In addition, chemotherapy or targeted therapy was administered as a supplementary treatment. Unfortunately, the overall prognosis was not good, with recurrence and metastasis occurring within 1–2 years after surgery.

The gold standard for diagnosing colonic lymphoma is pathological examination [5]. Imaging findings reveal differences between typical adenocarcinoma of the colon mucosa and primary colon lymphoma. In contrast-enhanced CT examination, colon carcinoma is typically characterized by local wall thickening accompanied by uneven enhancement, and smaller lesions are often difficult to detect. In contrast, primary colon lymphoma usually shows a very regular external contour, which is often easier to identify [6]. Nowadays, advanced diagnostic tools, such as Next Generation Sequencing (NGS) allowing for, have significantly improved our ability to detect specific genetic features that are indistinguishable based solely on their morphological characteristics [7]. However, many cases have been reported with intussusception without sufficient time for pathology results before surgery [8,9]. The diagnostic awareness of clinicians must be heightened. Additionally, according to the literature review, most double primaries occur in elderly individuals. Therefore, pathologists should be vigilant for small primary early malignant lesions in elderly cases. It is necessary and important for pathologists to perform accurate evaluations of the entire specimen, especially for luminal organs such as the proximal and distal regions, in addition to the main lesion.

The treatment plan for colon cancer typically involves surgery and chemotherapy. In the case of primary colonic lymphoma, Kavea et al. [5] proposed that chemotherapy is typically more effective in controlling lymphoma, while surgery is primarily reserved for emergency cases. Y-bo Cai et al. [10] suggested that surgical treatment might not improve the survival rate for patients with advanced, left hemicolonic lesions or asymptomatic colon lymphoma, but could be the best option for patients with early-stage, right hemicolonic lesions or DLBCL. In B.M. Smith's case [11], the surgical plan was postponed, and the patient was referred for oncologic treatment. According to Won RP [12], surgical intervention is typically necessary by the time of lymphoma diagnosis, given the lack of specific symptoms in the early stage. The best prognosis for patients is often achieved with surgery followed by adjuvant chemotherapy. However, a study by Maguire LH [13] reported increased short-term mortality in patients with primary lymphoma after surgery.

In our case, the patient presented with intestinal obstruction and intussusception preoperatively, and there was no opportunity to further diagnose the specific type of tumor. Therefore, surgery was the only but best choice at the time. The presence of two types of cancer in our case was identified through postoperative pathological examination. The adenocarcinoma was found to be at an early stage, while the main tumor consisted predominantly of lymphoma. As a result, the subsequent chemotherapy focused primarily on treating the lymphoma. Based on the previous literature review, it can be observed that the treatment approach for double primaries should be determined based on the specific staging of each tumor. When necessary, a multidisciplinary team (MDT) discussion should be conducted, taking into consideration additional factors such as genetic testing results, in order to reach a conclusion.

In conclusion, we must carefully consider the possibility of rare pathological diseases to make a correct diagnosis, especially when preoperative examinations are limited. Pathologists must conduct a meticulous evaluation of the entire specimen, particularly in cases involving elderly patients, to ensure the early detection of potential malignant tumor changes is not overlooked. The optimal treatment plan should be formulated based on the specific staging of the tumor and the individual circumstances.

Table 1
Summarizing the various cases reported in the literature of a synchronous colonic adenocarcinoma and colon malignant lymphoma.

Study	Said Haddadi [14]	Jun Kataoka [15]	Juan-Juan Li [16]	Wang Wei [17]	Makoto Saito [18]	Michael Zapata Palomino [19]	Hung-Hsin Lin [20]	Deuk Young Lee [21]	Jin Xiaoli
Report year	2021	2021	2020	2019	2022	2022	2014	2014	2024
Age	77	78	67	78	71	72	81	79	73
Gender	M	M	M	M	M	F	M	F	F
Type of adenocarcinoma	Well differentiated	Moderately differentiated	Moderately differentiated	Adenocarcinoma	Well differentiated	Moderately differentiated	Moderately differentiated	Poorly differentiated	Well differentiated
Location of adenocarcinoma	Flexura hepatica coli	Ascending colon	Sigmoid colon	Sigmoid colon	Sigmoid colon	Ascending colon	Sigmoid colon	Ileocecal region	Ileocecum
Type of lymphoma	MALT	DLBCL	MALT	DLBCL	Follicular lymphoma	Lymphoplasmablastic lymphoma	LGBCL	AITL	DLBCL
Location of lymphoma	Transverse colon	Ascending colon	33 cm from the anal	Ascending colon	Rectum	Ileocecum	Sigmoid colon	Pericolic lymph node	Ascending colon
distance	10 cm	Collision	/	/	/	Collision	Collision	/	5 cm
diagnose time	Synchronize	Synchronize	5 months	Synchronize	6 months	Synchronize	Synchronize	Synchronize	Synchronize
Symptoms	Abdominal pain,melena	Anemia	Hematochezia	Abdominal mass	Lower abdominal discomfort	Black stools,weightlose, asthenia, and adynamia	Dry cough,TB infection	Abdominal pain, anorexia, nausea and melena	Abdominal pain
TNM[a]	T4aN1M0	T2N0M0	T3N1Mx	T3N0M0	T1N0M0	T2N0M0	T2N1M1	T4N1M0	T1N0M0
Lymph nodes[b]	1/17	0	1/12	0	/	0/32	1/20	1/37	0/25
Treatment	Surgery+chemotherapy (capecitabine)	Surgery+chemotherapy ([c]r-chop)	Surgery+chemotherapy (folfox6)	Surgery+chemotherapy	ESD + Rituximab	Surgery+chemotherapy	Surgery+mfolfox6+ anti tb	Surgery	Surgery+chemotherapy
Prognosis	Tumor recurrence and metastasis in 2 years	Alive for 4 years	Suspected metastasis, died in 10 months	Died of a stroke after 15 months	Alive for 3 years	Alive	Stable for 24 months	Not mentioned	Tumor recurrence in 1 year and died in 17 months

Abbreviations: MALT, mucosa associated lymphoid tissue; DLBCL, diffuse large B-cell lymphoma; AITL,angioimmunoblastic T-cell lymphoma; FL, Follicular lymphoma; EDS, Endoscopic Submucosal Dissection; LGBCL, low-grade B-cell lymphoma;TB, Tuberculosis.

[a] TNM,TNM for adenocarcinoma ; [b]lymph nodes, lymph nodes withadenocarcinomaadenocarcinoma metastases ; [c]R-CHOP, rituximab+CHOP regimen.

Authors' contribution

Xiaoli Jin wrote the manuscript. Xiaoli Jin, Dongjie Shen and Xiaochun Fei collected the images. Xiaoli Jin, Ru Zhou and Jiankang Shen collected relative articles. Dongjie Shen, Ru Zhou and Jiankang Shen edited the manuscript. All authors reviewed the manuscript.

Ethical approval

The study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Ruijin Hospital Lu Wan Branch. Written informed consent was obtained prior to the study.

Consent for publication

Written informed consent was obtained from individual(s) for the publication of any potentially identifiable images or data included in this article.

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Availability of data and materials

All data generated and analyzed during this study are included in this article and are available from the corresponding author upon reasonable request.

Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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