Diagnostic and therapeutic challenges of locally advanced colon cancer complicated with acute lymphoblastic leukemia: A case report

YUPING ZENG[1,2], SONG MU[1,2], GUOSHENG LI[1,2], ZHENGZI LIANG[1,2], QINGHUA JI[1,2], YUNHUAN ZHEN[1,2], WENLING WANG[1,3] and WEIWEI CHEN[1,2]

[1]Colorectal Tumor Center, Affiliated Hospital of Guizhou Medical University, Guiyang, Guizhou 550004, P.R. China; [2]Department of Clinical Medicine, Guizhou Medical University, Guiyang, Guizhou 550004, P.R. China; [3]Department of Oncology, Affiliated Hospital of Guizhou Medical University, Guiyang, Guizhou 550004, P.R. China

Received September 7, 2025; Accepted March 26, 2026

DOI: 10.3892/ol.2026.15627

Abstract. Colorectal cancer (CRC) is the second most common malignant tumor in China, characterized by a steadily increasing annual incidence. Acute lymphoblastic leukemia (ALL) is a malignant clonal disorder originating from lymphoid progenitor cells that predominantly affects children and adolescents. Its incidence is relatively lower in adults than in children, however they typically experience poorer prognoses. Although CRC and ALL each have distinct pathological and epidemiological profiles, their coexistence as synchronous or metachronous double primary malignancies in the same patient is rare and their treatment strategies differ. The current study presents a case of locally advanced colon cancer concurrent with ALL, in which the patient underwent radical colon cancer surgery after achieving complete remission of ALL through induction chemotherapy.

Introduction

Colorectal cancer (CRC) and acute lymphoblastic leukemia (ALL) are two distinct malignant neoplasms with differing origins, biological characteristics and epidemiological features. CRC is a malignant tumor derived from the colorectal epithelial cells, and is ranked third for incidence and second for cancer-related mortality worldwide (1). Over recent years, the overall incidence of CRC has shown a consistent upward trend (2), with a particularly pronounced increase in early-onset cases (diagnosis at age ≤50 years) (3). By contrast, ALL is a malignant clonal disorder arising from lymphoid progenitor cells (4). In 2021, the numbers of new cases of ALL and ALL-associated deaths worldwide exceeded 100,000 and 70,000, respectively (5). China substantially contributes to the global burden of ALL, ranking among the countries with the highest incidence and mortality rates worldwide (5). Although the incidence is relatively higher in children than in adults, the overall prognosis of adult ALL is markedly worse than that in pediatric patients (4). From the perspective of tumor biology, CRC has an insidious onset and progresses relatively slowly. It primarily grows through local invasion and can metastasize via lymphatic vessels (to lymph nodes) and blood vessels (to the liver and lungs) (6). Conversely, ALL has an acute onset and rapid progression, characterized by systemic dissemination. As the disease progresses, the malignant cells proliferate within the bone marrow, suppressing normal hematopoiesis, and can quickly enter the peripheral blood and infiltrate lymph nodes, liver, spleen and the central nervous system (3).

Against this backdrop, when CRC and ALL coexist as synchronous double primary cancer (SDPC), the complexity of diagnosis and treatment increases substantially. Diagnostically, the acute onset of ALL, accompanied by systemic symptoms, cytopenia and coagulopathy, can easily mask the relatively insidious gastrointestinal symptoms of CRC (such as hematochezia or abdominal pain), leading to missed or delayed diagnosis of the latter. Therapeutically, their standard treatment regimens are fundamentally conflicting: The myelosuppression caused by ALL induction chemotherapy critically increases the risk of perioperative infection and hemorrhage for CRC surgery. Conversely, emergency or time-sensitive surgery for CRC may induce or exacerbate life-threatening complications (such as disseminated intravascular coagulation) due to uncontrolled ALL and delay the crucial treatment for this acute, fatal disease. Therefore, formulating a multidisciplinary, integrated strategy that prioritizes life-threatening emergencies and strategically sequences treatments is paramount for optimizing overall patient survival (7).

The present case highlights the importance of multidisciplinary team (MDT) collaboration in the diagnosis and treatment of complex double primary cancer. The case demonstrates that when two distinct malignancies occur

Correspondence to: Dr Weiwei Chen, Colorectal Tumor Center, Affiliated Hospital of Guizhou Medical University, 16 Beijing Road, Yunyan, Guiyang, Guizhou 550004, P.R. China
E-mail: weiweichen@gmc.edu.cn

Key words: colorectal cancer, acute lymphoblastic leukemia, double primary cancer, multidisciplinary team

simultaneously, it is essential to establish treatment priorities, balance drug efficacy against toxicity and formulate individualized therapeutic regimens.

Case report

A 61-year-old man with a history of hypertension, type 2 diabetes and coronary artery disease presented to the Affiliated Hospital of Guizhou Medical University (Guizhou, China) in May 2025 with bleeding gums, melena, fatigue, fever and cough. The patient reported no prior family history of malignant tumors or hereditary diseases. Blood cell analysis revealed trilineage cytopenia (Table I). Blood biochemical test demonstrated an elevated C-reactive protein level of 94.82 mg/l (reference range, <5 mg/l). Laboratory evaluation of coagulation revealed notably prolonged prothrombin time and activated partial thromboplastin time, with values of 17 sec (reference range, 10-15 sec) and 51.8 sec (reference range, 28-44 sec), respectively. Sputum culture yielded *Klebsiella pneumoniae*. For the bone marrow sear, bone marrow fluid was routinely aspirated from the posterior superior iliac spine, immediately mixed with EDTA-K_2 anticoagulant and submitted for examination within 2 h. Upon receipt of the specimen, a small volume of undiluted bone marrow fluid was placed on one end of a clean glass slide and spread using a spreader at a 30-45˚ angle to prepare a single-layer smear with distinct head, body, and tail sections. The smear was naturally dried at room temperature, fixed with pure methanol for 3-5 min at room temperature, and then stained with Wright-Giemsa composite stain for 15-20 min at room temperature. Morphological examination was performed using an Olympus CX43 light microscope equipped with 10X, 40X and 100X oil immersion objectives, and differential counting was conducted under the oil immersion lens at high magnification. Bone marrow aspiration demonstrated hypocellularity, an abnormal granulocyte-to-erythrocyte ratio, and abnormal lymphoid hyperplasia with 40-54% blasts and immature lymphocytes (Fig. 1A).

Flow cytometric immunophenotyping analysis was performed. Bone marrow aspirate samples were collected in EDTA-K_2 anticoagulant tubes and processed within 24 h. Immunophenotyping was performed using the following fluorescent monoclonal antibodies: CD45-V500-C (cat. no. 647450), CD10-PE (cat. no. 332776), CD19-PE-Cy7 (cat. no. 341103), CD20-APC-Cy7 (cat. no. 335829), CD34-PerCP-Cy5.5 (cat. no. 347213), CD38-FITC (cat. no. 340909), CD81-APC (cat. no. 551112), HLA-DR-PerCP-Cy5.5 (cat. no. 347401), CD5-PE-Cy7 (cat. no. 348810), CD7-PE (cat. no. 332774), CD36-PE (cat. no. 570214), CD117-APC (cat. no. 333233), CD123-PE (cat. no. 554529), CD72-Pacific Blue (cat. no. 338710) and FACS lysing buffer (cat. no. 349202; BD Biosciences). All antibodies were purchased from BD Biosciences except for CD72-Pacific Blue, which was from BioLegend, Inc. A 100-μl aliquot of sample was incubated with the antibodies for 15 min at room temperature in the dark, followed by red blood cell lysis for 10 min. After centrifugation and washing, cells were resuspended in phosphate-buffered saline. Data acquisition was performed on a BD FACSCanto II flow cytometer (BD Biosciences), with at least 50,000 events recorded per sample. Data analysis was conducted using FlowJo software version 10.8.1 (BD Biosciences) based on forward and side scatter gating strategies. Flow cytometric immunophenotyping analysis revealed blasts accounting for 23.75% of nucleated cells, expressing CD10, CD19, CD20, CD72, CD34, CD38, CD81 and HLA-DR (Fig. 1B), but negative for CD5, CD7, CD36, CD117 and CD123. Granulocytes comprised 13.53% of nucleated cells and were predominantly mature neutrophils. These findings were consistent with B-cell ALL (B-ALL) immunophenotype.

Bone marrow chromosome karyotype analysis demonstrated a normal karyotype (46,XY), whereas leukemia-associated gene testing by targeted next-generation sequencing (NGS) detected an *IKZF1* mutation, with no fusion genes identified, including *BCR::ABL1, SIL::TAL1, E2A::HLF, TEL::AML1, E2A::PBX1, MLL::AF4, MLL::AF6, MLL::AF9, MLL::AF10, MLL::ELL, MLL::ENL, CBFβ::MYH11, DEK::CAN, AML1::ETO or PML::RARα*. Electrocardiography indicated an acute anteroseptal and anterior wall myocardial infarction (MI), despite normal cardiac enzymes. Echocardiography showed left atrial enlargement and segmental left ventricular wall motion abnormalities on dynamic images, and a left ventricular ejection fraction of 50% (Fig. 2).

