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Single Case

Metachronous Sigmoid Carcinoma and Mantle Cell Lymphoma in Intestines

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Keywords

Multiple primary malignant tumors · Mantle cell lymphoma · Sigmoid carcinoma

Abstract

It is rare that colon carcinoma and mantle cell lymphoma (MCL) occur one after another in intestines. We found two malignancies of sigmoid carcinoma and MCL in a single patient, who had initially been diagnosed with sigmoid carcinoma and treated with radical resection in our hospital. Good postoperative recovery was reported without recurrence signs, which lasted for 7 years and 5 months until polyps of sigmoid colon were found by colonoscopy. Biopsy and immunohistochemistry revealed MCL, but the patient refused treatment. One year later, MCL was diagnosed again in the transverse colon. The patient is currently under observation and has not received treatment for MCL.

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Introduction

Multiple primary malignant tumors (MPMTs), first proposed by Billroth in 1889, refers to 2 or more independent primary malignant tumors occurring simultaneously or successively in one or more organs of the same individual [1]. Each tumor must be malignant and have its distinct pathological morphology except for metastasis or recurrence, which are the diagnostic criteria of MPMTs put forward by Warren and Gates [2]. MPMTs can be divided into synchronous carcinoma (SC) and metachronous carcinoma (MC) depending on whether or not the tumors occur simultaneously. SC occurred within 6 months while the occurrence of MC must be spaced more than half a year apart [3]. There was a higher incidence in patients with MC than it in patients with SC [4]. The most common site of MPMTs was the same organ, followed by paired organs or the organs of the identical system [5].

One clinical work manifested that the prevalence of MPMTs was 1.09% (167 of 15,321) [6]. However, most MPMTs are double primary tumors and the occurrence rate of triple tumors and quadruple tumors is less common than double primary malignancy. Among the malignant tumors, only 0.5% were triple tumors and 0.3% were quadruple tumors [7]. The occurrence of MPMTs may be caused by some factors such as genetic predisposing factor, hyp immunity, radiotherapy and chemotherapy, environmental factors, and unhealthy lifestyles. An MPMTs patient who suffered from ovarian and breast cancer was found to have copy-neutral loss of heterozygosity of PALB2 by conducting whole-genome sequencing [8]. A combination of genetic susceptibility and environmental exposure to asbestos and ultraviolet radiation could lead to MPMTs in a family [9]. Radiotherapy and chemotherapy may be the cause of gastric adenocarcinoma after treatment of lymphoma [10].

Mantle cell lymphoma (MCL) and sigmoid colon cancer are two different malignancies. MCL is a type of B-cell non-Hodgkin lymphoma, and most MCL patients were middle-aged and old-aged males with a median age of 61 years [11]. The most common site of involvement other than lymph nodes is the gastrointestinal tract [11]. MCL has the invasive biological characteristics of medium and high malignant lymphoma, and its response to treatment is similar to that of indolent lymphoma, so it is considered as an incurable disease [12]. Researchers found patients over 60 years old or with spleen involvement who had a poor prognosis [11]. Besides, in terms of immunohistochemical results, if the overlapping degree between the reticular structure of the follicular dendritic cell and tumor cells was less than 90% or the Ki-67-positive index was greater than 40%, the patient's prognosis was also poor [11]. Colon cancer, one of the most common malignancies and sigmoid colon cancer being the most common, ranks third in the estimated cancer incidence and mortality rate in the United States in 2018 [13].

It is rare to have colon carcinoma and MCL of the colon at the same time, and to our knowledge, only a few cases have been reported [14–16]. However, there have been no reports of cases where MCL of the colon occurred years after colon cancer resection without recurrence of colon cancer. In this study, we report the case of a male patient (69 years old) who suffered from MCL of the intestines 7 years after having had a radical resection of sigmoid carcinoma, aiming to deepen our understanding of this kind of disease and preliminarily explore the relationship between MCL and sigmoid colon cancer.

Case Report

A male patient, aged 69 years and a native of the Guangdong province, had had a history of hypertension for more than 10 years and long-term oral administration of amlodipine for blood pressure control. He also had a history of chronic cholecystitis, gallstone, and hyperplasia of the prostate. His father had lung cancer and bowel cancer and his mother died of coronary heart disease. He denied a habit of smoking and drinking.

