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Mantle cell lymphoma with multiple lymphomatous polyposis and intussusception: A case report

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Abstract. Mantle cell lymphoma (MCL) is a rare malignant lymphoma of the gastrointestinal (GI) tract that may present as multiple lymphomatous polyposis (MLP); however, MLP with intussusception is rarely reported in MCL. In the present study, a 54-year-old male patient was diagnosed with MCL, presenting with numerous polypoid lesions of the complete GI tract combined with ileocecal intussusception. Right hemicolectomy was performed in order to prevent complicated intussusception and for tumor debulking. In addition, 6 cycles of chemotherapy were performed with the rituximab plus hyper-CVAD regimen. Subsequent to the planned chemotherapy cycles, follow-up examination demonstrated a complete response and the remission lasted for 3 years until the present time.

Introduction

Mantle cell lymphoma (MCL) is a non-Hodgkin's lymphoma composed of small lymphoid cells. MCL usually occurs in males with a median age of 60 years; however, its frequency accounts for ~4% of all lymphomas in the Western countries (1). It commonly involves the gastrointestinal (GI) tract and may present as multiple lymphomatous polyposis (MLP), which frequently occurs in the colon and small bowel (2). However, numerous sessile or polypoid lesions may be identified throughout the GI tract (3).

Malignant lymphoma is an uncommon cause of intussusception, which is estimated to cause <1% of all intussusception cases (4). MLP combined with intussusception is rare in MCL patients. Only a limited number of MCL cases with intussusception have been previously reported (5-7). The current study presented a case of GI tract MCL with MLP and ileocecal intussusception that was effectively treated with surgery and chemotherapy.

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Case report

A 54-year-old male was referred to the Division of Gastroenterology and Hepatology (Korea University College of Medicine, Seoul, Korea) with abnormal computed tomography (CT) findings in the right lower abdomen (June 2012). The patient had been diagnosed with stage I bladder cancer 2 years earlier, and had undergone transurethral resection of the bladder tumor and intracavitary instillation of mitomycin. No evidence of bladder cancer recurrence was observed during the 2 years of follow-up. Upon referral to the Division of Gastroenterology and Hepatology, intussusception and a mass in the terminal ileum were identified by performing contrast-enhanced abdominal CT scans (Fig. 1). Physical examination revealed normal vital signs and a soft distended abdomen with normoactive bowel sounds. The initial laboratory findings were as follows: hemoglobin level, 14.2 g/dl (normal range: 12.0-17.0 g/dl); white blood cell count, 8,000/μl (normal range: 4,500-11,000/μl); platelet count, 171,000/μl (normal range: 150,000-400,000/μl); and C-reactive protein level, 0.6 mg/dl (normal range: 0-5.0 mg/dl). Blood biochemical analyses revealed no pathological findings, while the β_2-microglobulin and lactate dehydrogenase (LDH) levels were normal. Written informed consent was obtained from the patient.

A total colonoscopy (CF-H260AL; Olympus Optical, Tokyo, Japan) revealed ileocolic intussusception and a large mass in the distal ileum (Fig. 2A). The mass had a smooth rubber-like surface, fungating shape with multilobular contour and a diameter of ~4-8 mm. Multiple round nodules were also identified in the distal ileum (Fig. 2B) and rectum. Esophagogastroduodenoscopy (GIF-H260; Olympus Optical) revealed a polypoid tumor that measured ~30 mm in the high body of the stomach (Fig. 2C) and multiple small subepithelial nodular lesions from the bulb to the second portion of the duodenum (Fig. 2D). Multiple biopsies of the complete GI tract presented diffuse infiltration of monotonous small-to-medium sized, lymphoid cells. In addition, immunohistochemical analysis of the biopsy tissues demonstrated positive staining for CD20, CD5, Bcl-2, CD43 and