Given the concurrent respiratory infection, gastrointestinal bleeding and acute MI (ECG-only), the treatment regimen included: 1 g meropenem by intravenous infusion every 8 h for 7 days; 250 μg/h somatostatin by continuous micro-pump infusion for 3 days; 40 mg esomeprazole by intravenous infusion every 12 h for 5 days; and transfusion of two therapeutic doses of ABO-identical platelets and a total of 4 units of ABO-identical suspended red blood cells, among other measures. Cardiology consultation prioritized ALL treatment due to normal cardiac biomarkers/function, with MI symptom monitoring. On day 4, the patient underwent one cycle of induction therapy consisting of blinatumomab, vincristine and dexamethasone, administered as follows: Blinatumomab at 9 μg daily on days 1-6, followed by 35 μg daily on days 7-14; vincristine at 2 mg on days 1 and 8; and dexamethasone at 15 mg daily on days 1-14. During the treatment period, the patient developed grade 4 leukopenia/neutropenia/thrombocytopenia, grade 3 anemia, coagulopathy and recurrent lower gastrointestinal bleeding (≤1,000 ml) with hemorrhagic shock. After transfusion and resuscitation, platelet count and coagulation parameters normalized, but hematochezia persisted. On day 18, bone marrow flow cytometry confirmed complete remission (CR) with 0.07% blasts and evidence of hematopoietic recovery (Fig. S1). A colonoscopy revealed a sigmoid neoplasm and rectal ulcer (Fig. 3A and B). Colonoscopy biopsies confirmed sigmoid adenocarcinoma and rectal adenoma with low-grade intraepithelial neoplasia (Fig. 3C and D). An abdominal CT staged the sigmoid adenocarcinoma as cT3N2M0 IIIC (Fig. 4). At day 35, after MDT discussion, laparoscopic radical resection was performed and the pathology report included the following: i) The tumor measured 8x3x1 cm at 3 cm above the peritoneal reflection; ii) there was moderately differentiated adenocarcinoma invading the subserosa; iii) there were 0/11 lymph node metastases, but two tumor deposits were identified (Fig. 5A); and iv) the results of immunohistochemistry revealed that the tumor was: $MLH1^+$, $MSH2^+$, $MSH6^+$, $PMS2^+$, $HER2^{1+}$, Ki-67 (~90%) and p53 (wild-type; Fig. 5B-H).

Pathological tissue HE staining was performed using the HE staining kit (cat. no. EE0012; Shandong Sparkjade

Table I. Key results of the peripheral blood cell analysis of the patient.

Day	WBC, x10^9/l	NEUT#, x10^9/l	RBC, x10^{12}/l	HGB, g/l	PLT, x10^9/l
Day 1	0.8	0.19	1.83	50	9
Day 2	0.71	0.2	2.11	56	8
Day 4	0.8	0.21	2.11	59	13
Day 6	0.37	0.2	2.06	60	16
Day 8	0.32	0.19	2.14	62	31
Day 13	1.31	1.05	2.1	61	51
Day 18	1.61	0.89	2.09	64	51
Day 28	7.41	5.87	2.78	84	100
Day 29	5.4	4.1	2.61	78	102

WBC, white blood cell, normal range: 3.5-9.5x10^9/l; NEUT, neutrophil count, normal range: 1.8-6.3x10^9/l; RBC, red blood cell, normal range: 4.3-5.8x10^{12}/l; HGB, hemoglobin, normal range: 130-175 g/l; PLT, platelets, normal range: 125-350x10^9/l.

Scientific Instruments Co., Ltd.), which includes hematoxylin, 1% hydrochloric acid alcohol differentiating solution, and eosin staining solution. The procedure involved baking at 65˚C for 60 min, and dewaxing in xylene I and II for 10 min each, followed by hydration through a graded ethanol series. Hematoxylin staining was performed at room temperature for 5-8 min, followed by differentiation with 1% hydrochloric acid alcohol for 3-5 sec, and bluing under running water for 10 min. Eosin staining was then performed at room temperature for 1-3 min, after which the sections were dehydrated using a graded ethanol series, cleared in xylene and mounted with neutral balsam.

For immunohistochemical analysis, tissue specimens were fixed in 4% paraformaldehyde, routinely embedded in paraffin, and sectioned into 4-μm thick serial slices using a microtome. Following deparaffinization, rehydration and antigen retrieval, endogenous peroxidase activity was blocked with 3% hydrogen peroxide at room temperature (25˚C) for 10 min in the dark. To reduce non-specific binding, goat serum (Beijing Zhongshan Golden Bridge Biotechnology Co., Ltd.) diluted 1:5 was applied for 20 min at room temperature. Primary antibodies used in this study were as follows: MLH1 (cat. no. ZM-0154; diluted 1:100), MSH2 (cat. no. ZA-0702; diluted 1:100), MSH6 (cat. no. ZA-0541; diluted 1:100), PMS2 (cat. no. ZA-0542; diluted 1:100), HER2 (cat. no. ZM-0065; diluted 1:100), Ki-67 (cat. no. ZM-0167; diluted 1:100) and p53 (cat. no. ZM-0408; diluted 1:100) (all purchased from Beijing Zhongshan Golden Bridge Biotechnology Co., Ltd.), and all primary antibodies were incubated at 37˚C for 1-2 h. The HRP-conjugated goat anti-mouse/rabbit IgG secondary antibody (cat. no. PV-9000; Beijing Zhongshan Golden Bridge Biotechnology Co., Ltd.) was diluted 1:200 and incubated at room temperature for 30 min. After DAB chromogenic detection, sections were counterstained with hematoxylin, dehydrated, cleared and mounted. Observations and imaging were performed using an Olympus BX53 upright optical microscope (Olympus Corporation) equipped with 10X, 40X and 100X objective lenses.

The final pathology confirmed a diagnosis of pT3N1cM0 stage IIIB sigmoid adenocarcinoma. Postoperative day 10 bone marrow flow cytometric immunophenotyping analysis demonstrated normocellularity with no evidence of residual leukemia cells (no leukemia-related immune phenotype was observed), and sustained hematological CR. Following MDT consensus, adjuvant chemotherapy for colon cancer was deferred to prioritize consolidation and maintenance therapy for ALL. A timeline describing the treatment course of the patient was prepared for clearer review (Fig. 6).

Following ALL induction therapy and radical colon cancer surgery, the gastrointestinal bleeding, gum bleeding, anemia and infection symptoms resolved, with bone marrow function restored to normal. The patient is currently in CR with minimal residual disease (MRD) negativity for ALL and was advised to initiate post-remission consolidation therapy, potentially with multi-agent chemotherapy combined with blinatumomab. Due to the age of the patient, chemotherapy doses may be reduced to lower treatment intensity. However, after consultation, the patient temporarily declined further treatment and was discharged for recuperation on day 49. After the last follow-up in July 2025, the patient could not be contacted.

Discussion

ALL development is closely linked to genetic alterations, primarily characterized by chromosomal abnormalities and gene mutations. Chromosomal abnormalities encompass numerical changes (such as hyperdiploidy) and structural aberrations (such as translocations, inversions and duplications). These alterations frequently generate fusion genes such as *BCR::ABL1*, *KMT2A* (formerly MLL) rearrangements and *ETV6::RUNX1*, which compromise genomic stability and disrupt transcriptional regulation (8). Key mutations in genes that regulate cell proliferation, differentiation, apoptosis and genomic stability, such as *PAX5* and *IKZF1*, further contribute to the development of lymphocytic leukemia (9). These molecular profiles inform targeted therapy selection, refine relapse risk stratification and predict long-term survival outcomes (10).

