Clinical Case Report

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Coexistence of colon adenocarcinoma, diffuse large B-cell lymphoma, and myelodysplastic syndrome

A case report

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Abstract

Rationale: Cases of coexistence of 2 cancers, such as colorectal cancer and diffuse large B-cell lymphoma (DLBCL), colorectal cancer and myelodysplastic syndrome (MDS), and DLBCL with MDS, have been reported, whereas the coexistence of 3 different cancers in a patient is extremely rare. Here we report a case of co-occurrence of colon adenocarcinoma, DLBCL, and MDS in a 78-year-old Chinese man.

Patient concerns: He presented to our hospital with palpable lumps in the abdomen without any of the following symptoms including abdominal pain, fever, contact pain, tenesmus, changes in bowel habits and shape, nausea, and vomiting.

Diagnoses: The patient was first diagnosed with sigmoid colon adenocarcinoma and DLBCL in the right ascending colon using enhanced computed tomography, colonoscopy, and immunohistochemistry. After resection of the sigmoid adenocarcinoma and DLBCL, MDS was diagnosed according to the results of routine blood tests, bone marrow aspiration smear, and flow cytometry.

Interventions: Overall, the patient was treated with surgical resection of the sigmoid adenocarcinoma and DLBCL of the colon, combined with 4 cycles of chemotherapies targeting MDS.

Outcomes: Blood test results and follow-up indicated that the treatment regimen showed promising outcomes.

Lessons: In conclusion, a case of synchronous existence of colon cancer, DLBCL, and MDS is reported, which suggests that careful attention should be paid clinically to checking the state of bone marrow for elderly cancer patients. Efforts are also needed to establish an effective system for distinguishing the origin of multi-existent cancers and to develop effective therapeutic regimens for multi-existent cancers with fewer side effects.

Abbreviations: CT = computed tomography, DLBCL = diffuse large B-cell lymphoma, MDS = myelodysplastic syndromes, PET-CT = positron emission tomography-computed tomography.

Keywords: coexistence, colon adenocarcinoma, diffuse large B-cell lymphoma, myelodysplastic syndrome

1. Introduction

Colorectal cancer is currently ranked as the third most lethal cancer in the United States. Of the colorectal cancers, the vast majority (>95%) are adenocarcinomas, which occur in the mucus-making glands lining the colon and rectum.[1] Colonoscopy is the method used for the diagnosis of colorectal cancer and for adenoma removal.[2] The common treatments include surgical resection, radiofrequency ablation, cryosurgery, chemotherapy, radiation therapy, and targeted therapy.[1]

Diffuse large B-cell lymphoma (DLBCL) accounts for 30% to 58% of non-Hodgkin lymphoma cases. Its incidence rate in Europe is 3.8 of 100,000/year.[3] Diagnosis of DLBCL is generally performed in a hematopathology laboratory morphologically, immunochemically, and genetically. Chemotherapy is commonly used for treatment.[3,4]

Myelodysplastic syndromes (MDS) are a group of clonal hematopoietic stem cell malignancies with significant morbidity and high mortality. The incidence of MDS is >1/30,000/year in the United States.[5,6] The commonly used diagnostic tests are blood tests, bone marrow histology and immunohistochemistry, karyotyping, molecular typing and point mutation analysis, and flow cytometry. Therapeutic treatment includes bone marrow transplantation and chemotherapy.[6]

Cases of patients with coexistence of 2 malignancies,[7–9] such as colon cancer with DLBCL,[7,10] gastric-intestine cancer with MDS,[11] and DLBCL with MDS,[7,12] have been reported. However, synchronous occurrence of colon cancer, DLBCL, and MDS has not been reported to our knowledge, and thus, no

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Written informed consent was obtained from the patient for publication of the case.

The authors have no conflicts of interest to disclose.

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diagnosis and treatment standards for this type of case have been established. Here we report a case with these 3 malignancies coexisting in the same patient.

2. Case report

This study was approved by the Ethics Committee of Huashan Hospital. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from the individual participant included in the study.

