

Simultaneous occurrence of colonic adenocarcinoma and MALT lymphoma: A series of three cases

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Moreover, in all three cases, a coexisting MALT lymphoma was diagnosed in the colon (1 case), in both colon and adjacent lymph nodes (1 case) or in colonic lymph nodes and omentum (1 case). In the last case, a post-operative bone marrow biopsy revealed extensive infiltration of the bone marrow, due to which the patient received postoperative chemotherapy. Diagnostic and treatment issues are briefly discussed.

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Abstract

Simultaneous development of adenocarcinoma and primary B cell lymphoma of mucosa-associated lymphoid tissue (MALT) lymphoma of the colon is rare; only one case has so far been reported out of 13 cases with the coexistence of colonic adenocarcinoma with involvement of the colon by lymphoma. We hereby present three more cases, two females (aged 75 and 71 years) and a male (aged 72 years). All three underwent colectomy based on a preoperative biopsy revealing colonic carcinoma. Histological examination of the resection specimens disclosed a colonic adenocarcinoma in two cases, whereas a tubulovillous adenoma with superficial foci of intraepithelial adenocarcinoma was seen in the third

INTRODUCTION

Colonic adenocarcinoma is the third most commonly diagnosed cancer worldwide^[1]. In contrast, extranodal marginal zone B-cell lymphoma [lymphoma of the mucosa-associated lymphoid tissue (MALT) type] is rare, constituting 6%-8% of non Hodgkin lymphomas. The colon is a rare location for the aforementioned lymphoma^[2]. Only one case of simultaneous occurrence of adenocarcinoma and MALT lymphoma of the colon has so far been reported^[3] out of 13 cases with the coexistence of colonic adenocarcinoma and involvement of the colon by lymphoma^[3-13]. We hereby report three more cases.

Table 1 Details of immunostains performed

	P/M (clone)	Company	Dilution	Treatment
CD3	M mouse (LN10)	Novocastra	1:200	PT
CD5	M rabbit (SP19)	DakoCytomation	1:50	PT
CD10	M mouse (56C6)	Novocastra	1:25	PT
CD20	M mouse (L26)	Novocastra	1:50	PT
CD21	M mouse (1F8)	DakoCytomation	r. t. u.	S1700
CD23	M rabbit (SP23)	DakoCytomation	1:50	PT
CD34	M mouse (QBEnd/10)	DakoCytomation	1:50	PT
CD35	M mouse (Ber-MAC-DRC)	DakoCytomation	1:30	S1700
CD43	M mouse (MT1)	Novocastra	1:50	PT
CD61	M mouse (Y2/51)	DakoCytomation	1:40	S1700
CD138	M mouse (MI15)	DakoCytomation	r. t. u.	ER1
cyclin D1	M rabbit (SP4)	DakoCytomation	r. t. u.	PT
Glycophorin A	M mouse (JC159)	DakoCytomation	1:100	PT
MPO	P rabbit	DakoCytomation	1:2500	PT
IgA	M mouse (6E2C1)	DakoCytomation	1:70	TR
IgG	M mouse (A57H)	DakoCytomation	1:70	TR
IgM	M mouse (R1/69)	DakoCytomation	1:100	TR
κ light chains	P rabbit	DakoCytomation	1:60.000	PT
λ light chains	P rabbit	DakoCytomation	1:60.000	PT
Bcl-2	M mouse (124)	DakoCytomation	1:40	PT

MPO: Myeloperoxidase; M: Monoclonal; P: Polyclonal; r. t. u.: Ready to use; PT: Dako Target Retrieval Solution, pH 9; S1700: Dako, Envision FLEX Target Retrieval Solution, low pH; ER1: Bond Epitope Retrieval Solution 1; TR: Trilogy, Cell Marque.

CASE REPORT

Case 1

A 75-year-old female was referred due to anemia, weakness, fatigue and presence of blood in the stools (positive Mayer test). Lower gastrointestinal endoscopy revealed a polypoid mass located about 4 cm proximal to the anal verge. An abdominoperineal resection was performed which showed a 7-cm polypoid tumor. Adjacent to the aforementioned tumor, a 1.5-cm large solid, whitish area was detected. A postsurgical work-up of upper endoscopy, abdominal computed tomography and bone marrow examination was negative for lymphoma involvement. The patient received no further treatment. Although she missed scheduled follow ups, she has since been readmitted due to intermittent incomplete intestinal obstruction. She is alive, 20 mo post-operatively.