The diagnosis of ALL utilizes the Morphology, Immunology, Cytogenetics, Molecular Genetics framework, with classification adhering to the WHO 2022 (fifth edition) criteria (11). Treatment initiation is recommended upon

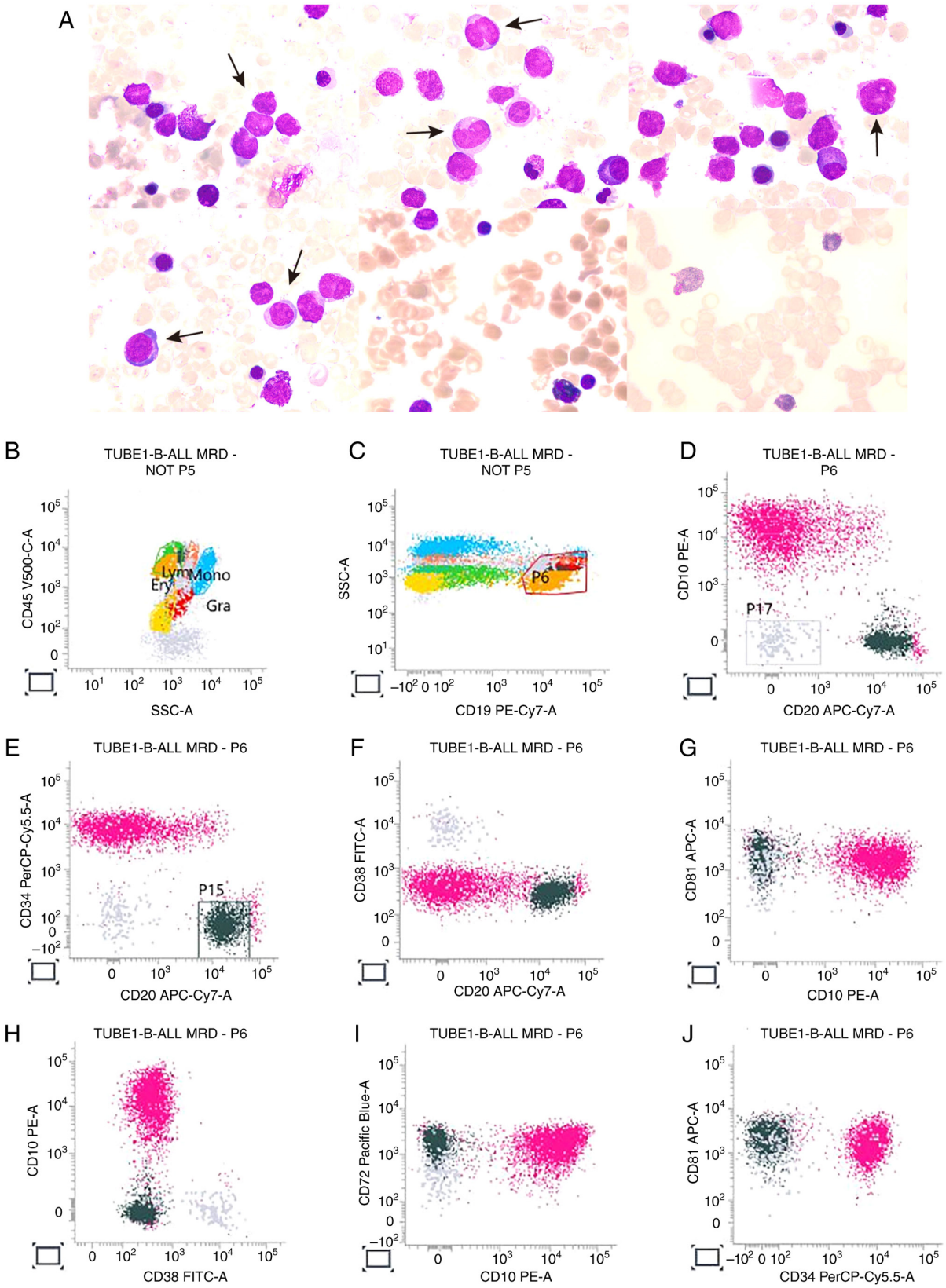

Figure 1. Bone marrow cytology and representative flow cytometric immunophenotyping plots. (A) Bone marrow smear revealed hypocellularity with abnormal lymphoid hyperplasia predominated by lymphoblasts and prolymphocytes, accompanied by hypoplasia of the myeloid and erythroid lineages, absence of megakaryocytes and rare platelets (magnification, x200). Arrows indicate abnormal B lymphocyte clusters. (B) Gating of bone marrow cells (P5) based on CD45 vs SSC, with separation of Lym, Mono, Ery, and Gra. (C) $CD19^{+}$ B-lineage cells (P6) were isolated from P5. (D and E) Within P6, plasma cells or plasmablasts (P17, $CD10^{-}$ and $CD20^{-}$) and normal mature B lymphocytes (P15, $CD34^{-}$ and $CD20^{bright}$) were gated as internal controls, while pro-B lymphocytes were identified as $CD10^{+/bright}$, $CD34^{+/bright}$, $CD20^{-/dim}$ cells. (F-J) Immunophenotypic validation of pro-B lymphocytes, confirming the aberrant phenotype: $CD10^{bright}$, $CD19^{+}$, $CD20^{dim}$, $CD72^{+}$, $CD34^{+}$, $CD38^{dim}$, $CD81^{dim}$, HLA-DR^{+}, which were consistent with a B-cell ALL immunophenotype. The magenta cell clusters in (D-J) represent the majority of B lymphocytes with the aforementioned abnormal phenotype. P5, population 5; P6, population 6; P17, population 17; P15, population 15; SSC, side ccatter; Lym, lymphocytes; Mono, monocytes; Ery, erythrocytes; Gra, granulocytes; CD, cluster of differentiation; HLA-DR, human leukocyte antigen D-related.

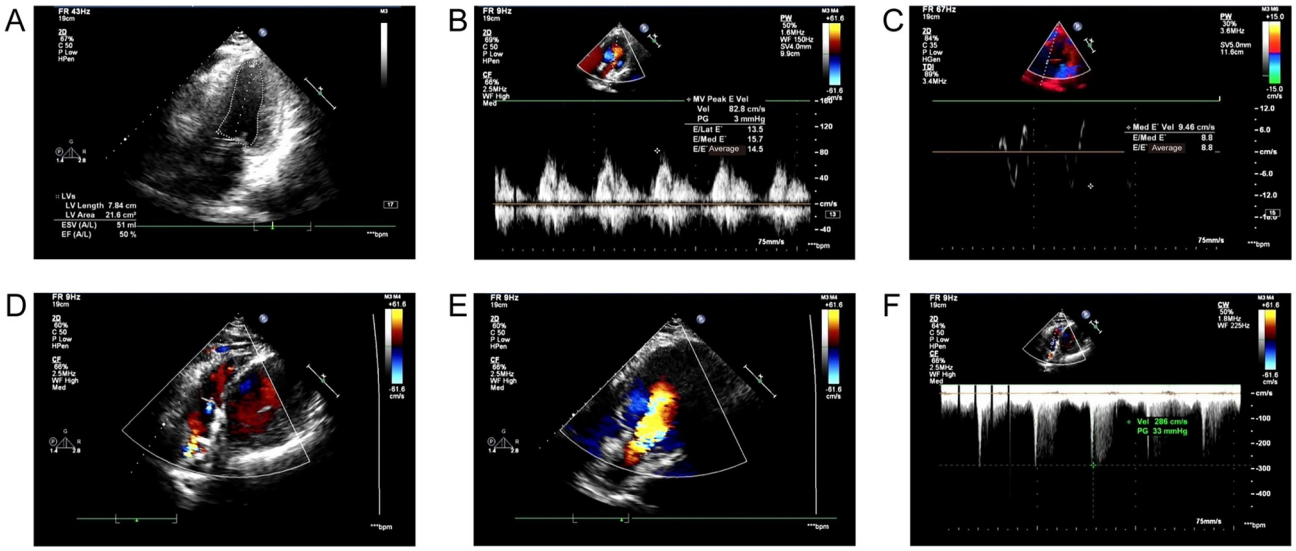

Figure 2. Echocardiographic assessment of left ventricular function and hemodynamics. (A) Left ventricular systolic function: Apical biplane view showing an EF of 50%, at the lower limit of normal. (B) Mitral inflow Doppler: PW Doppler demonstrated a peak E velocity of 82.8 cm/sec, consistent with normal filling dynamics. (C) TDI: TDI at the mitral annulus yielded an average E/e' ratio of 8.8, falling within the borderline range. (D) Atrioventricular valve color Doppler: CDFI showed normal flow across the mitral and tricuspid valves. (E) Tricuspid regurgitation color Doppler: CDFI revealed mild tricuspid regurgitation. (F) Tricuspid regurgitation CW Doppler: Peak velocity of tricuspid regurgitation measuring 286 cm/sec, with a PG of 33 mmHg. EF, ejection fraction; LV, left ventricular; PW, pulsed-wave; E, early diastolic mitral inflow velocity; TDI, tissue Doppler imaging; E/e', ratio of mitral early diastolic flow velocity to mitral annular early diastolic tissue velocity; CDFI, color Doppler flow imaging; CW, continuous-wave; PG, peak gradient; FR, frame rate; ESV, end-systolic volume; CF, color flow; MV, mitral valve.

