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Diffuse gastrointestinal involvement of mantle cell lymphoma

Mantle hücreli lenfomanın diffüz gastrointestinal tutulumu

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The gastrointestinal tract is the predominant site of appearance of extranodal non-Hodgkin lymphomas. The most frequent endoscopic finding of mantle cell lymphoma is multiple lymphomatous polyposis, which is a very rare entity. Multiple lymphomatous polyposis is characterized by multiple polypoid lesions involving long segments of the gastrointestinal tract and it accounts for 2% of primary gastrointestinal tract lymphomas. A 68-year-old patient was admitted to our clinic with intermittent diarrhea, weight loss, hematochezia and fatigue. Multiple lymphomatous polyposis was detected on the endoscopic evaluations. Gastrointestinal mantle cell lymphoma was confirmed with histopathological and immunohistochemical studies on biopsy specimens from colon, small intestine and stomach. The patient was successfully treated by combination chemotherapy.

Key words: Mantle cell lymphoma, multiple lymphomatous polyposis, gastrointestinal involvement

Gastrointestinal sistem ekstranodal non Hodgkin lenfomaların en sık görüldüğü yerdir. Mantle hücreli lenfomanın en sık endoskopik bulgusu multipl lenfomatöz polipozistir. Multipl lenfomatöz polipozis oldukça nadir bir durumdur. Multipl lenfomatöz polipozis gastrointestinal sistem segmentlerini tutan multipl polipoid lezyonlarla karakterizedir ve primer gastrointestinal lenfomaların %2'sini oluşturmaktadır. 68 yaşındaki hasta aralıklı diare, hematokezya ve güçsüzlükle kliniğimize başvurdu. Endoskopik değerlendirmede multipl lenfomatöz polipozis görüldü. Kolon, ince barsak ve mide biyopsi örneklerinin histopatolojik ve immunohistokimyasal değerlendirmesinde mantle hücreli lenfoma tanısı doğrulandı. Hasta kombinasyon tedavisi ile başarılı şekilde tedavi edildi.

Anahtar kelimeler: Mantle hücreli lenfoma, multipl lenfomatöz polipozis, gastrointestinal tutulum

INTRODUCTION

The gut mucosa contains more lymphocytes than the other immune system organs. However, paradoxically, only 10% of lymphomas occur in the gut. The stomach and small intestine are vulnerable organs to primary gastrointestinal (GI) lymphoma, while esophageal and colorectal lymphomas are very rare (1). Mantle cell lymphoma (MCL) comprises 2.5%-7% of all non-Hodgkin lymphomas (NHL), and the GI tract is involved in about 20% of cases (2). Morphological, immunohistochemical, and molecular studies are essential for diagnosis of MCL. Tumor cells typically express CD5 and cyclin D1 markers. Multiple lymphomatous polyposis (MLP) is an uncommon disease that is regarded as the intestinal form of MCL (1). Most MLP cases occur in elderly patients, usually over 50 years, and presenting symptoms are abdominal pain, melena, hematochezia, and fatigue. Any part of the GI tract may be involved, but diffuse GI involvement of MCL is a rare condition. We describe and discuss the clinicopathologic features of a MLP case that affected the stomach, small intestine and colon.

CASE REPORT

A 68-year-old man admitted to our clinic with intermittent bloody diarrhea, epigastric pain, hematochezia, fatigue, weakness and weight loss (6 kg/4 months). He had no important personal pathologic history. The symptoms of disease started five months prior to admission with marked fatigue. On admission, the general condition of the patient was poor. His pulse rate was 78 beats/min and blo-

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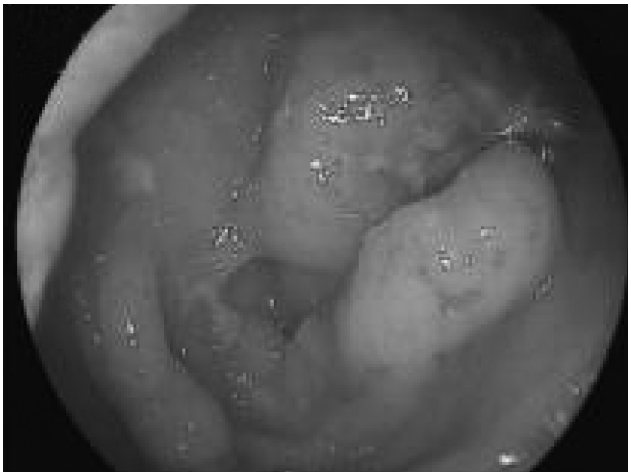

Figure 1. Colonoscopic view showing multiple polyps.