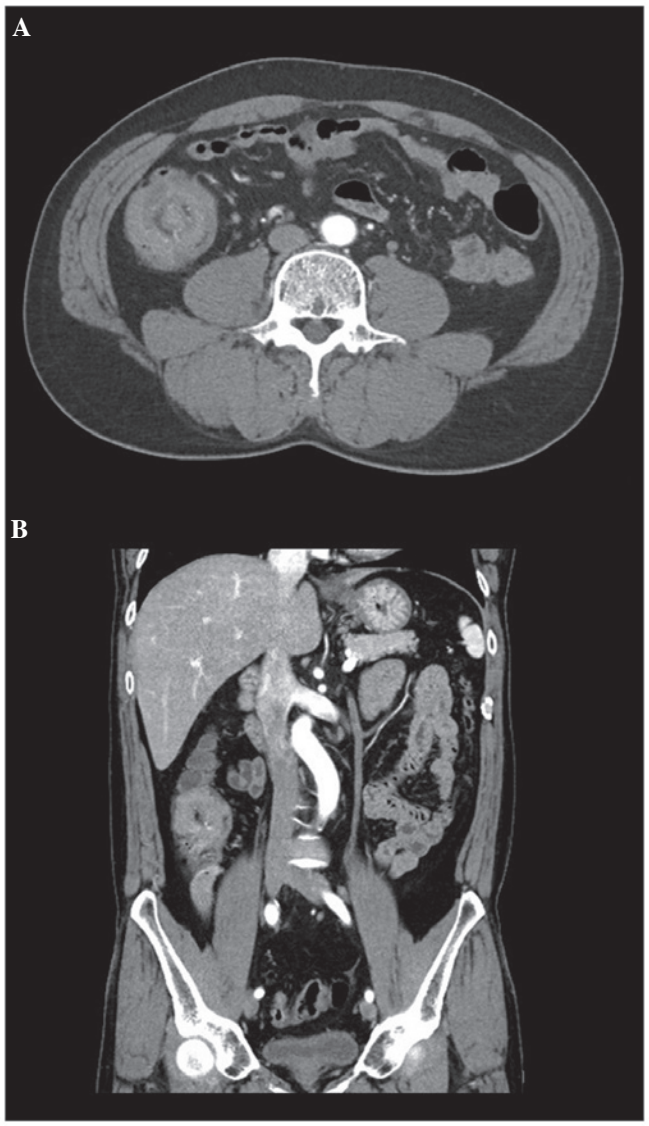

Figure 1. Contrast-enhanced abdominal computed tomography (CT) scan of the abdomen demonstrate (A) the finding of a target like an ileocolic intussusception and (B) round mass lesion with focal enhancement.

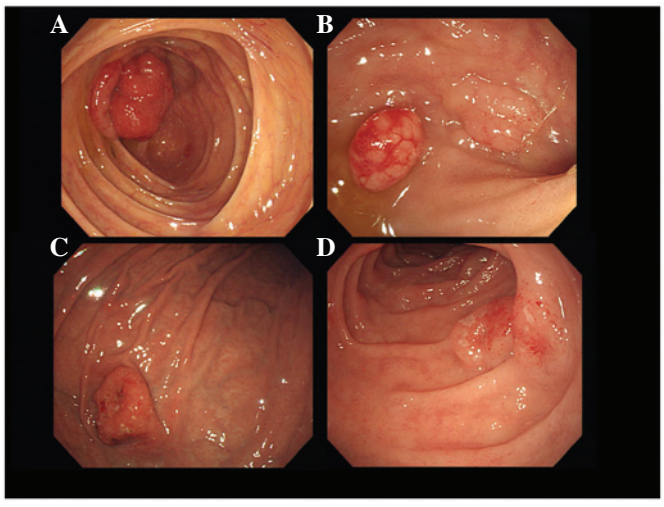

Figure 2. Endoscopic findings revealing: (A) Intussusceptum in the cecum and large mass of the terminal ileum; (B) multiple round nodular lesions in the distal ileum; (C) a large mass with multiple mucosal defects in the stomach; and (D) multiple small subepithelial nodular lesions in the duodenum.

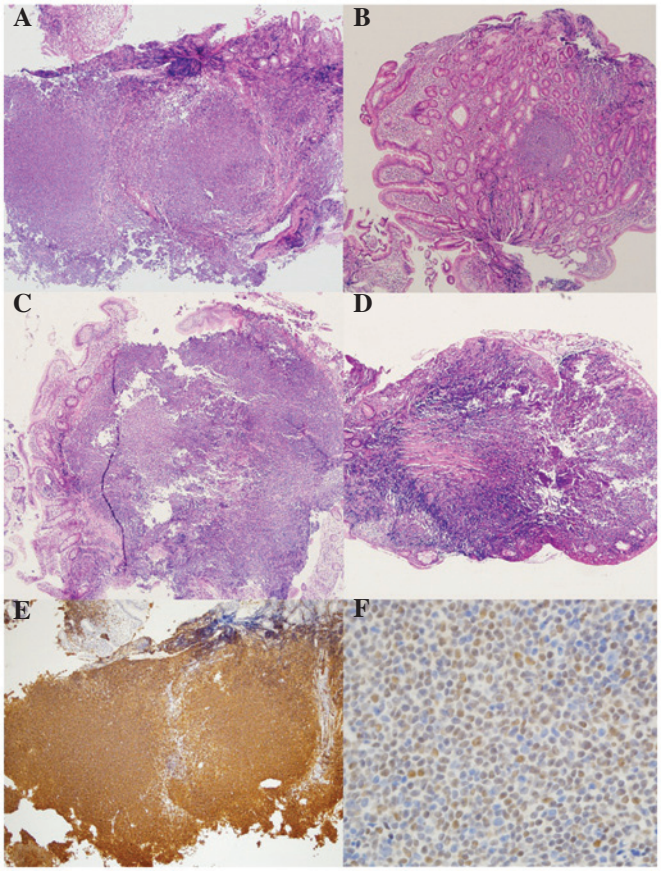

Figure 3. Histopathological and immunochemical analysis revealing diffuse lymphomatous proliferation invading the gastrointestinal tract. Immunohistochemical analysis for (A) stomach, (B) duodenum, (C) terminal ileum, and (D) rectum tissues (hematoxylin and eosin stain; magnification, x100). Also, the tissues showed positive staining for (E) CD20 (magnification, x100) and (F) cyclin D1 (magnification, x400).

