Solitary Primary Gastric Mantle Cell Lymphoma

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Mantle cell lymphoma (MCL) is a relatively rare subgroup of non-Hodgkin’s lymphoma that is characterized by an aggressive and severe disease course with frequent involvement of regional lymph nodes and/or early metastasis. Because most cases of MCL are diagnosed in the advanced stages, clinical data on extranodal or early stage MCL is lacking, and MCL that is both extranodal and diagnosed during the early stages is even more rare. There have been several case reports on primary gastric MCL, which comprise a type of extranodal MCLs. However, to our knowledge, there have been no reports on solitary primary gastric MCL without regional lymph node involvement or distant metastasis. Recently, the authors experienced an uncommon case of MCL with the aforementioned characteristics that was managed with chemotherapy followed by allogeneic stem cell transplantation.

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Key Words: Mantle cell lymphoma; Stomach; Primary; Solitary, Cyclin D1 positive

INTRODUCTION

Mantle cell lymphoma (MCL) is a unique subgroup of non-Hodgkin’s lymphoma, which accounts for approximately 6% of non-Hodgkin’s lymphoma. MCL is characterized by t(11;14) (q13;q32) and cyclin D1 overexpression in a vast majority of cases. It is also characterized by aggressive disease course with many cases being diagnosed in the advanced stages, and frequent involvement of regional lymph nodes and/or early metastasis. In addition to the regional lymph nodes, extranodal sites such as gastrointestinal tract are frequently involved. According to previous studies, the frequency of extranodal involvement was reported up to 80%, and 15% to 30% of MCL had gastrointestinal tract involvement. However, solitary and primary involvement of extranodal sites is rare, and solitary primary extranodal MCL diagnosed in the early stage is even rarer. To the best of our knowledge, a few cases on primary gastric MCL were reported, but there had been no documented reports dealing with solitary primary gastric MCL without regional lymph node involvement or distant metastasis.

Herein, we report the first case of primary gastric MCL which was found as solitary lesion in the stomach without any regional lymph nodes involvement or distant metastasis.

CASE REPORT

A 48-year-old man presented to the department of gastroenterology with epigastric soreness of 8 months’ duration. On arrival, his vital signs were stable: blood pressure was 110/70 mm Hg, pulse rate was 70 beats/min, and body temperature was 36.8°C. On physical examination, no mass could be palpated, no organ enlargement such as hepatosplenomegaly or lymph node enlargement was noted, and neither tenderness nor rebound tenderness was present. Initial laboratory findings were as follows: hemoglobin, 13.0 g/dL; white blood cell count, 5,750/μL (45.6%: neutrophils); platelet count, 215,000/μL; blood urea nitrogen, 13 mg/dL; creatinine, 1.1 mg/dL; total protein, 6.4 g/dL; albumin, 3.4 g/dL; total bilirubin, 0.62 mg/dL; alkaline phosphatase, 70 IU/L; alanine aminotransferase, 24 IU/L; aspartate aminotransferase, 23 IU/L; gamma glutamyl transferase, 13 IU/L; lactate dehydrogenase, 388 IU/L; prothrombin time, 13.1 sec (INR, 0.98); amylase, 83 IU/L; ESR, 17 mm/hr; CRP, 2.570 mg/L; alpha-fetoprotein, 7.1 ng/mL. Hepatitis B surface antigen (HBsAg) was positive, and hepatitis B envelope antigen/antibody...
(HBeAg/Ab) was positive/negative. Antibody against hepatitis B surface antigen (anti-HBs Ab) and antibody against hepatitis C (anti-HCV Ab) were all negative. Initial gastrofiberscopic examination showed two masses: a 3×3×1.5 cm sized smaller crater-like ulcerating mass with central ulceration (1×1 cm) on the high-body anterior wall and a 6.5×4.5×2.5 cm sized larger swimming goggle shaped ulcerofungating mass with central ulceration (2.5×2 cm) on the low-body along the greater curvature (Fig. 1).