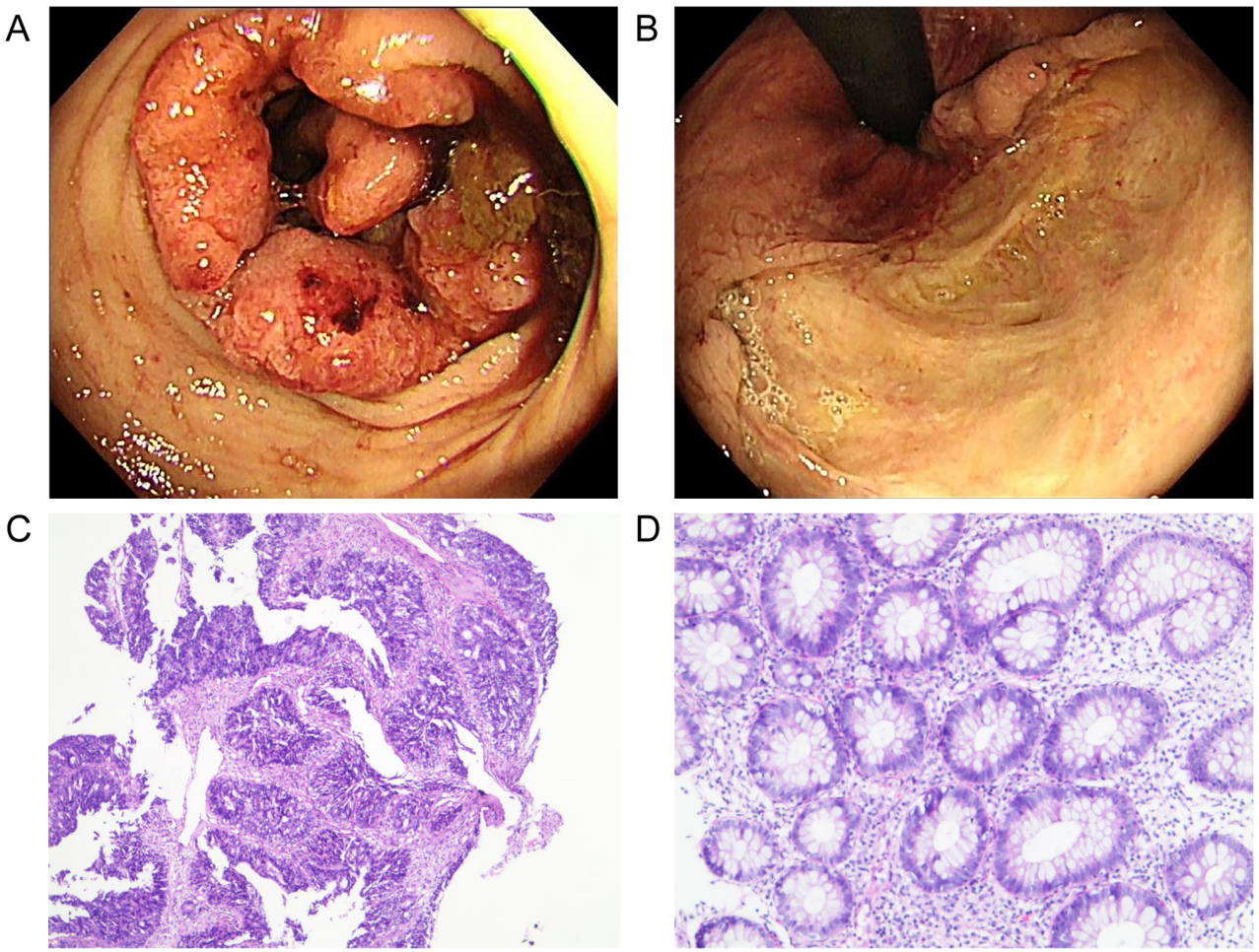

Figure 3. Colonoscopy images and tissue biopsy pathology. (A) Colonoscopy revealed a sigmoid colon mass with active bleeding. (B) Colonoscopy revealed a rectal ulcer involving the dentate line. (C) Biopsy pathology report confirmed sigmoid colon adenocarcinoma (magnification, x100). (D) Biopsy pathology report confirmed rectal adenoma with low-grade intraepithelial neoplasia (magnification, x100).

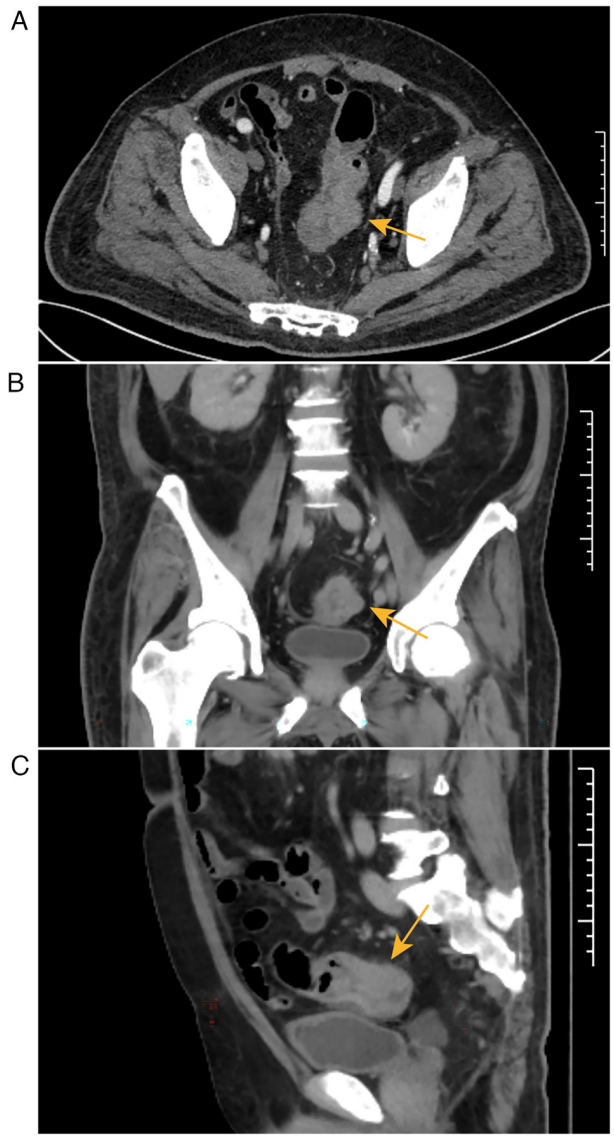

Figure 4. Contrast-enhanced CT of the abdomen reveals irregular wall thickening of the sigmoid colon with heterogeneous enhancement, luminal narrowing and serosal irregularity. (A) Axial CT scan image. (B) Coronal CT scan image. (C) Sagittal CT scan image. CT, computed tomography.

confirmed diagnosis and a standardized risk-stratified regimen, formulated according to disease subtype, genetic profile, clinical prognostic group and treatment tolerance, should be implemented to optimize outcomes (11,12).

Prognostic risk stratification in adult ALL incorporates: i) Clinical factors, including age and initial white blood cell count; ii) biological markers, including immunophenotype and cytogenetic/molecular risk category; and iii) treatment response, including post-remission MRD status (12).

High-risk genetic abnormalities associated with poor prognosis and ALL include: i) Hypodiploidy (<44 chromosomes); ii) *KMT2A* rearrangements; iii) *ZNF384* rearrangements; iv) *MYC* rearrangements; v) *TP53* mutations; vi) *IKZF1* mutations; and vii) *BCR::ABL1*-like ALL (such as JAK-STAT pathway mutations and *ABL*-homologous kinase rearrangements) (11,12). High-risk patients with ALL require intensified chemotherapy combined with molecularly targeted agents tailored to specific abnormalities (11,12). For example, individuals with *ABL*-class fusion genes (such as *BCR::ABL1*) should receive tyrosine kinase inhibitors, whereas $CD20^+$ cases (≥20% expression) benefit from rituximab. Patients exhibiting persistent MRD negativity despite adverse clinical/genetic features should undergo allogeneic hematopoietic stem cell transplantation during the first CR (11,12).

Morphological and immunophenotypic analyses confirmed B-ALL in the patient described in the present case report. Cytogenetics demonstrated a normal karyotype, while molecular testing identified an *IKZF1* mutation without detectable fusion genes, including *BCR::ABL1*, *KMT2A::AF4*, *KMT2A::AF6*, *CBFB::MYH11*, *RUNX1::RUNX1T1* (formerly *AML1::ETO*) or *PML::RARA*. *IKZF1* encodes the transcription factor IKAROS, a zinc finger DNA-binding protein essential for lymphoid development (13). Loss of IKAROS function confers leukemia-initiating potential through enhanced self-renewal and dysregulated proliferation (13). *IKZF1* deletions are associated with therapy resistance and poor prognosis (13), evidenced by a median survival of 1-2 months untreated compared with chemotherapy-induced 3-year survival rates of 32.4-33.7% (median survival; 18-24 months) (14) and a high 3-year cumulative relapse incidence of 50-60% (15). Emerging targeted strategies have shown the synergistic efficacy of chidamide and venetoclax in *IKZF1*-deleted B-ALL. Chidamide potentiates venetoclax-induced apoptosis by reducing mitochondrial membrane potential, downregulating anti-apoptotic proteins (such as MCL-1), upregulating BIM and elevating γ-H2AX (a DNA damage marker), offering a novel approach currently in phase I/II trials (16-18). However, other targeted agents for *IKZF1* mutations remain investigational and lack established clinical application guidelines.