The patient was a 78-year-old man from Shanghai. In May 2017, he presented to our hospital with palpable lumps in the abdomen without any of the following symptoms including abdominal pain, fever, contact pain, tenesmus, changes in bowel habits and shape, nausea, and vomiting. Enhanced computed tomography (CT) revealed that the ascending colon was regionally thickened unevenly, most likely to be colon cancer. Colonoscopy revealed a different type of biological ulcer in the sigmoid colon 30 cm from the anus, which was about 20×10 mm, had a dirty appearance on the surface, had a crisp texture, and bled easily upon touch. This lesion was diagnosed as an intraepithelial neoplasia and a high-grade local cancer. In the ascending colon, there was severe acute and chronic inflammation in the mucosa with erosion, and a lesion that was 3/5 of the circumference of the colon, with an uneven and dirty appearance, crisp texture, and bled easily upon touch, resulting in local mild stenosis in the colon around which the endoscope could still pass.

On May 25, 2017, blood tests showed that he had low hemoglobin anemia (Table 1). On May 26, 2017, in the Department of General Surgery of our hospital, laparoscopic resection was performed to remove the right half colon, the sigmoid colon, and the sigmoid mesocolon. During the surgery, right upper abdominal adhesions, a lump in the middle of the ascending colon, and an ulcer in the middle of the sigmoid colon were found (Table 1). Pathological evaluation revealed a grade II ulcerated adenocarcinoma, which was at T3N0M0 according to tumor node metastasis staging, in the sigmoid colon (Table 1, Fig. 1A–C), and a non-Hodgkin lymphoma of DLBCL lesion in the right ascending colon (Table 1, Fig. 1D–F). The DLBCL was graded at stage IV A (Ann Arbor, International Prognostic Index 3, high risk). On June 10, 2017, positron emission tomography-computed tomography (PET-CT) revealed that fluorodeoxyglucose metabolism was increased in the anastomotic stoma after surgical resection. Whole-body (including brain) PET-CT showed a senile brain with bilateral basal ganglia lacunar. The patient recovered well after the surgery and was transferred to the Department of Hematology for further treatment of the lymphoma.

Upon admission to the Department of Hematology on June 26, 2017, physical examination showed that every tested parameter was normal (Table 1). Blood tests showed a white blood cell count of 4.22×10^9/L, hemoglobin level of 103 g/L, and platelet count of 44×10^9/L (Table 1). On June 27, 2017, bone marrow aspiration smears showed typical active hyperplasia symptoms and dyshematopoiesis (Table 1, Fig. 1G and H). Flow cytometry showed 13% abnormal myeloid progenitor cells in the bone marrow (Table 1). The patient was diagnosed with MDS-excess blasts 2 according to the WHO classification, which was highly risky with an International Prognostic Scoring System score of 2.5, and treated from June 28 to August 24, 2017 with a chemotherapy regimen comprising rituximab 600 mg D1+, methylprednisolone 40 mg D1–7+G-CSF 300 μg D3–4, 9–10+, decitabine 25 mg D4–8+, aclacinomycin 10 mg D7–10+, cytosine arabinoside (cytarabine) 12.5 mg q12 h D7–13.

On August 24, 2017, karyotyping showed a chromosome type of 46XY. Whole-genome microarray analysis revealed one chromosome abnormality of uniparental disomy (UPD) (11p), which was not among the chromosome abnormalities previously reported to be related to malignant blood diseases (Table 1).

The patient's health conditions were monitored on August 24, October 23, and December 28, and tests showed a normal white blood cell count and increased hemoglobin level. However, bone marrow hyperplasia was still active (Table 1) after 3 consolidation chemotherapies on August 26, 2017; October 24, 2017; and December 29, 2017 (regimen: rituximab rituxan mabthera 600 mg D0+G-CSF 75 μg D0–9+, decitabine 25 mg D1–5+, aclacinomycin 10 mg D3–6+, cytarabine 12.5 mg q12 h D3-). The patient was further treated 3 times with the same chemotherapeutic regimen with the last chemotherapy given in July 2018, and restaging after the therapy showed that the 3 tumors were in a state of complete remission.[13] After a 1-month follow-up, the patient died of stroke in August 2018.