The biopsy specimen obtained from the low-body showed

Fig. 1. Initial gastrofiberscopy shows a goggle-shaped ulcerofungating mass on the low body along the greater curvature (A) and a crater-like ulcerative mass with bleeding on the high-body anterior wall (B).

Fig. 2. Gastric mucosal biopsy from the low body shows diffuse infiltration of medium-sized lymphoid cells with a dispersed chromatin pattern (A, H&E stain, ×40; B, ×400).

Fig. 3. Immunohistochemistry with the same specimen from Fig. 2 shows that these cells were diffusely and strongly positive for CD20 (A, ×40) and cyclin D1 (B, ×400).
diffuse infiltration of relatively monotonous, medium-sized lymphoid cells with dispersed chromatin pattern (Fig. 2). These cells were diffusely and strongly positive for CD20 (Fig. 3A), CD5, CD43, and cyclin D1 (Fig. 3B), but negative for CD3, CD21, CD10, and TdT. Some bcl-6-positive cells were also seen. Most cells were positive for Ki-67 (Fig. 4A). Therefore, it could be diagnosed as mantle cell lymphoma, blastoid variant. The biopsy specimen obtained from the high-body showed focal lymphoid infiltration in lamina propria (Fig. 4B). These infiltrates were mixture of CD20-positive B cells and CD3-positive T cells. However, immunostain for cyclin D1 was negative and Ki-67 labeling was low. Because the mucosa was intact and the lymphoid infiltrates were localized, the biopsy might be obtained from the periphery of the ulcerating lesion, representing chronic follicular gastritis. Therefore, the possibility of concomitant MCL could not be completely ruled out, which might have been due to inadequate amount of biopsy specimen.

On endoscopic ultrasonography, the larger swimming goggle shaped ulcerofungating mass on the low-body seemed to have advanced to the muscularis propria without involvement of the serosa (Fig. 5). Abdominal computed tomography (CT) scan showed 6.5×2.5 cm sized lobulated enhancing mass with ulceration in the center, which was located on the low-body. However, neither definite metastatic lesion nor regional lymph node involvement was seen. Colonoscopy, chest CT, bone scan, PET-CT scan, and bone marrow biopsy were performed for further staging work-up but no regional lymph node involvement or distant metastasis was found. Conventional cytogenetic analysis was also performed with the specimen obtained from the bone marrow biopsy; the karyotype was 46,XY and no abnormal clone was detected.

Therefore, the patient was diagnosed as stage 1E MCL, and was treated with hyperCVAD/MA (cyclophosphamide 300 mg/m², vincristine 2 mg, doxorubicin 50 mg/m², dexamethasone 40 mg; alternated with methotrexate 1 g/m² and cytarabine 1 g/m² every 4 weeks or earlier). Follow-up gastrofiberscopy performed 26 days after third cycle showed that the mass on the high-body had been completely resolved leaving behind only a scar, and the lesion on the low-body had markedly decreased in size (Fig. 6A).

Because of prolonged febrile neutropenia after third cycle, the dose was reduced by 25% on fourth cycle. The patient was scheduled to undergo stem cell transplantation after the completion of fifth cycle, but since not enough stem cell could be collected for autologous stem cell transplantation, the patient underwent allogeneic stem cell transplantation instead 69 days after fifth cycle. Follow-up gastrofiberscopy performed 40 days after allogeneic stem cell transplantation showed that the mass on the low-body had completely resolved (Fig. 6B). He has completely recovered afterwards and is currently being followed-
up at the outpatient department without any complaints and further complications.