Blinatumomab, a bispecific T-cell engager antibody targeting CD3 and CD19, bridges T cells with $CD19^+$ B-lineage tumor cells to activate cytotoxic killing (19). When combined with standard ALL regimens, it markedly reduces MRD and improves prognosis; Food and Drug Administration approval covers B-cell precursor ALL in first/second CR with MRD ≥0.1% (19). A phase II trial by Bassan *et al* (20) demonstrated MRD negativity rates increasing from 72 to 93% in Philadelphia chromosome-negative (Ph^-) B-ALL, with 3-year survival rate of >80% and cumulative relapse rates declining to 20-30%. Similarly, a phase II study at The First Affiliated Hospital of Soochow University (Suzhou, China) reported that reduced-intensity chemotherapy (idelalisib/vindesine/dexamethasone) administered sequentially with blinatumomab achieved 94% CR and 86% MRD negativity at 2 weeks in adult patients with Ph^- B-ALL, with all patients attaining CR after 4 weeks of blinatumomab. At the median 11.5-month follow-up, 1-year overall survival (OS) was 97.1% and progression-free survival was 82.2% (21). These outcomes confirm the synergistic efficacy of chemotherapy-blinatumomab combinations in enhancing remission depth and MRD clearance. In the present case report, given the $CD19^+$ status, age (>60 years) and comorbidities (hypertension/diabetes/coronary heart disease) of the patient, palliative induction with glucocorticoids and vinca alkaloids was initiated alongside blinatumomab to achieve MRD^- CR and extend survival.

Central nervous system leukemia (CNSL) is a major cause of relapse in acute leukemia, particularly in ALL (10). The Chinese Society of Clinical Oncology (CSCO) Guidelines

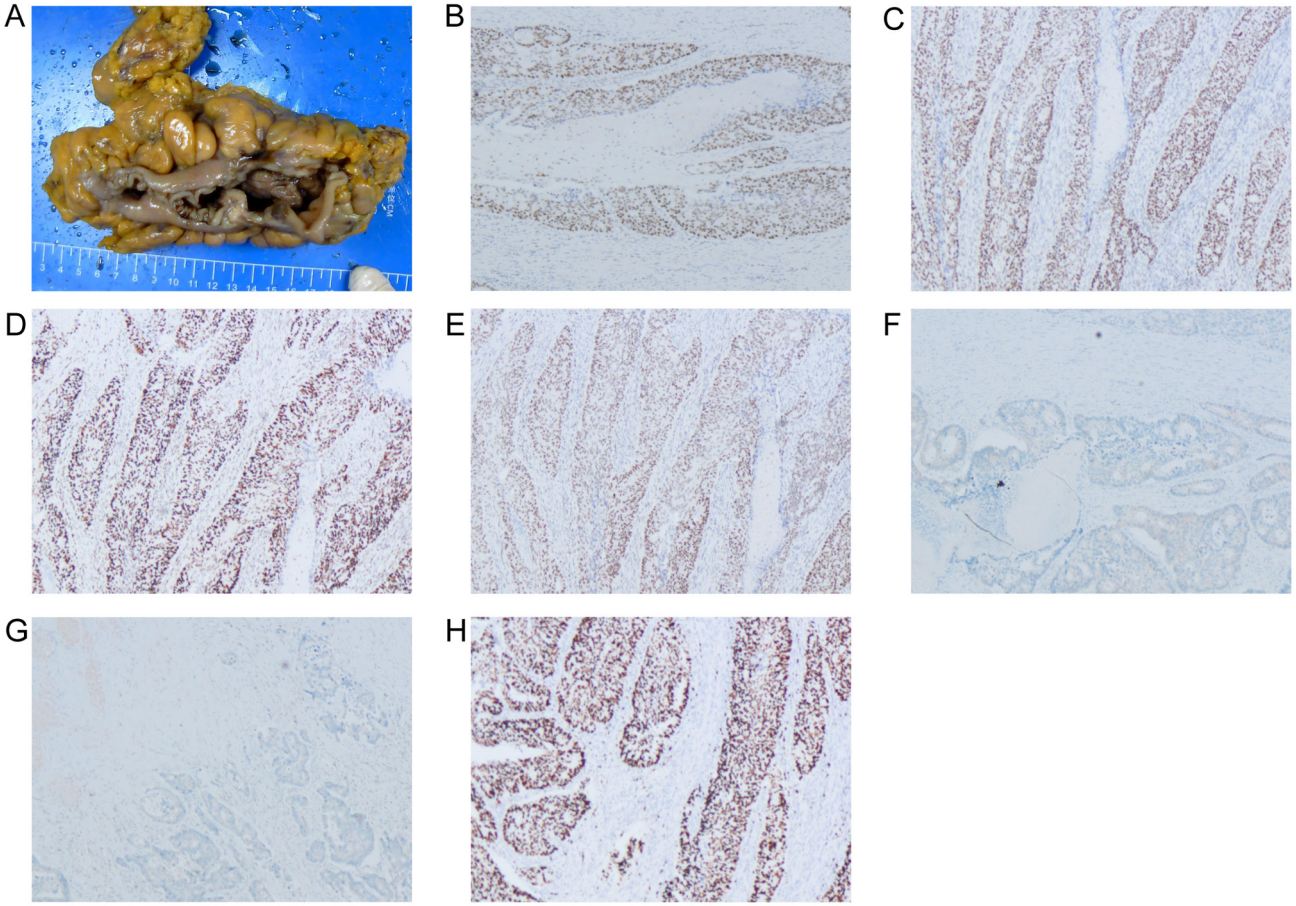

Figure 5. Pathological specimen of the sigmoid colon tumor and representative micrograph of immunohistochemical staining in colon carcinoma tissue. (A) The intestinal segment measured 11 cm in length and 4.5 cm in diameter, with a tumor located 3 cm above the peritoneal reflection line on the mucosa, measuring ~8.0x3.0x1.0-cm, and situated 2.5 cm from the proximal resection margin and 7.0 cm from the distal resection margin. (B) MLH1 staining of tumor tissue showing diffuse, strongly positive brown staining in the nuclei of tumor cells (magnification, x100). (C) MSH2 staining of tumor tissue showing diffuse, strongly positive brown staining in the nuclei of tumor cells (magnification, x100). (D) MSH6 staining of tumor tissue showing diffuse, strongly positive brown staining in the nuclei of tumor cells (magnification, x100). (E) PMS2 staining of tumor tissue showing diffuse, strongly positive brown staining in the nuclei of tumor cells (magnification, x100). (F) HER2 staining of tumor tissue showing weak, incomplete membranous staining (light brown) in tumor cells, consistent with the $HER2^{1+}$ immunophenotype (magnification, x100). (G) P53 staining of tumor tissue showing scattered nuclear positivity in tumor cells with mixed intensity brown staining, consistent with wild-type TP53 (magnification, x100). (H) Ki-67 staining of tumor tissue showing diffuse and strong nuclear positivity (brown staining) in tumor cells, with a proliferation index of ~90% (magnification, x100).

for Hematological Malignancies (Version 2025) (22) and the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia (version 2.2025) (11) both emphasize early CNSL prophylaxis for all adult patients with ALL. Recommended preventive strategies include intrathecal chemotherapy, cranial radiotherapy, high-dose systemic chemotherapy or a combination of these (11,22). Intrathecal chemotherapy, the cornerstone of CNSL prevention, is typically administered during early induction or consolidation-intensification phases, provided that no primitive cells are detected in the peripheral blood and blood counts have recovered to a safe range (11,22). Prophylactic cranial radiotherapy is generally reserved for high-risk patients >18 years of age, or those >40 years old who are not candidates for hematopoietic stem cell transplantation and is typically delivered during consolidation after remission or in the maintenance phase (11,22).

In the present case, the patient exhibited no clinical signs of CNS involvement at initial diagnosis. Although guideline-recommended CNS prophylaxis was indicated, the critical condition of the patient, marked by life-threatening comorbidities, chemotherapy-induced myelosuppression with complications during induction therapy, and limited tolerance to further aggressive treatment, precluded the safe administration of intrathecal or high-dose systemic chemotherapy. Furthermore, the patient and family declined additional consolidation therapy following colon cancer surgery. Consequently, CNS-directed prophylactic treatment was not implemented during the clinical course.