3. Discussion

Here we report for the first time an extremely rare case of coexistence of colon cancer, lymphoma, and MDS. This case tells us that special caution should be taken in the diagnosis of the patients with multicancers, and an effective testing system should be established to define the origin of coexistent cancers. Moreover, effective treatments for patients with multiple cancers need to be developed.

Three coexistent cancers may originate from the same source[14] or generate independently.[8] Although the colon adenocarcinoma and DLBCL were diagnosed in the same time, the relationship between these 2 malignancies regarding to their origin is not clear. When MDS was diagnosed, no chemotherapy had been applied, indicating that the origin of MDS in the present case was not secondary to chemotherapeutic treatment.[15] It is not excluded that it could be secondary to metastasis of the colon adenocarcinoma and DLBCL, which were diagnosed before MDS. The chromosome abnormality of UPD (11p) was not among the genetic abnormalities previously reported to be related to blood malignancies, suggesting that it might be a new genetic defect contributing to the coexistence of the 3 cancers in the patient. An aging-related immune-watch mechanism defect could also result in the co-occurrence of the cancers.[1,3] The coexistence of 3 cancers in our case further supports the need for an effective differentiation system to be established to define the origins of different coexisting cancers.

In the present case, when the patient was diagnosed with colon adenocarcinoma and DLBCL, his routine blood test results did not show MDS. Only after the bone marrow aspiration smear test was performed was MDS discovered, suggesting that precautions should be clinically taken to examine the status of bone marrow when a patient is diagnosed with any cancer to identify coexistent MDS, especially in elderly patients.

Currently, patients with multiple cancers are treated with various therapeutic regimens and generally have a poor prognosis with a survival period of several months.[12] The patient in the present case was treated with surgical resection of the lesions in

Table 1

Medical examination results.