**DISCUSSION**

MCL is a relatively uncommon and aggressive disorder, being incurable in many cases, with median survival of three to four years in affected patients. Current World Health Organization guideline suggests that morphological examination and immunophenotyping, with demonstration of cyclin D1 protein overexpression and/or t(11;14)(q13;q32), are needed for confirmative diagnosis of MCL. Morphologically, MCL is generally classified into several subgroups: classic, small cell, blastoid, marginal zone-like, and pleomorphic with some interplay between them. Among these subgroups, the blastoid subgroup has the worst prognosis and it is composed of variable cell population in size and shape, with frequent mitotic figures, oval to irregular nuclear contours, pale cytoplasm, and prominent nucleoli. Immunophenotypically, MCL resembles that of a mature B-lymphocyte (CD10−, CD19+, CD20+, CD22+, CD43+, CD79a+) with coexpression of the T-cell antigen CD5; in contrast to CLL, cells are usually CD23 negative. In addition, cyclin D1 is almost always overexpressed, making it the most important and useful finding for diagnosing MCL. Furthermore, t(11;14)(q13;32) is also seen in most of the MCL patients, although some cases of t(11;14)(q13;32) negative MCL have been reported. However, chromosomal study with the lymphoma mass was not performed in this patient.

In general, early stage MCL is rare since MCL is diagnosed in the advanced stages commonly accompanied by regional lymph node involvement, hepatosplenomegaly, bone-marrow involvement, and leukemic spread. Primary focus of MCL being other than the lymph nodes, i.e., extranodal, is also rare. There have been some case reports on primary gastric MCL, but systemic involvement or regional lymph node involvement was always present. There was one case report on solitary primary gastric MCL, but gastric MCL was accompanied by synchronous early gastric cancer in this case. Primary extranodal MCL without regional involvement and/or distant metastasis is even rarer, which has been reported by Estrozi et al.; it was primary cutaneous blastoid subgroup of MCL in right temporal region without regional lymph node involvement and distant metastasis (stage 1E). As far as we know there have been no reports on isolated primary gastric MCL in which solitary mass in the stomach was the only tumor focus without regional lymph node involvement and/or distant metastasis.

Unfortunately there is no established standard treatment guideline in patients with MCL. However, the consensus for the treatment of MCL is either with myeloablative regimens followed by autologous stem cell transplantation after initial CHOP- (cyclophosphamide, vincristine, doxorubicin, and prednisone) or DHAP- (dexamethasone, high-dose Ara-C, and cisplatin) like induction therapy, or with upfront dose intensification (HyperCVAD/MA plus rituximab, a monoclonal antibody against the protein CD20). But, since MCL has very aggressive disease course and is often diagnosed in the advanced stages, the treatment is often unsuccessful. Despite of the initial response to chemotherapy, the disease may relapse in many patients. Therefore, in order to improve the treatment outcomes, various intensive chemotherapy combinations, radiotherapy, stem cell transplantation, and molecular targeted approaches have been tried. Among aforementioned three cases of primary gastric MCL, one case reported a 60-year-old man with systemic lymph node involvement who was treated with HyperCVAD/MA plus rituximab followed by stem cell transplantation. He had no recurrence for 50 months thereafter. Another case reported a 65-year-old man with synchronous colonic MCL who was treated with COP (cyclophosphamide, vincristine, prednisone). He also had a complete resolution after six cycles. In the last case report, a 74-year-old man with regional lymph node involvement suffering from long-standing crohn’s disease was treated with rituximab-CHOP. The patient had maintained complete remission state for 18 months after completion of 2 cycles. In our case, the patient was very responsive to HyperCVAD/MA, showing dramatic size reduction of the gastric MCL on follow-up gastrofiberscopy resulting in complete remission. But unfortunately, he could not undergo autologous stem cell transplantation because not enough stem cells could be collected.

![Fig. 6.](image) After the third cycle of chemotherapy, the huge ulcerofungating mass on the low-body along the greater curvature is markedly reduced in size (A). After allogenic stem cell transplantation, the lesion has completely resolved, leaving behind only a scar (B).
for autologous stem cell transplantation. This might have been due to bone marrow suppression after intensive chemotherapy. Due to the fact that no established standard treatment guideline exist, not to mention that for each stages of MCL, many doctors follow similar treatment protocol regardless of the stage at diagnosis and thus managing toxicity is another problem MCL patents have to face.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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