To the best of our knowledge and based on the latest search results, no other case reports of CRC and adult B-ALL presenting as synchronous double primary malignancy have been identified to date. Table II (23-34) summarizes several previously reported cases of multiple primary cancers involving CRC and hematological malignancies analogous to the present case. Among these, synchronous presentations (diagnostic interval <6 months) constituted only a minority, with the specific combination of CRC and ALL being exceptionally rare. The observed trend in this series may reflect that a shorter diagnostic interval between the two malignancies is

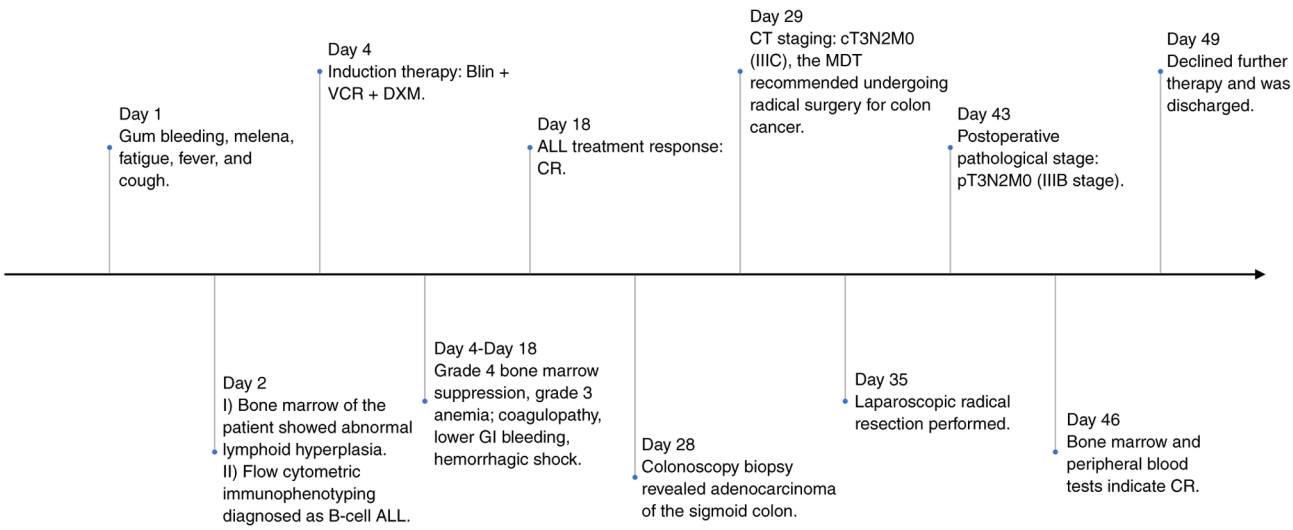

Figure 6. Chronological timeline chart regarding the treatment process of the patient. Blin, blinatumomab; VCR, vincristine; DXM, dexamethasone; ALL, acute lymphoblastic leukemia; CR, complete remission; GI, gastrointestinal; MDT, multidisciplinary team.

associated with reduced OS, although this preliminary observation is constrained by the limited number of available cases and requires validation in larger cohorts.

Review of these cases illustrates that the coexistence of CRC and hematological malignancy, particularly as synchronous primary malignancy, poses notable diagnostic and therapeutic challenges. Profound immunosuppression and thrombocytopenia secondary to the hematological disease or its treatment can critically increase the peri-operative risk, complicating or delaying necessary colorectal surgery. Conversely, surgical intervention for CRC may itself precipitate or exacerbate life-threatening complications of the concurrent hematological malignancy, such as disseminated intravascular coagulation or severe infection.

Consequently, managing these dual diagnoses necessitates a meticulously planned, multidisciplinary approach. The cornerstone of this approach involves dynamic risk assessment to prioritize the most immediately life-threatening condition, strategically sequencing treatments (such as chemotherapy, surgery and radiotherapy) and proactively managing overlapping toxicities. The present case underscores the exceptional rarity and clinical complexity inherent in this scenario and exemplifies the critical importance of integrated, individualized treatment planning to optimize outcomes for coexisting high-risk malignancies.

In the present case, ALL and colon cancer were diagnosed within 6 months of each other, therefore fulfilling the definition of SDPC (35). Although diagnosed after ALL, the insidious progression of colon cancer suggested its precedence. However, the patient described the gastrointestinal bleeding during the initial disease phase as melena (rather than hematochezia or bright red blood), which led to the initial consideration of upper gastrointestinal bleeding secondary to ALL-associated thrombocytopenia. Throughout the treatment course of the patient, it can be observed that symptoms related to colon cancer were relatively insidious and were easily minimized by complications associated with ALL, which highlights the complexity and difficulty of diagnosis in colon cancer concurrent with ALL. Currently, the exact pathogenesis of such dual primary cancers remains uncertain. Current evidence implicates synergistic genetic, environmental and immunological mechanisms in SDPC pathogenesis. Germline mutations [such as *TP53*, *APC*, *ATM*, *BRCA1/2* and mismatch repair (MMR) genes] induce DNA replication errors, chromosomal/genomic instability and cell cycle dysregulation, driving hereditary cancer syndromes (36), including Lynch syndrome (LS), familial adenomatous polyposis (FAP) and MUTYH-associated polyposis (37). While MMR defects are solid tumor hallmarks, their hematological roles remain unclear. Pedroni *et al* (38) reported constitutional MMR deficiency from biallelic PMS2 mutations causing four malignancies (sigmoid colon, jejunum and duodenal adenocarcinomas, and lymphoblastic lymphoma) within a decade.

According to the 2025 CSCO Guidelines for Colorectal Cancer (39), genetic testing for LS is recommended for individuals if their family history includes at least two histopathologically confirmed CRC cases (where two are first-degree relatives), along with any one of the following criteria: i) At least one case involves multiple CRCs (including adenomas); ii) at least one case was diagnosed before the age of 50 years; and iii) at least one family member has an extra-colonic LS-associated malignancy (such as gastric, endometrial, small intestinal, ureteral/renal pelvic, ovarian or hepatobiliary cancer).

In the present case, the patient denied that they had any family history of malignancies and showed no clinical features indicative of FAP or Peutz-Jeghers syndrome. Therefore, based on the current CSCO guidelines, the patient did not meet the criteria for routine LS screening. Additionally, germline genetic testing is not currently reimbursed under the national medical insurance policy of China, which further contributed to the decision not to pursue such testing. The patient showed intact MMR protein expression without loss on pathology. Nevertheless, underlying MMR mutations cannot be excluded due to immunohistochemical heterogeneity, functional MMR pathway compensation and potential discordance from microsatellite instability testing when missense mutations occur. However, the concurrent development of ALL and CRC in the

Table II. Summary of cases of CRC concurrent with primary HM in the literature.

First author, year	Case	Age, years/sex	HM	First primary malignancy	Priority treatment	Treatment		Interval, months	Survival, months	Cause of death	(Refs.)
						CRC	HM				
Bhattachar *et al*, 2022	1	28/F	T-ALL	T-ALL	T-ALL	PRT	BFM 2002	2	8	ALL recurrence	(23)
	2	27/M	AML-M2	AML-M2	-	None	3+7	0.23	0.57	Septic shock	
Chang *et al*, 2011	1	86/M	DLBCL	DLBCL	DLBCL	Surgery	R-COP x3, R-OP x5	3.5	N/A	Alive	(24)
Tian *et al*, 2025	1	75/M	SLL	SLL	-	Surgery	N/A	<6	>8	Alive	(25)
Fujita *et al*, 2021	1	68/M	AML	AML	AML	Surgery	CAG x2, 3+7	<6	6	Sepsis, circulatory failure	(26)
Prabakaran *et al*, 2001	1	11/M	ALL	ALL	ALL	Surgery, 5-Fu	mBFM	24	~27	N/A	(27)
Nagata *et al*, 1987	1	47/M	AMML	AMML	AMML	Surgery	VCR + DNR + CTX + 6-MP	>6	N/A	Alive	(28)
Yashige *et al*, 1989	1	78/M	ALL	CC	CC	Surgery	VDS + L-ASP + ADM + PDN	72	90	Pneumonia	(29)
Alkhayyat *et al*, 2020	1	30/M	APL	RC	RC	CRT x5, surgery, XELOX x4	ATRA	>6	N/A	N/A	(30)
Zarrabi *et al*, 1979	1	57/F	AML	CRC	CRC	Surgery, RT	Ara-C, DNR	42	57	N/A	(31)
	2	37/F	AMML	CRC	CRC	Surgery, TI, CYT	Ara-C, DNR	30	42	N/A	
	3	66/M	AEL	CRC	CRC	Surgery, CYT, VCR	None	36	48	N/A	
Abbaoui *et al*, 2024	1	15/M	ALL	ALL	ALL	Surgery, FOLFOX	N/A	73	N/A	Alive	(32)
Zhu *et al*, 2024	1	66/F	AEL	CC	AEL	Surgery, CT	MA, DA, HA	120	N/A	N/A	(33)
Tailor *et al*, 2012	1	38/M	AML	CC	CC	Surgery, 5-Fu	DA, MACE, FLAG-IDA, SCT	96	N/A	Alive	(34)

CRC, colorectal cancer; CC, colon cancer; RC, rectal cancer; F, female; M, male; HM, hematological malignancy; T-ALL, acute T-lymphoblastic leukemia; AML, acute myeloid leukemia; AML-M2, acute myeloid leukemia with maturation; DLBCL, diffuse large B-cell lymphoma; SLL, small lymphocytic lymphoma; ALL, acute lymphoblastic leukemia; AMML, acute myelomonocytic leukemia; APL, acute promyelocytic leukemia; AEL, acute erythroid leukemia; PRT, palliative radiotherapy; CRT, chemoradiotherapy; XELOX, Capecitabine, Oxaliplatin; RT, radiotherapy; 5-Fu, 5-fluorouracil; TI, triethylene thiophosphoramide; CYT, cyclophosphamide; VCR, vincristine; FOLFOX, 5-fluorouracil, leucovorin, oxaliplatin; CT, chemotherapy; BFM 2002, Berlin-Frankfurt-Munster 2002 Protocol; 3+7, anthracyclines (3 days) + cytarabine (7 days); R-COP/R-OP, R-rituximab, C-cyclophosphamide, O-vincristine, P-prednisone; mBFM, modified Berlin-Frankfurt-Munster; CTX, cyclophosphamide; 6-MP, 6-mercaptopurine; VDS, vindesine; L-ASP, L-Asparaginase; ADM, Adriamycin; PDN, prednisone; ATRA, All-trans retinoic acid; CAG, cytarabine, aclarubicin, G-CSF; G-CSF, granulocyte colony-stimulating factor; Ara-C, cytarabine; DNR, daunorubicin; MA, mitoxantrone + cytarabine; DA, daunorubicin + cytarabine; HA, homoharringtonine + Cytarabine; MACE, amsacrine + etoposide + cytarabine; FLAG-IDA, fludarabine + cytarabine + G-CSF + idarubicin; SCT, stem cell transplantation; N/A, not available.

patient may represent a chance co-occurrence and clinical data are insufficient to confirm an underlying hereditary syndrome.