Case 2

A 71-year-old female was admitted due to a fainting episode. She mentioned a loss of 20 kg over the past year and had anemia. Colonoscopy revealed a tumor of the ascending colon; a biopsy diagnosed it as adenocarcinoma. The patient underwent a right hemicolectomy which revealed an 8.5 cm large, constricting ulcerated tumor 12 cm from the ileocaecal valve. The patient received no adjuvant therapy. She has since been regularly followed up and is alive and well 4 years post-operatively.

Case 3

Colonoscopy of a 72-year-old male with anemia showed the presence of a polyp at the ascending colon, histologically shown to be a tubulovillous adenoma with superficial foci of intraepithelial adenocarcinoma. A subsequent right hemicolectomy specimen revealed a 4.5 cm large, fungat-

ing tumor at a distance of 7.6 cm from the ileocecal valve upon incision. He had no history of fever, loss of weight or night sweats. Clinical examination showed no peripheral lymphadenopathy or hepatosplenomegaly. However, a post-operative bone marrow biopsy revealed infiltration (almost 80% of the total marrow area) by a CD20 (+), CD5 (-), CD10 (-), CD23 (-), CD43 (-), cyclin D1 (-) B cell lymphoid population, consistent with the MALT lymphoma previously diagnosed. Consequently, the patient was staged as IV A (Longano Staging system)^[14] and was treated with six cycles of FCR [Fludarabine, Cyclophosphamide and Rituximab (monoclonal anti-CD20 antibody)]. He is alive and well 18 mo post-operatively.

Histological examination of the three cases

Surgical specimens were fixed in a 10% buffered formal solution and processed according to standard protocols. 4 μm thick, deparaffinised sections were stained with Haematoxylin-Eosin^[15]. Moreover, immunostains with primary antibodies (Table 1) were performed.

Case 1: Histology showed the polypoid tumor to be a tubulovillous adenoma with superficial foci of high grade intraepithelial neoplasia (i.e., *in situ* adenocarcinoma), without invasion of muscularis mucosae or submucosa (Figure 1A). The whitish area had histological and immunohistochemical features of an extranodal marginal zone B-cell lymphoma (of MALT type) with prominent plasmacytic differentiation and cIgλ clonality (Figure 1B-F). Two out of twenty two colonic lymph nodes retrieved were involved by lymphoma. A postsurgical bone marrow biopsy revealed no involvement of the bone marrow.

Case 2: Histology showed the colonic tumor to be a moderately differentiated adenocarcinoma infiltrating the

