Case Report

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Early Gastric MALT Lymphoma

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The endoscopic findings of mucosa-associated lymphoid tissue (MALT) lymphoma were classified into exophytic and infiltrative types by Palmer and Seifert. Normal-appearing gastric MALT lymphoma is quite uncommon, and only one case had been reported in the literature. Here we report the case of a 49-year-old woman who underwent esophagogastroduodenoscopy for health screening. Endoscopy revealed indistinct follicular gastritis mucosal change and a duodenal ulcer scar, and random biopsy was taken from her stomach to check for the presence of *Helicobacter pylori* (*H. pylori*). Biopsy revealed chronic gastritis with *H. pylori*, and atypical lymphoid infiltration highly suggestive of MALT lymphoma. Polymerase chain reaction study using primers specific for immunoglobulin heavy chain gene showed a clonal B cell lymphoproliferation consistent with MALT lymphoma. Treatment with amoxicillin, clarithromycin, and omeprazole for *H. pylori* rendered complete resolution of the disease. In conclusion, follicular gastritis may be a high-risk condition that gives rise to MALT lymphoma, and further investigation is indicated.

After Isaacson and Wright first introduced a distinct group of extranodal malignant lymphoma arising from mucosa-associated lymphoid tissue (MALT), literature is replete with this low-grade B-cell lymphoma of MALT type.[1] The association of *Helicobacter pylori (H. pylori)* infection and formation of MALT lymphoma in the stomach has also been observed.[2-5] The endoscopic findings of MALT lymphoma were classified into exophytic and infiltrative types by Palmer and Seifert.[6,7] Cammarota *et al*. reported a normal-appearing gastric MALT lymphoma, in which the diagnosis was made by chance.[8] Here we report a case of MALT lymphoma presented with follicular gastritis on endosopic examination. The polymerase chain reaction (PCR) using primers specific for amplifying the third complementary determining region of immunoglobulin heavy chain gene eventually showed a clonal B cell lymphoproliferation consistent with MALT lymphoma.

CASE REPORT

A 49-year-old woman had a health screening done in our hospital in August 2000. As a component of our screening, esophagogastroduodenoscopy (EGD) revealed fine granular gastric mucosal change (Fig. 1) and a duodenal ulcer scar. Random biopsy was taken from several sites of the stomach mucosa to check for the presence of *H. pylori*. Pathology revealed chronic gastritis with frequent *H. pylori*, and atypical lymphoid infiltra-

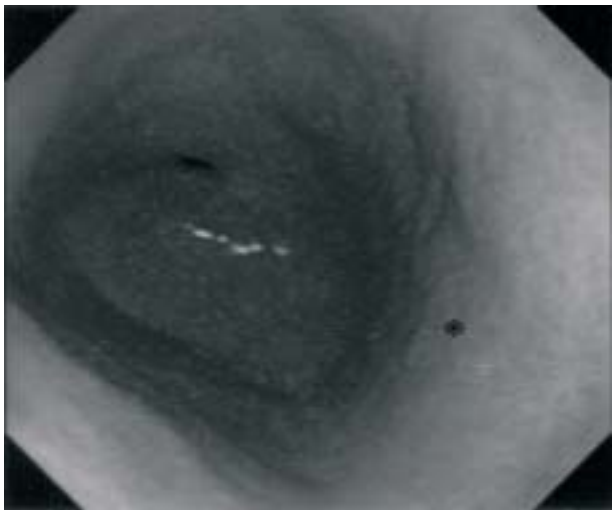

Fig. 1. Endoscopic view of gastric antrum and lower body showing indistinct mucosal change (asterisk).

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tion highly suggestive of MALT lymphoma (Fig. 2).