Date	Medical examination	Results
May 25, 2017 (preresection)	Routine blood tests	WBC: 6.32×10^9 cells/L; RBC: 4.16×10^{12} cells/L; Hb: 112 g/L; PLT: 195×10^9/L; neutrophils: 75%; lymph cells: 10%; monocytes: 15%
May 26, 2017	Surgical observation	Right upper abdominal adhesions; a lump with a diameter of 5 cm in the middle of the ascending colon; an ulcer with a diameter of 2.5 cm in the middle of the sigmoid colon; mesenteric lymph nodes in the ascending mesocolon; no tumors involving both the cutting edges; no metastasis in 2 intestinal lymph nodes (0/2); inflammation in the appendix.
	Pathological examination	Adenocarcinoma: grade II ulcerated; in the sigmoid colon; CK (+), p53 (+). Non-Hodgkin's lymphoma or DLBCL: in the right ascending colon; CK (−), Vim (+), CD2 (−), Ki67 (50% +), p53 (−), CD5 (−), Syn (−), CD138 (−), CD20 (+), CD3 (−), Bcl2 (+), Bcl6 (partially +), MUM-1 (partially +), PAX-5 (+), CD10 (few +), CyclinD1 (−), CD23 (−), CD43 (−), CD79a (+).
June 2, 2017	Routine blood tests	WBC: 4.6×10^9 cells/L; RBC: 3.7×10^{12} cells/L; Hb: 100 g/L; PLT: 166×10^9/L; neutrophils: 67%; lymph cells: 15%; monocytes: 15%; immature granulocytes: 3%
June 26, 2017 (prechemotherapy)	Physical examination	Body temperature 37°C, normal mucocutaneous zone, no enlargement in the body superficial lymph nodes, no subcutaneous bleeding, no icteric sclera, no lip cyanosis, clear lung breath sounds without dry or moist rales, heart rate of 80 beats/min, regular heart rhythm, even abdomen and soft abdominal wall, no whole abdominal tenderness, no muscle tension and rebound, no palpable liver or spleen under rib cage (palpation), no percussion pain in the liver and kidneys, no red swelling of joints or lower extremity edema.
	Routine blood tests	WBC: 4.22×10^9 cells/L; RBC: 3.66×10^{12} cells/L; Hb: 103 g/L; PLT: 44×10^9/L; neutrophils: 71%; lymph cells: 14%; monocytes: 12%; immature granulocytes: 1%
June 27, 2017	Bone marrow aspiration smear	Active bone marrow nucleated cells; normal ratio of bone marrow granulocytes to nucleated erythrocytes; bone marrow blasts increased to 12%; blasts were medium sized, fewer, and blue, occasionally showing fine particles in the cytoplasm; there was folding, twisting, and notches in some nuclei, occasionally showing Auer bodies, fine granular chromatin, and 1–3 nucleoli; there were binucleated blasts. Granulates seemed to be actively proliferating. Some neutrophils showed vacuoles in the cytoplasm and loss of granules. Some myelocytes were small. Some mature neutrophils had nonsegmented nuclei. Erythroid hyperplasia was observed with most middle and late erythroblasts, and occasionally 3 nucleated intermediate erythroblasts. The mature RBCs were not even in size. There were 207 megakaryocytes on the whole slides, consisting of 3/50 immature megakaryocytes, 30/50 granular megakaryocyte, 7/50 platelet-producing megakaryocytes, 10/50 small, tiny megakaryocytes, 2-, 3- and multinucleated megakaryocytes, and platelets.
	Flow cytometry	13% Abnormal myeloid progenitor cells in the bone marrow (CD7+, CD117+, CD36+, CD4+, CD38+, CD33+/−, CD13+/−).
July 11, 2017 (postchemotherapy)	Routine blood tests	WBC: 2.69×10^9 cells/L; RBC: 2.89×10^{12} cells/L; Hb: 83 g/L; PLT:34×10^9/L; neutrophils: 64%; lymph cells: 22%; monocytes: 14%
August 24, 2017	Routine blood tests	WBC: 7.69×10^9 cells/L; RBC: 4.12×10^{12} cells/L; Hb: 118 g/L; PLT: 163×10^9/L; neutrophils: 72%; lymph cells: 11%; monocytes: 16%
	Bone marrow smears	Active bone marrow hyperplasia with 1% myoblasts
	Flow cytometry	0.8% Myelodysplastic primitive myeloid
	Karyotyping and whole-genome microarray analysis	46XY; chromosome abnormality of UPD (11p).
October 23, 2017	Routine blood tests	WBC: 6.2×10^9 cells/L; RBC: 4.63×10^{12} cells/L; Hb: 130 g/L; PLT: 150×10^9/L; neutrophils: 78%; lymph cells: 10%; monocytes: 12%.
	Bone marrow smears	Active hyperplasia; some myeloblasts.
	Flow cytometry	Approximately 1.3% bone marrow blasts
December 28, 2017	Routine blood tests	WBC: 4.74×10^9 cells/L; RBC: 4.44×10^{12} cells/L; Hb: 128 g/L; PLT: 192×10^9/L; neutrophils: 71%; lymph cells: 14%; monocytes: 15%.
	Bone marrow smears	Active hyperplasia; 1% myeloblasts
	Flow cytometry	Approximately 1.5% bone marrow blasts

CK = cytokeratin, Hb = hemoglobin, PLT = platelet, RBC = red blood cell, WBC = white blood cell, UPD = uniparental disomy.

the colon combined with several cycles of rituximab targeting DLBCL and chemotherapeutic treatments targeting MDS. Although these treatments resulted in some positive outcomes, our follow-up was not long enough, and the outcome was not optimal. The differences in age, sex, number of coincident tumors, and grade of tumors make the therapeutic regime and outcomes not comparable among the present patient and previously reported cases.[12] Effective treatments for patients with multiple cancers still need to be developed, and therapeutic agents that can effectively target all coexistent cancers simultaneously with few side effects are particularly in demand.

In conclusion, a case of coexistence of colon adenocarcinoma, DLBCL, and MDS was reported. This case suggests that it is necessary to pay careful attention to checking the state of bone marrow for elderly cancer patients. Moreover, an effective system for distinguishing the origins of the coexistent cancers is needed,