Figure 4. Surgically-resected specimen. A mass that acts as a leading point is observed at the distal ileum.

cyclin D1 (Fig. 3); therefore, the diagnosis was confirmed to be MCL. A positron emission tomography (PET) scan indicated intense hyper-metabolism of all digestive structures, extending from the stomach to the rectal wall. Furthermore, a bone marrow biopsy and chromosomal study were also performed; however, no abnormal results were observed. The MCL International Prognostic Index score (8) was 8.1, and the disease was classified as stage IV according to the Ann Arbor staging system (9).

The patient underwent right hemicolectomy with distal ileum resection and ileocolic anastomosis (Fig. 4). After 20 days, chemotherapy with rituximab plus hyper-CVAD (R-hyper-CVAD) was administered, with alternating course A and B regimens for cycles during 6 months [course A: Rituximab (375 mg/m^2, intravenous, IV, day 1), cyclophosphamide (300 mg/m^2, IV, day 2-4), vincristine (1.4 mg/m^2, IV, day 5 and 12), doxorubicin (1.6 mg/m^2, IV, day 5-7) and dexamethasone; course B: Rituximab (375 mg/m^2, IV, day 1), methotrexate (1,000 mg/m^2, IV, day 2), leucovorin (15 mg every 6 h, IV, 10 times, day 3-5) and cytarabine (3 g/m^2, every 6 h, IV, day 3 and 4)]. Following 6 planned cycles of R-hyper-CVAD, upper and lower endoscopic examinations demonstrated complete remission and absence of polypoid lesions in the GI tract. The remission lasted over 18 months and a follow-up PET scan revealed no abnormal hypermetabolic lesions. There was no evidence of recurrence in abdominal CT and endoscopic examination until the present time.

Discussion

MCL is a mature B-cell non-Hodgkin's lymphoma that, according to previous epidemiological data, comprises up to 4% of all lymphoma cases (1). Although various studies have demonstrated improvement of the median survival using aggressive chemotherapeutic strategies, the prognosis of MCL remains unfavorable (10-13). MCL generally occurs in adults with a median age of 60 years and has a male predominance (14). Overexpression of cyclin D1 is a typical characteristic of MCL.

MLP was initially defined by Cornes in 1961 (15). It involves numerous polypoid lesions throughout the GI tract, caused by malignant lymphoma. Diffuse and nodular polypoid lesions are a characteristic feature at presentation; therefore, involvement of the GI tract must be investigated by endoscopic examination in lymphoma patients. Common clinical symptoms include abdominal pain, diarrhea and weight loss, while protein-losing enteropathy, chylous ascites, intestinal malabsorption and perforation are less frequently observed (16). In rare cases, MCL with MLP results in intestinal obstruction or intussusception. Several previous studies have analyzed the clinical features and outcome of MLP (16); however, no standardized therapeutic options exist for GI cases of MCP with MLP.

Only a limited number of MCL cases presenting with intussusception have been reported (5-7). In the majority of cases, patients were treated with the R-CHOP chemotherapy regimen (cyclophosphamide, doxorubicin, vincristine and prednisone, in combination with rituximab) and surgical resection. However, it has been suggested that the R-Hyper-CVAD regimen (cyclophosphamide, vincristine, doxorubicin, dexamethasone, cytarabine and methotrexate, in combination with rituximab) is associated with improved response rates in MCL (17). The main concern in the present case was the risk of remission failure or severe complications, such as intestinal obstruction due to unresolved intussusception. Therefore, prior to chemotherapy, the patient underwent right hemicolectomy for tumor debulking and prevention of complications. Subsequently, R-hyper-CVAD chemotherapy was administered.

In asymptomatic patients, it remains unclear whether surgery prior chemotherapy is required and whether 6 cycles of chemotherapy are appropriate to treat MCL with intussusception. However, the therapeutic strategy in the present study demonstrated marked results and good response. Progress in the current patient suggested that complete remission may be achieved in MCL with MLP following the administration of R-hyper-CVAD. In conclusion, operative bowel resection may be a feasible option in MCL, when MLP is associated with asymptomatic intussusception.

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