The patient underwent radical resection of a sigmoid carcinoma in our hospital on February 10, 2010. A polypoid mass and a cauliflower-like mass were found on the gross pathological examination, and infiltration into the submucosa was observed with the naked eye. Microscopic examination of the masses showed sigmoid colon tubular adenocarcinoma grade II infiltrating into the deep muscle layer (Fig. 1). Six chemotherapy treatment courses of CF+5-FU + oxaliplatin were administered after conducting surgery. During this period, the patient felt mild sensory abnormalities in the extremities, without abdominal pain, distension, nausea, vomiting, cold, fever, cough, and expectoration. Periodic reexamination showed no recurrence of the tumor.

On July 26, 2017, a syncope occurred after some activity as a result of fever and lack of food intake. The patient fell over and the occipitalia hit the ground, being unconscious for about 3 min, of which he recovered. CT examination suggested brain atrophy with no bleeding. At reexamination of the electron colonoscopy on August 1, 2017, multiple polypoid eminences of sigmoid colon were found with a high possibility of inflammatory hyperplasia (Fig. 2). Microscopic examination of the polyps showed a large number of hyperplastic lymphoid cells under the mucosa with a single shape (Fig. 3a, b). On examination of immunohistochemistry (IHC), hyperplastic lymphocytes were positive for CD5 (Fig. 3c), cyclin D1 (Fig. 3d), CD20 (Fig. 3e), CD79 α , Bcl-2, CD43, and Ki-67 (40%) (Fig. 3f), and negative for CD10 (Fig. 3g) and CD23 (Fig. 3h). In combination with morphology and IHC, the patient was diagnosed with MCL. Bone marrow cytology and bone marrow pathology showed no involvement of the lymphoma. Special stain for Fe, PAS, and Ag showed to be negative. PET/CT examination indicated no increased glucose metabolism. The blood routine tests remained normal: WBC, $7.88 \times 10^9/L$; RBC, $4.23 \times 10^{12}/L$; HGB, 137g/L; PLT, $132 \times 10^9/L$. Transverse colonic polyps were found during a repeat colonoscopy review on July 26, 2018. IHC results were similar to those of last year, and the diagnosis of MCL was rendered again.

Discussion

In this case, the pathological diagnosis confirmed that two types of malignant tumors, sigmoid carcinoma and MCL, developed at different times. The time interval was more than 6 months, which was consistent with the diagnosis of MPMTs. Although sigmoid colon cancer is common and mantle cell tumors of the intestinal tract are not rare, it is rare for the same person to have both. Six similar cases reported in the literature and our case are summarized and listed in Table 1 [14–18]. Among them, 4 cases were SC and the remaining 3 cases were MC. No cases of MCL occurring before bowel cancer were found. All cases occurred in middle-aged or old-aged males, with an average age of 73.6 years (54–83 years old) and a median age of 75 years.

The etiology and mechanism of MPMTs have not been defined yet, which may be related to genetic susceptibility, genetic factors, radiotherapy and chemotherapy, living environment, and lifestyle [19, 20]. Patients with MPMTs are more likely to carry harmful mutations than those with a single primary cancer [21]. The direct relative of the patient in this case was also an MPMTs patient with lung cancer and bowel cancer. Hence, the patient has two types of tumors that may be genetic. He had also received radiotherapy and chemotherapy before suffering from MCL, which may be the cause of MCL.

On account of the lower rates of MPMTs and the diversity of clinical features, MPMTs should be distinguished from metastatic cancer [6]. Tumor cells invade lymphatic vessels, blood vessels, or other pathways and transfer from the primary site to another site for further growth, forming the same type of tumor as the primary tumor, which is the process of metastasis. Lymphoma was misdiagnosed as metastatic gingival carcinoma because the clinical presentation of maxillofacial lymphoma is very similar to that of squamous cell carcinoma [22]. Of course, metastatic cancer can camouflage and also present different morphology from the original site of the tumor, so that it is easy to be misdiagnosed as MPMTs. It was reported that Hodgkin lymphoma involving the tonsils has been misdiagnosed as tonsil cancer [23].

Because of different pathological types of tumors and time intervals for diagnosis, MPMTs have different treatment principles. For SC, life-threatening tumors or tumors with a poor prognosis should be treated first, while for MC, one tumor can be treated at a time [24]. In this case, the patient was diagnosed with two types of tumors with a long time interval, and sigmoid carcinoma was resected without recurrence. Although the MCL of the intestinal tract he suffered from had no other systemic involvement, the tumor proliferation index Ki-67 was high. He was supposed to be hospitalized but kept waiting.