At present, there is no unified standard, guideline or protocol for the treatment of multiple primary tumors (35). Management typically requires MDT communication to implement an individualized comprehensive treatment strategy that integrates tumor-related factors, patient performance status and treatment preferences. The decision-making process critically depends on a dynamic assessment of the relative immediacy of life-threatening risks posed by each malignancy (35).

At initial diagnosis, the patient in the current case report presented with active B-ALL accompanied by severe thrombocytopenia and coagulopathy, which led to life-threatening gastrointestinal bleeding. Performing radical colon cancer surgery at that stage carried a high risk of perioperative major hemorrhage and infection, and would have postponed essential leukemia treatment. By contrast, delaying colon surgery carried the primary risk that the tumor may induce further fatal bleeding due to subsequent chemotherapy-induced thrombocytopenia, or that tumor progression might lead to complications such as intestinal obstruction. After comprehensive MDT deliberation, given that untreated adult ALL is rapidly fatal (40), whereas colon cancer progression without acute complications is relatively indolent, the leukemia constituted the primary and immediate survival threat. Therefore, the MDT decided to prioritize ALL induction therapy to rapidly achieve hematological remission and correct coagulopathy, thereby creating safer conditions for future surgery. This aligns with the imperative to address the most imminent life-threatening condition first.

Following the successful achievement of complete hematological remission from ALL, marrow function recovered sufficiently. The immediate threat was thus controlled and the clinical focus shifted to definitively treating the secondary malignancy. The patient subsequently underwent successful radical colon cancer surgery. Postoperative pathology confirmed pT3N1c (stage IIIB) colon cancer, characterized by the presence of tumor deposits, which is associated with a notable risk of systemic recurrence (41,42). The standard of care for stage IIIB colon cancer, per NCCN and European Society for Medical Oncology guidelines, is adjuvant chemotherapy, such as capecitabine plus oxaliplatin (CAPEOX) or folinic acid, fluorouracil and oxaliplatin (FOLFOX), to reduce recurrence risk and improve OS (41,42). For the decision regarding adjuvant chemotherapy for colon cancer, a risk-benefit assessment was meticulously revisited. A clinical cohort study conducted by Nors *et al* (43) showed that the 5-year cumulative incidence of recurrence for patients with stage III colon cancer was 24.6-35.3%, representing a primarily medium to long-term risk. In patients with untreated colon cancer, the risk of recurrence is highest in the early postoperative period, especially within the first 2 years (43). A study by Sargent *et al* (44), which pooled data from 18 phase III clinical trials involving 20,898 patients with colon cancer, demonstrated that fluorouracil-based adjuvant chemotherapy can improve disease-free survival and OS in patients with stage III colon cancer, markedly increasing OS rates. Furthermore, the meta-analysis results indicated that comprehensive postoperative adjuvant therapy could reduce the early recurrence risk of colon cancer by 40% and increase the 8-year OS rate in patients with stage III colon cancer by 10% (44). Although standard adjuvant chemotherapy (such as FOLFOX/CAPEOX) can markedly reduce the long-term recurrence risk, the associated myelosuppression would have an additive effect with ALL maintenance therapy, substantially increasing the risk of severe infection, bleeding and treatment interruption, potentially risking the achieved leukemia remission. The MDT considered that, due to the highly aggressive, acute-onset and rapidly progressive nature of ALL, leukemia relapse remained immediately life-threatening in the short term, whereas the progression of colon cancer after radical surgery was not currently a major contributor to the immediate mortality risk of the patient in this case. When treatment toxicities conflict, priority should be given to ensuring the continuity and safety of leukemia therapy. Consequently, in the present case report, the decision was made to postpone adjuvant chemotherapy for colon cancer, with plans to reassess after the intensity of ALL treatment decreased and the bone marrow function of the patient had sufficiently recovered. Although this individualized approach deviates from the standard pathway for colon cancer treatment, it is based on considerations aimed at maximizing the OS of the patient.

In the present case report, follow-up was short and the patient declined further antitumor therapy, notably limiting the assessment of long-term outcomes. Therefore, prognosis for either B-ALL or stage IIIB colon cancer cannot be determined from the patient. The present case report mainly highlights short-term decision-making and peri-treatment coordination, and longer follow-up is required to evaluate prognosis and late events for both malignancies.

In conclusion, the management of locally advanced colon cancer concurrent with ALL requires multidisciplinary collaboration to assess treatment priority, balance drug efficacy against toxicity, and formulate an individualized therapeutic regimen adapted to the treatment response and tolerance of the patient, while concurrently determining the optimal timing for local surgical intervention.

Acknowledgements

Not applicable.

Funding

The present study was funded by the Guizhou Provincial Basic Research Program (Natural Science) (grant no. [2022]340, zk[2025] General Program 475) and the Cultivation Project of Guizhou Medical University (grant no. 20NSP039).

Availability of data and materials

The data generated in the present study are not publicly available due to relevant national regulations and the protection of patient's privacy but may be requested from the corresponding author.

Authors' contributions

YZh, WW and WC conceived the study. SM, GL, YZh and WC designed the study methodology. YZe was responsible for the collection of case data and literature. SM, GL, ZL, QJ, YZh, WW and WC were responsible for analysis of case data and

literature. YZh, WW and WC interpreted the data. WW and WC acquired the funding. YZe wrote the original draft. WC reviewed and edited the manuscript. YZe and WC confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

All patient-related medical records and information presented in this article, along with the publication of this case report, were obtained with the patient's written informed consent.