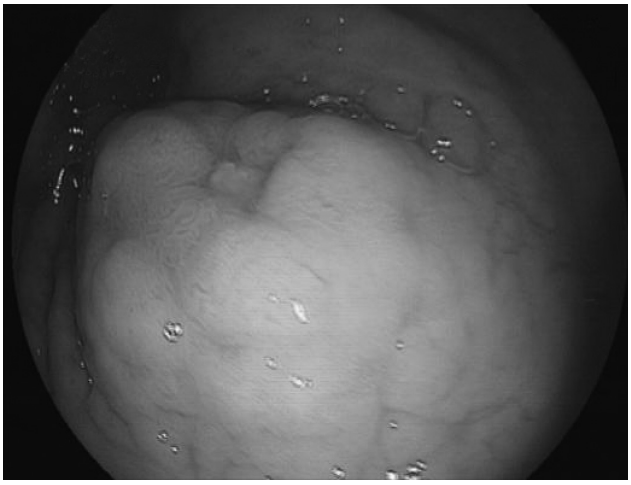

Figure 2a. Endoscopic view of gastric mucosa and polyp with ulcer on its surface.

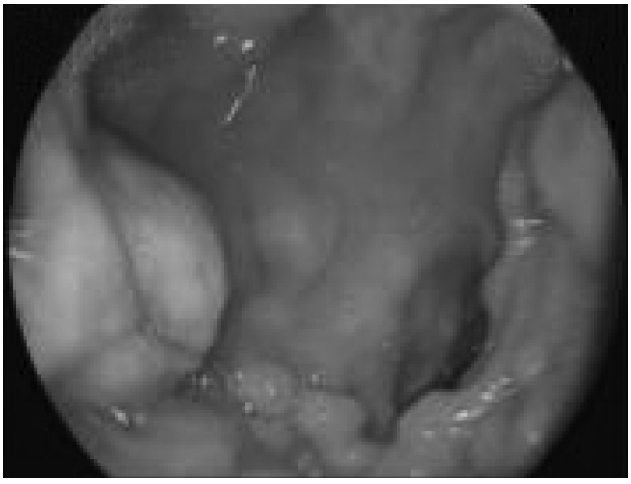

Figure 2b. Endoscopic view of duodenum showing multiple polyps.

od pressure 110/90 mmHg. Cervical and inguinal lymph nodes were palpable. The abdomen was distended with no tenderness. Hepatomegaly and splenomegaly were present, palpable 4 cm and 2 cm below the costal margins, respectively. Laboratory studies included the following: hemoglobin 7.8 g/dl (normal 12-16), white blood cell count 4200/mm^3 (4000-10200), C-reactive protein 53 (0-5), erythrocyte sedimentation rate 64 mm/L hour (0-20), blood urea nitrogen 57 mg/dl (5-20), creatinine 3.6 mg/dl (0.8-1.4), and LDH 421 IU/L (240-480). On the microbiologic and parasitologic examination of the stool, no pathology was determined. Colonoscopy revealed diffuse colonic polyposis (Figure 1). Similar lesions were seen at the terminal ileum and ileocecal valve. Multiple gastric (Figure 2a) and duodenal (Figure 2b) polyposis were detected on upper GI endoscopy. Endoscopic biopsy specimens were taken from the polypoid lesions of the stomach, duodenum and colon. Endoscopic biopsy samples showed small- and medium-sized diffuse lymphocytic infiltration in lamina propria (Figure 3). Since these lesions suggested polypoid lymphoma, immunohistochemical testing was required for diagnosis. Immunophenotypic examination showed light chain restriction, indicating monoclonal B cell proliferation, and the lymphoid cells stained positive for CD20, CD5 (Figure 4) and cyclin D1 (Figure 5), but negative for CD10. Computed tomography of abdomen and mediastinum showed lymphadenopathy, hepatosplenomegaly, and polyps in the stomach, which increased thickness of stomach and colon. Barium contrast radiography demonstrated diffuse involvement of the small intestine with polypoid masses. Bone marrow biopsy was normal. According to these findings, we diagnosed the case as MCL. For treatment, the patient received systemic combination chemotherapy consisting of cyclophosphamide, doxorubicin, vincristine and prednisolone. During the follow-up, polyp size and number were significantly diminished in the colon (Figure 6) and duodenum (Figure 7) on the endoscopic evaluation.