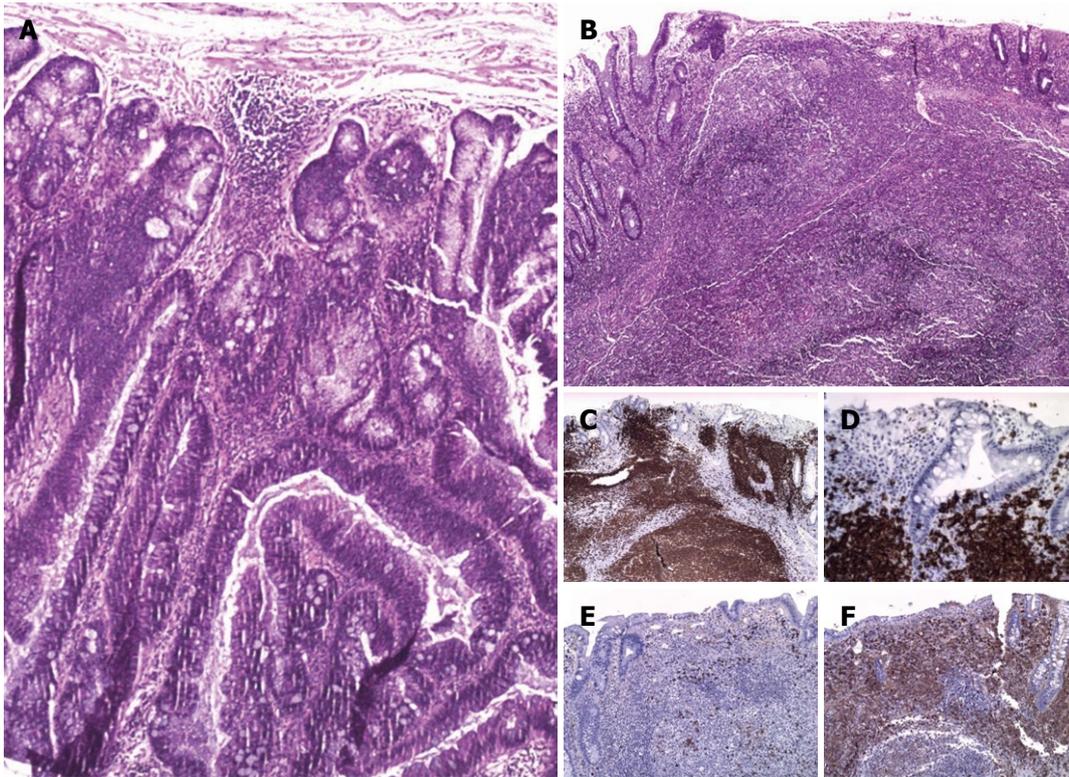


Figure 1 Histological examination of Case 1. Tubulovillous adenoma with superficial foci of high grade intraepithelial neoplasia (A: HE, $\times 4$); coexisting colonic lymphoma of MALT type [B: HE, $\times 4$; C: CD20, $\times 4$; D: CD20, $\times 20$ (lymphoepithelial lesions); E: κ light chain, $\times 4$; F: λ light chain, $\times 4$].

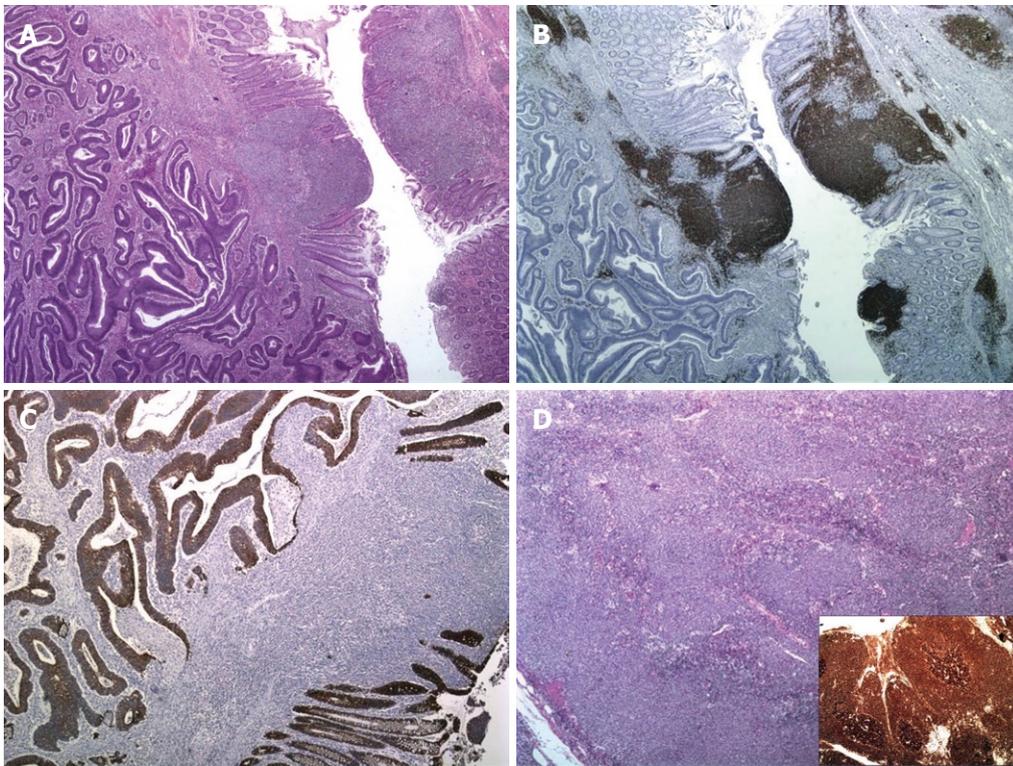


Figure 2 Histological examination of Case 2. Colonic lymphoma of MALT type adjacent to a moderately differentiated adenocarcinoma (A: HE, $\times 4$; B: CD20, $\times 4$; C: CKAE1/AE3, $\times 20$). Colonic lymph node involved by lymphoma [D: HE, $\times 4$; CD20, $\times 4$ (inset)].