The relationship between colorectal cancer and MCL of the intestinal tract is unclear. After searching the literature, we found they either occur at the same time or MCL appears after intestinal cancer. Whether intestinal cancer is a cause of lymphoma is still unknown. Their occurrence may be accidental. MPMTs are easy to miss, leading to delayed or incorrect treatment, so early diagnosis is important. Their pathogenesis needs further study.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare no conflicts of interest.

Author Contributions

Q.Y. was responsible for the acquisition, analysis and interpretation of data for the work and drafting the paper. Q.-Y.L. participated in writing and revising the paper. D.-M.W. and

D.-Z.L. were both in charge of the design of the work, correcting the draft, final approval of the version to be published, and agreement to be accountable for all aspects of the work.

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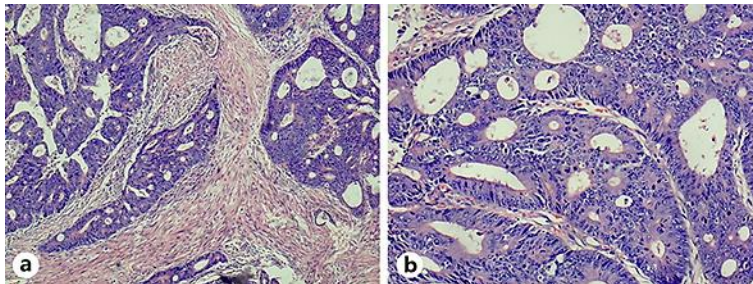


Fig. 1. Adenocarcinoma which is tubular, moderately differentiated, infiltrating into the deep muscle layer. **a** H&E, magnification $\times 40$. **b** H&E, magnification $\times 100$.

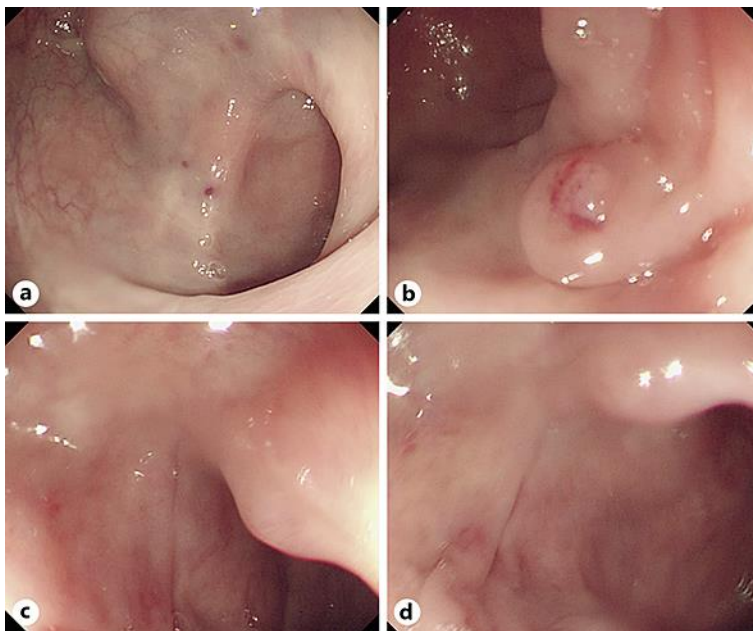


Fig. 2. Endoscopic image: anastomosis was found 20 cm away from the anus edge, and the mucosa of the anastomosis was smooth, with no erosion, ulcer or tumor (**a**). Three polypoid growths were seen 45 cm away from the anal margin (**b–d**), with a size of about 0.2 cm \times 0.2 cm to 0.4 cm \times 0.4 cm, and one polyp surface was flushed (**b**).