DISCUSSION

Primary GI lymphomas are rare conditions. They are most common in the stomach, followed by small intestine and colon. Approximately 15%-30% of primary extranodal lymphomas occur in the GI tract, although primary GI tract lymphomas account for only 1% to 10% of all GI malig-

nancies (3). NHL of the GI tract, which is the most common extranodal site, accounts for 4%-20% of all NHLs (4). The great majority of GI tract lymphomas present with a generally solitary lesion, but not with multifocal involvement of the GI tract (5).

MCL is a distinct clinicopathologic entity of NHL, characterized by a monotonous proliferation of small- to medium-sized lymphocytes with coexpression of CD5 and CD20, and an aggressive and incurable clinical course. MCL comprises 2.5%-7% of all NHL, and the GI tract is involved in about 20% of cases (2). The most frequent endoscopic finding of MCL is MLP. MLP is characterized by multiple polypoid lesions involving long segments of the GI tract and accounts for 2% of primary GI tract lymphomas (6).

MLP is an extremely rare disease. Males are more frequently affected than females and the disease usually appears during the fifth and sixth decades of life. Abdominal pain, diarrhea, hematochezia, and palpable mass are the most common presenting manifestations. Our patient presented predominantly with weight loss, hematochezia and diarrhea. In the series of Ruskone-Fourmestraux et al. (7), the colon and rectum were affected in about 90% of cases, followed by the small bowel, stomach, and duodenum, respectively, in 69%, 57% and 52%. However, our patient's presentation is rare in the literature because of the involvement of the whole GI tract (8).

The prognosis of GI MCL is poor, with a mean survival time of less than three years. Response to chemotherapy is seen in up to half of the patients (9). COP (cyclophosphamide, doxorubicin, prednisolone), anthracycline-containing regimens, and CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) are used as conventional chemotherapies for MCL. Infiltrating lymphoma cells expressed CD20 molecules on their surfaces. Another treatment for MCL is rituximab (a chimeric monoclonal antibody). This chimeric antibody binds specifically to the CD20 antigen. Single-agent rituximab has produced response rates of about 30%, and when combined with an anthracycline-containing regimen, response rates increase to above 90% (10). Because this lymphoma occurs in the elderly population, stem cell transplantation is not feasible.

In conclusion, GI lymphomatous polyposis is a rare disease. Abdominal pain, diarrhea, hematoche-

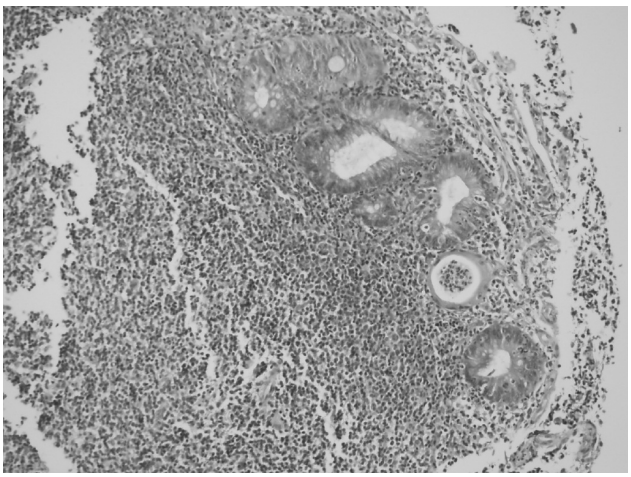

Figure 3. Histopathologic view of MCL (hematoxylin and eosin).