The confirmation test for MALT lymphoma was performed by PCR study described as follows. DNA was extracted from a 50 μ-sliced paraffin embedded tissue using PUREGENE DNA isolation kit (Genetra Inc., Minneapolis, MN USA). DNA quality and quantity were determined by GeneQuant II (Pharmacia Biotech, Piscatway, NJ USA). Each PCR reaction proceeded in 25 μL reaction mixture containing 1 unit Tag Polymerase (Promega, Madison, WI USA) and performed as previously described.[9] PCR reactions were performed using a PE 9600 thermocycler (PE Applied Biosystem, Foster City, CA USA.). A first round consisting of 30 cycles of denaturation (94 °C for 15 seconds), annealing (58 °C for 15 seconds) and extension (72 °C for 20 seconds) was used with the FR3A (5′ ACA CGG C(C/T) (G/C) TGT ATT ACT GT 3′) for the 3′ end of the variable segment (framework 3) and JH (5′ TGA GGA GAC GGT GAC C 3′) primers for the joining segment. Seminesting was performed by using 0.5 μL initial amplification product as the template in a second reaction consisting of 30 cycles of denaturation (94 °C for 15 seconds), annealing (58 °C for 15 seconds) and extension (72 °C for 20 seconds) using an internal VLJH primer (5′ GTG ACC AGG GT (G/T/A/C) CCT TGG CCC CAG 3′) for the J segment and the FR3A primer. PCR products were followed to electrophoresis at 130V for 40 minutes using ethidium bromide-stained 12% polyacrylamide gels (acrylamide: bisacrylamide = 29:1) and detected by ultraviolet transillumination. The expected length of final products was about 80 to 150 base pairs. Each experiment contained 3 sample tests, a positive control test, 3 healthy control tests and a negative control test (Fig. 3). The duplicate PCR result was made in a separate experiment. For optimizing PCR reaction, we used different initial quantities of template DNA, 200 (C1), 100 (C2) and 50 ng (C3), from sample crude DNA in the PCR reaction. The C3 reaction represented monoclonal result and showed the reproductive result in duplicate reaction. In addition, we found 25 ng DNA was enough to make a reliable result by using the 100 (HC1), 50 (HC2) and 25 ng (HC3) of DNA extracted from the reactive lymph node as templates in the first round PCR, and the polyclonal result of each reaction revealed multiple bands. These above results suggested that monoclonal B cell DNA might be present in this investigated specimen, consistent with MALT lymphoma (Fig. 3).

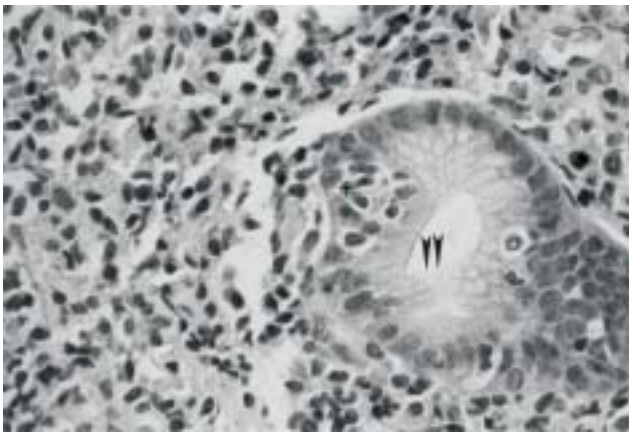

Fig. 2. Gastric biopsy showing characteristic lymphoepithelial lesion in MALT-lymphoma composed of a group of small lymphocytic aggregate within the gastric gland (asterisk). The stroma is being heavily infiltrated by mature-appearing small lymphocytes and plasma cells. Two bacilli morphologically compatible with *H. pylori* are also present (arrowhead) (H&E, original magnification 400X).