colonic wall and the surrounding adipose tissue, but not extending to or beyond the serosa. Adjacent to the carci-

noma, areas of extranodal marginal zone B-cell lymphoma (of MALT type) were identified (Figure 2A-C), involving

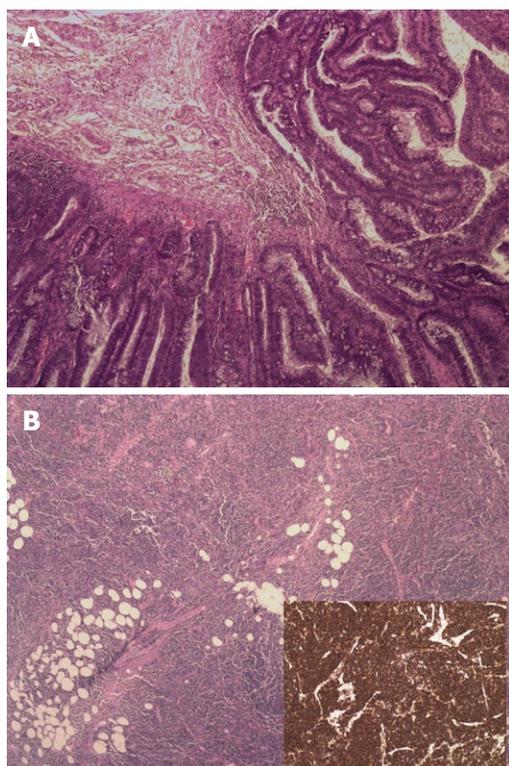


Figure 3 Histological examination of Case 3. Focus of *in situ* adenocarcinoma within a tubulovillous colonic adenoma (A: HE, $\times 4$). Omentum involved by lymphoma of MALT type [B: HE, $\times 4$; CD20, $\times 4$ (inset)].

22 out of 34 totally excised colonic lymph nodes as well (Figure 2D). No bone marrow involvement was detected.

Case 3: Histological examination revealed a tubulovillous adenoma containing superficial foci of well differentiated colonic adenocarcinoma infiltrating the submucosa (Figure 3A). No secondaries were found in the 12 colonic lymph nodes retrieved; nevertheless, both these lymph nodes and a 5-cm large fragment of omentum were involved by an extranodal marginal zone B-cell lymphoma (of MALT type) (Figure 3B).

DISCUSSION

Our cases are, to the best of our knowledge, the second ever reported concerning simultaneous occurrence of adenocarcinoma and MALT lymphoma of the colon. Out of 13 cases of coexisting adenocarcinoma and lymphoma of the colon^[3-13], only one is a MALT type lymphoma^[3]; the rest usually deal either with another type of primary colonic lymphoma, mostly mantle cell lymphoma^[5,9,11], or with involvement of the colon by an extracolonic lymphoma.

Two issues are to be noted: (1) whereas the presence of lymphocytes in the vicinity of colonic carcinomas is common, these cells are not always reactive. The presence of a dense lymphocytic infiltrate should therefore alert the pathologist to carefully assess its morphology, immunophenotype and clonality in order to rule out a

coexisting MALT lymphoma; and (2) in a case when such a lymphoma is diagnosed, it is important to closely scrutinize colonic lymph nodes for their eventual involvement.

In all three cases, MALT lymphoma was only diagnosed in the excision specimen, with no previous clinical symptoms attributable to it. The simultaneous diagnosis of a lymphoma in a colectomy specimen led to a different post-operative work-up, including a bone marrow biopsy, in order to exclude extracolonic extension of the lymphoma.

Since no etiological factor for primary colonic lymphomas has been determined until now, its coexistence with colonic adenocarcinoma might rather be attributed to the advanced age of the patient in all cases.

Treatment of colon MALT lymphoma is not standard. However, there is a general agreement that surgical treatment alone is effective for localized disease, while combined chemotherapy is the mainstay for disseminated disease^[16]. The role of inclusion of Rituximab (monoclonal anti-CD20 antibody) to the chemotherapy has not yet been commented on in this rare entity. In our case series, surgical resection was the only treatment for two patients with local disease, whereas the third patient, due to disseminated disease with bone marrow involvement, also received post-operative combined chemo-immunotherapy.

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