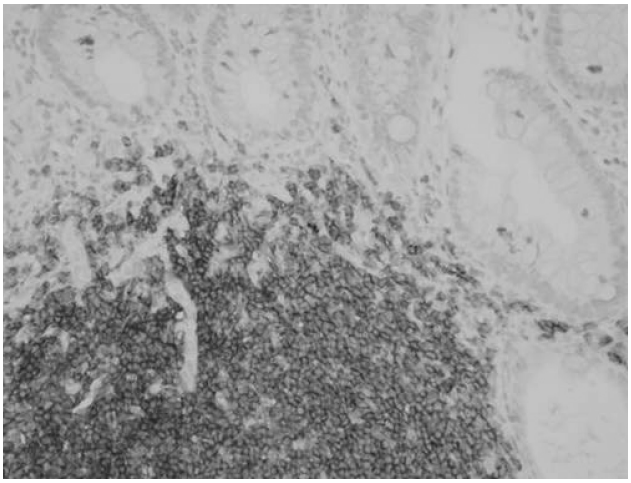

Figure 4. Lymphoid cells immunostained positive for CD20.

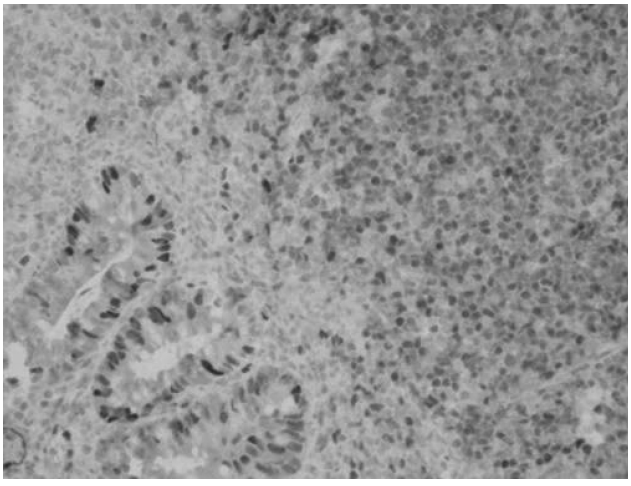

Figure 5. Lymphoid cells stained positive for cyclin D1.

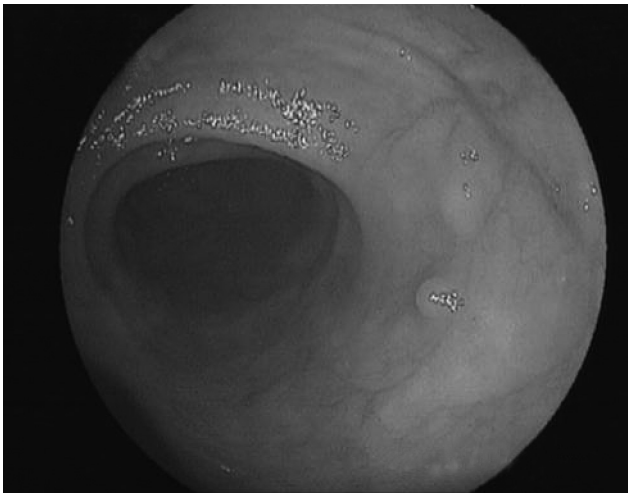

Figure 6. Endoscopic view of colon after chemotherapy.

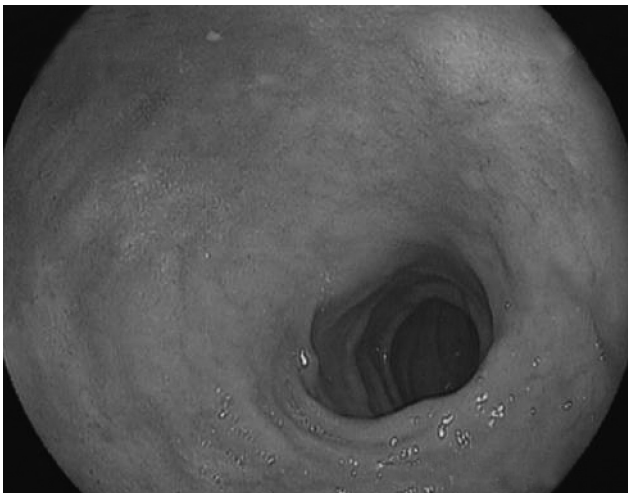

Figure 7. Endoscopic view of duodenal mucosa after chemotherapy.

zia, weight loss and organomegaly are the most common presenting manifestations. For this reason, GI involvement of lymphomas is very important, and all patients with diagnosis of lymphoma complaining of GI symptoms must be carefully evaluated.

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