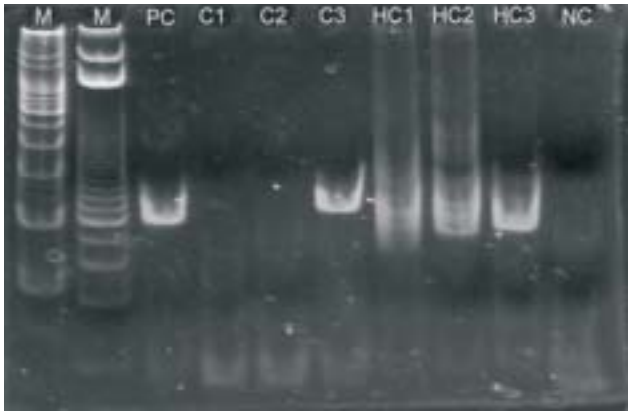

Fig. 3. Polyacrylamide gel photograph of IgH PCR product electrophoresis showing a clonal rearrangement band (C3). (Lane 1 M, 100 bp size marker; lane 2 M, 20 bp size marker; PC, positive control (100 bp); C1, 200-ng sample DNA; C2, 100-ng sample DNA; C3, 50-ng sample DNA; HC1, healthy control (100 ng DNA); HC2, healthy control (50 ng DNA); HC3, healthy control (25 ng DNA); NC, negative control (no DNA) (IgH = immunoglobulin heavy chain; PCR = polymerase chain reaction).

Treatment with amoxicillin 1000 mg, clarithromycin 500 mg, and omeprazole 20 mg twice daily for 1 week was given. The follow-up EGD in October 2000 showed identical finding, and the biopsy revealed residual MALT lymphoma. The second follow-up EGD in January 2001 with a biopsy revealed complete resolution of the disease.

DISCUSSION

In 1982, Isaacson and Wright first introduced a distinct group of extranodal malignant lymphoma arising from MALT. This group of lesion was a low-grade B-cell lymphoma of MALT type.[1]

The association of *H. pylori* infection and formation of MALT in the stomach was substantiated.[2,3] Association was also seen between *H. pylori* and gastric lymphoma.[4,5] The above evidence suggested that *H. pylori* infection is an essential factor in the formation of low-grade gastric MALT lymphoma. Regression of MALT was observed after the eradication of *H. pylori* with antibiotic treatment.[10,11]

The endoscopic findings of MALT lymphoma were described by Seifert *et al*.[7] in 1993. Two types of tumor could be differentiated by their appearance on endoscopy - exophytic and infiltrative types. [6,7] An exophytic - type tumor could be classified according to the system of Palmer; it is easily recognized as malignancy on endoscopy, and the diagnosis confirmed by endoscopic biopsy. The infiltrative type tumor is difficult to differentiate by means of endoscopy and biopsy, and it can be classified as elevated, flat or cavitated. The elevated type presents as thickened mucosal folds (giant folds) with or without erosion or ulceration. The flat type shows erosive mucosal changes with multiple erosions or a granular pattern. The cavitated type displays multiple, occasionally single, flat and irregular ulceration.

The endoscopic finding of granular pattern of the flat type could also be described as follicular gastritis. Follicular gastritis is highly correlated with *H. pylori*-caused severe, active gastritis. It is mostly prevalent in the young pylori-infected patients with duodenal ulcer.[12] The progression from *H. pylori*-infected gastritis through lymphoid hyperplasia to monoclonal B-cell lymphoma has been reported.[13,14] The incidence of monoclonal B-cell populations in the follicular gastritis was higher than in both *H. pylori*-positive and *H. pylori*-negative control, and it disappeared after successful *H. pylori* eradication. This suggests that follicular gastritis may be strongly associated with MALT lymphoma.[15] The character of B-cell monoclonality in this patient could be confirmed by 1 dominant PCR product of V_H family-specific gene rearrangement.

We believe that we detected a MALT lymphoma in its very early stage before gross abnormal finding was discernible by endoscopy. The response of the tumor to the treatment for *H. pylori* made this postulate convincing. Follicular gastritis may be a high-risk condition that gives rise to MALT lymphoma, and further investigation is indicated.

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