Competing interests

The authors declare that they have no competing interests.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F: Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71: 209-249, 2021.
2. Bailey CE, Hu CY, You YN, Bednarski BK, Rodriguez-Bigas MA, Skibber JM, Cantor SB and Chang GJ: Increasing disparities in the age-related incidences of colon and rectal cancers in the United States, 1975-2010. JAMA Surg 150: 17-22, 2015.
3. Sung H, Siegel RL, Laversanne M, Jiang C, Morgan E, Zahwe M, Cao Y, Bray F and Jemal A: Colorectal cancer incidence trends in younger versus older adults: An analysis of population-based cancer registry data. Lancet Oncol 26: 51-63, 2025.
4. Kantarjian H, Pui CH and Jabbour E: Acute lymphocytic leukaemia. Lancet 406: 950-962, 2025.
5. Ni H, Shi Y, Wang M and Ji C: Analysis of global, regional, and national burden and attributable risk factors of acute lymphoblastic leukemia and acute myeloid leukemia from 1990 to 2021. PLoS One 20: e0330479, 2025.
6. Nuha N, Higgins SP, Czekay RP, Higgins CE, Guo L, Lee H and Higgins PJ: SERPINE1 drives molecular synergies in colorectal cancer. Am J Physiol Cell Physiol 330: C9-C25, 2026.
7. Basheer MI, Rana IA, Sheikh UN, Yusuf MA, Sindhu II and Loya A: Presentation of acute lymphoblastic lymphoma and colorectal carcinoma in the context of constitutional mismatch repair deficiency syndrome: A case report with literature review. J Cancer Allied Spec 8: e443, 2022.
8. Bloomfield CD, Lindquist LL, Arthur D, McKenna RW, LeBien TW, Nesbit ME and Peterson BA: Chromosomal abnormalities in acute lymphoblastic leukemia. Cancer Res 41(11 Pt 2): 4838-4843, 1981.
9. Garcia C, Miller-Awe MD and Witkowski MT: Concepts in B cell acute lymphoblastic leukemia pathogenesis. J Leukoc Biol 116: 18-32, 2024.
10. Pui CH, Carroll WL, Meshinchi S and Arceci RJ: Biology, risk stratification, and therapy of pediatric acute leukemias: An update. J Clin Oncol 29: 551-565, 2011.
11. National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Acute Lymphoblastic Leukemia. Version 2.2025. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1410. Accessed January 25, 2026.
12. Wang Y: Interpretation of Chinese guideline for diagnosis and treatment of adult acute lymphoblastic leukemia (2024). J Clin Hematol (China) 37: 453-456, 2024 (In Chinese).
13. Paolino J, Tsai HK, Harris MH and Pikman Y: IKZF1 alterations and therapeutic targeting in B-cell acute lymphoblastic leukemia. Biomedicines 12: 89, 2024.
14. Tang BQ, Cai ZH, Lin DN, Wang ZX, Liang XJ, Fan ZP, Huang F, Liu QF and Zhou HS: Prognostic significance of IKZF1 gene deletions in patients with B-cell acute lymphoblastic leukemia. Zhonghua Xue Ye Xue Za Zhi 43: 235-240, 2022 (In Chinese).
15. Deng SY, Ou JW, Huang ZC, Chen JJ, Cai ZH, Liu QF and Zhou HS: The value of minimal residual disease and IKZF1 deletion for predicting prognosis in adult patients with B-cell acute lymphoblastic leukemia. Zhonghua Xue Ye Xue Za Zhi 45: 257-263, 2024 (In Chinese).
16. Ou JW, Deng SY, Li J, Huang ZC, Cai ZH, Lin JP, Chen YF and Zhou HS: Synergistic effect of chidamide and venetoclax in IKZF1 deletion acute B lymphoblastic leukemia cells and its mechanism. Abstract P380. Eur Hematol Assoc Annu Congr. June 13-16, 2024; Madrid, Spain.
17. Zhao L, Sun L, Kong D, Cao R, Guo Z, Guo D, Li Q, Hao J, Li Y and Emails L: Chidamide and venetoclax synergistically regulate the Wnt/β-catenin pathway by MYCN/DKK3 in B-ALL. Ann Hematol 104: 489-501, 2025.
18. Hanbali A, Kotb A and Saleh M: B-Cell lymphoma 2 inhibition in acute lymphoblastic leukemia: Mechanisms, resistance, and emerging combinations with venetoclax. J Hematol 14: 193-201, 2025.
19. Jen EY, Xu Q, Schetter A, Przepiorka D, Shen YL, Roscoe D, Sridhara R, Deisseroth A, Philip R, Farrell AT and Pazdur R: FDA approval: Blinatumomab for patients with b-cell precursor acute lymphoblastic leukemia in morphologic remission with minimal residual disease. Clin Cancer Res 25: 473-477, 2019.
20. Bassan R, Chiaretti S, Della Starza I, Santoro A, Spinelli O, Tosi M, Elia L, Cardinali D, De Propris MS, Piccini M, *et al*: Up-front blinatumomab improves MRD clearance and outcome in adult Ph- B-lineage ALL: The GIMEMA LAL2317 phase 2 study. Blood 145: 2447-2459, 2025.
21. Lu J, Zhou H, Zhou X, Yang Y, Tong L, Miao M, Yang X and Chen S: Reduced-dose chemotherapy followed by blinatumomab in induction therapy for newly diagnosed B-cell acute lymphoblastic leukemia. Cancer Med 13: e7062, 2024.
22. Chinese Society of Clinical Oncology. Guidelines of Chinese Society of Clinical Oncology (CSCO) Hematological Malignancies. People's Medical Publishing House, Beijing, China, 2025 (In Chinese).
23. Bhattacharjee S, Ghosh S and Bhattacharyya M: Bleeding per rectum during induction chemotherapy: Looking beyond the leukaemia-2 case reports and review of literature. Indian J Cancer 59: 560-564, 2022.
24. Chang H, Chuang WY, Shih LY and Tang TC: Collision in the colon: concurrent adenocarcinoma and diffuse large B-cell lymphoma in the same tumour. Acta Clin Belg 66: 302-304, 2011.
25. Tian S, Wu F, Yang F, Min G and Chen H: Laparoscopic surgery for synchronous double colorectal cancer with obstruction, plus small B cell lymphoma: A case report. J Surg Case Rep 2025: rjae830, 2025.
26. Fujita H, Morohashi H, Sakamoto Y, Miura T, Sato K, Mitsuhashi Y, Umemura K, Ogasawara H, Hara Y, Kanda T, *et al*: A case of descending colon and rectal cancer with acute myeloid leukemia performed robot-assisted hartmann's procedure. Gan To Kagaku Ryoho 48: 599-601, 2021 (In Japanese).
27. Prabakaran S, Senthilnathan SV, Venkatadesikalu M, Prasad N and Sridharan S: Adenocarcinoma of the colon as a second malignancy in a child. Pediatr Surg Int 17: 475-477, 2001.
28. Nagata K, Fushimi K, Sugiura K, Miyake S, Maruyama H, Murohashi I and Murakami N: A case of successful surgical treatment of rectal cancer complicated by acute myelomonocytic leukemia. Gan No Rinsho 33: 1945-1949, 1987 (In Japanese).
29. Yashige H and Fujii H: Ph1 positive acute lymphoblastic leukemia with DIC after operation of colon and lung cancer. Rinsho Ketsueki 30: 1074-1078, 1989 (In Japanese).
30. Alkhayyat S: Rectal cancer complicated by acute promyelocytic leukemia. Cureus 12: e11118, 2020.
31. Zarrabi MH and Rosner F: Acute myeloblastic leukemia following treatment for non-hematopoietic cancers: Report of 19 cases and review of the literature. Am J Hematol 7: 357-367, 1979.
32. Abbaoui S, Zaari N, Ammor A and Benhaddou H: Adenocarcinoma of the colon in children with LAL: A case report. Int J Surg Case Rep 121: 109995, 2024.
33. Zhu B, Liu M, Mu T, Li W, Ren J, Li X, Liang Y, Yang Z, Niu Y, Chen S and Lin J: Quadruple primary tumors in a lynch syndrome patient surviving more than 26 years with genetic analysis: A case report and literature review. Front Oncol 14: 1382154, 2024.
34. Tailor IK, Cook J, Reilly JT, Dalley CD, Ezaydi Y, Kelsey PJ and Snowden JA: Acute myeloid leukaemia associated with Muir-Torre variant of hereditary non-polyposis colon cancer (HNPCC): Implications for inherited and acquired mutations in DNA mismatch repair genes. Br J Haematol 156: 289-291, 2012.

35. Lung Cancer Medical Education Committee of the Chinese Medical Education Association; Lung Cancer Alliance of Chinese Thoracic Surgery; Society of Tumor Ablation Therapy of the Chinese Anti-Cancer Association; Tumor Ablation Expert Committee of the Chinese Society of Clinical Oncology; Tumor Ablation Expert Group of the Chinese College of Interventionalists. Chinese expert consensus: multidisciplinary diagnosis and treatment of multiple ground-glass nodule like lung cancer (2024 edition). Zhonghua Nei Ke Za Zhi 63: 153-169, 2024 (In Chinese).
36. Garutti M, Foffano L, Mazzeo R, Michelotti A, Da Ros L, Viel A, Miolo G, Zambelli A and Puglisi F: Hereditary cancer syndromes: A comprehensive review with a visual tool. Genes (Basel) 14: 1025, 2023.
37. Ma H, Brosens LAA, Offerhaus GJA, Giardiello FM, de Leng WWJ and Montgomery EA: Pathology and genetics of hereditary colorectal cancer. Pathology 50: 49-59, 2018.
38. Pedroni M, de Leon MP, Bonetti LR, Rossi G, Viel A, Urso EDL and Roncucci L: Biallelic PMS2 mutations in a family with uncommon clinical and molecular features. Genes (Basel) 13: 1953, 2022.
39. Chinese Society of Clinical Oncology: Guideline of Chinese Society of Clinical Oncology (CSCO) Colorectal Cancer. People's Medical Publishing House, Beijing, China, 2025.
40. Baden D, Wolgast N, Altrock PM, Steinhäuser S, Voran J, Beder T, Hecht M, Baden C, Bastian L, Ronckers C, *et al*: Epidemiology, survival, and treatment of acute myeloid and lymphoblastic leukaemia in Germany: A nationwide population-based registry analysis. Lancet Reg Health Eur 59: 101503, 2025.
41. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology(NCCN Guidelines): Colon Cancer. Version 5.2025. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1428. Accessed February 6, 2026..
42. Argilés G, Tabernero J, Labianca R, Hochhauser D, Salazar R, Iveson T, Laurent-Puig P, Quirke P, Yoshino T and Taieb J: Localised colon cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 31: 1291-1305, 2020.
43. Nors J, Iversen LH, Erichsen R, Gotschalck KA and Andersen CL: Incidence of recurrence and time to recurrence in stage I to III colorectal cancer: A nationwide danish cohort study. JAMA Oncol 10: 54-62, 2024.
44. Sargent D, Sobrero A, Grothey A, O'Connell MJ, Buyse M, Andre T, Zheng Y, Green E, Labianca R, O'Callaghan C, *et al*: Evidence for cure by adjuvant therapy in colon cancer: Observations based on individual patient data from 20,898 patients on 18 randomized trials. J Clin Oncol 27: 872-877, 2009.