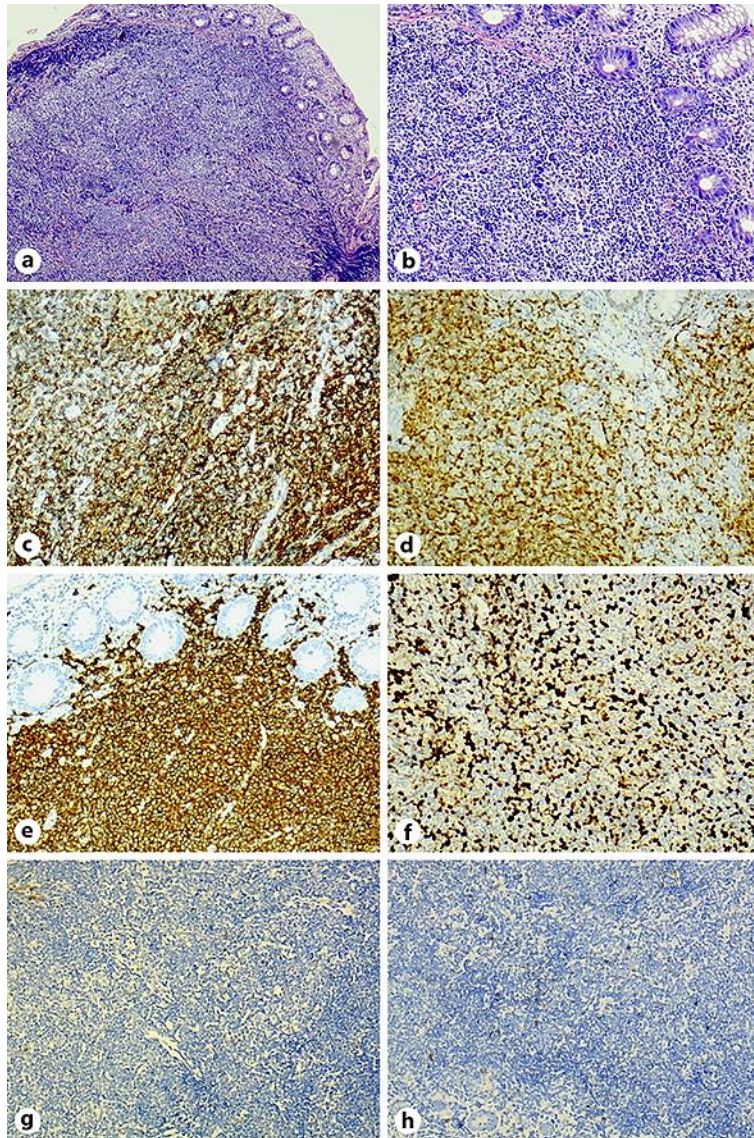


Fig. 3. A large number of lymphoid tissue hyperplasia under the mucosa of sigmoid colon, with a single morphology. **a** H&E, magnification $\times 40$. **b** H&E, magnification $\times 100$. **c** CD5, magnification $\times 100$. **d** cyclin D1, magnification $\times 100$. **e** CD20, magnification $\times 100$. **f** Ki-67, magnification $\times 100$. **g** CD10, magnification $\times 100$. **h** CD23, magnification $\times 100$.

Table 1. Simultaneous or metachronous colon carcinoma and MCL of colon reported in the literature

Author	Publication year/country	Age/Sex	Site of intestinal cancer/ MCL	TDMRC	IHC	Stage of MCL	Follow-up status
Handra-Luca [16]	2013/ France	80/ M	colorectum/colorectum	synchronous	CD20(+), CD5(+), bcl2(+), cyclin D1(+)	IV	NA
Liao et al. [18]	2009/ China	75/ M	sigmoid/duodenum	20 months after chemoradiotherapy	CD5(+), CD20(+), CD45(+), cyclin D1(+)	IV	died of profound multiple organ dysfunction syndromes in February 2005
Sztarkier et al. [17]	2009/ Israel	80/ M	sigmoid colon/bone marrow, colon and then massive	6 months later	CD20(+), cyclin D1(+), CD43(+)	NA	died 14 months after the original colectomy
Padmanabhan and Trainer [15]	2003/ USA	83/ M	cecum, colon, and terminal ileum with involvement of the regional lymph nodes/same as intestinal cancer	synchronous	CD20(+), cyclin D1(+), CD5 (+), BCL-2 (+), κ light chain (+), CD3(-), CD10(-).	NA	died of many causes after a month
Kanehira et al. [14]	2001/ USA	54/ M	hepatic flexure/ileum	synchronous	CD20(+), CD5(+), cyclin D1(+), CD10(-), CD23(-)	NA	alive and well 6 months after surgery
Kanehira et al. [14]	2001/ USA	74/ M	rectum/colon and lymph node	synchronous	CD20(+), CD5(+), cyclin D1(+), CD10(-), CD23(-)	NA	alive and well for 4 months after surgery
This study	1018/ China	69/ M	sigmoid/sigmoid, TRANSVERSE colon	7 years later	CD20(+), CD79α(+), CD5(+), Cyclin D1(+), CD43(+), Bcl-2(+), CD21(+), CD23(-), CD10(-), Ki-67 (40%)	I	alive and well for 13 months after suffering MCL

DTMRC, the diagnosis time of MCL related to intestinal cancer; M, male; NA, not available.