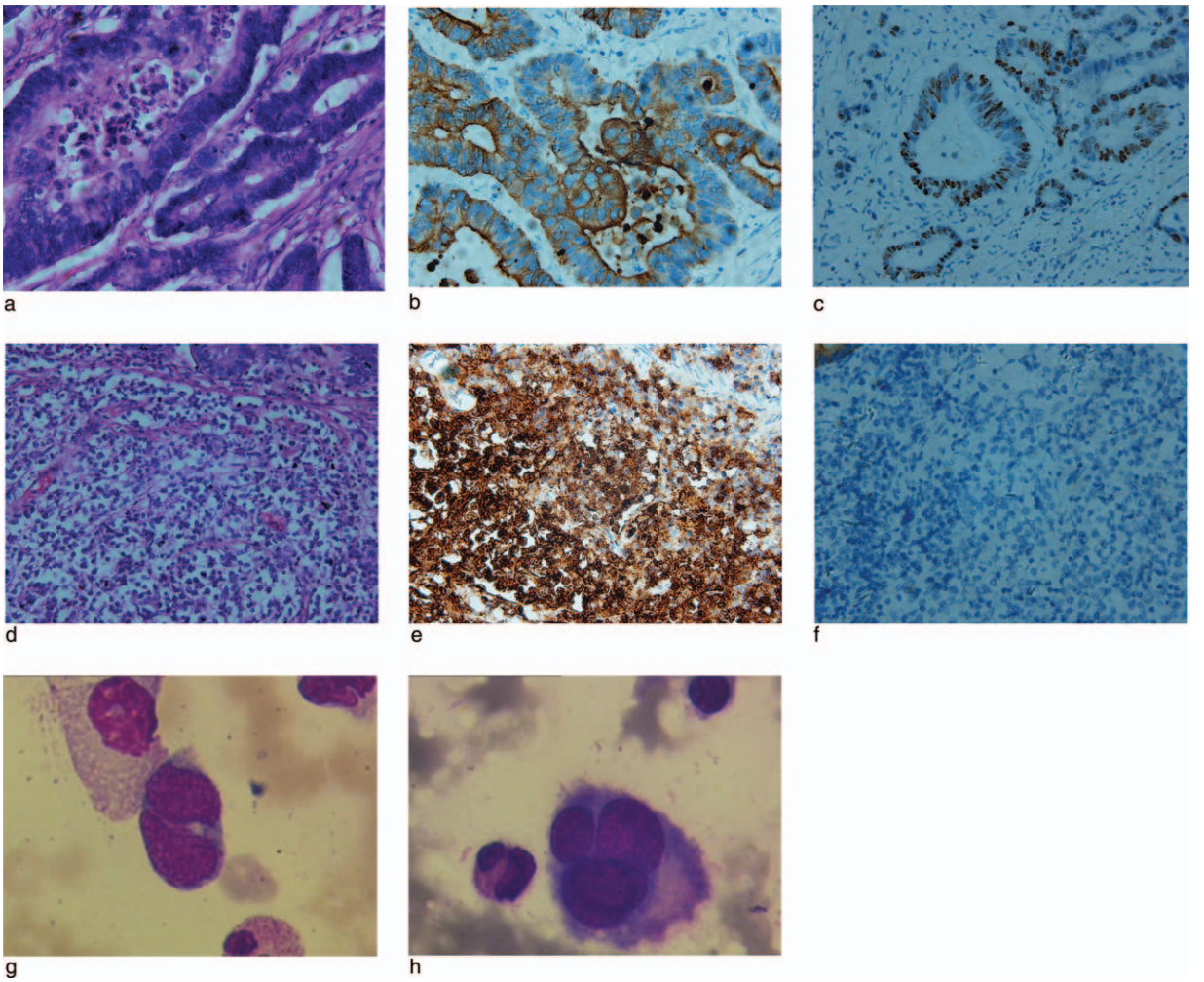

Figure 1. Coexistent malignancies in the patient. A–C, Sigmoid colon ulcerated adenocarcinoma. A, Hematoxylin and eosin (HE) staining (400×). B, Cytokeratin (CK) immunostaining (400×). C, p53 immunostaining (400×). D–F, Non-Hodgkin lymphoma in the right half colon. D, HE staining (400×). E, CD20 immunostaining (400×). F, CK immunostaining (400×). G–H, Bone marrow aspiration smears. G, Wright staining (1000×). H, Wright staining (1000×).

and effective therapeutic regimens for multi-existent cancers with few side effects need to be developed.

Author contributions

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