CASE REPORT

Regression of colonic low grade B cell lymphoma of the mucosa associated lymphoid tissue type after eradication of *Helicobacter pylori*

M Raderer, F Pfeffel, G Pohl, C Mannhalter, J Valencak, A Chott

Abstract

**Background**—Lymphoma of the mucosa associated lymphoid tissue (MALT) arising in the stomach has been shown to be related to *Helicobacter pylori* infection, and total regression of gastric lymphoma after successful eradication of *H pylori* has consistently been reported. MALT-type lymphomas at other localisations, however, has to our knowledge not been linked to *H pylori*, and eradication of the bacteria has not been studied for management of such lymphomas.

**Patient Method**—A 67 year old man was diagnosed with MALT-type lymphoma simultaneously involving the stomach and the colon descendens. In addition to the presence of MALT-type lymphoma, *H pylori* associated chronic gastritis was diagnosed, and treatment with clarithromycin, metronidazole, and omeprazole was initiated, resulting in its successful eradication.

**Results**—Follow up performed four months later showed regression of the colonic manifestation, whereas the gastric lymphoma did not respond to antibiotic treatment, as assessed by regular follow up for 14 months, in spite of its restriction to mucosa and submucosa. The patient was therefore treated with oral cyclophosphamide (100 mg a day) resulting in partial remission after seven months of continuous treatment. Because of the presence of residual lymphoma, additional irradiation was performed, which led to complete remission of the gastric lymphoma. The patient remains in complete remission 40 months after diagnosis and 26 months after initiation of treatment.

**Conclusion**—In the case of concurrent gastric and intestinal low grade MALT-type lymphoma, *H pylori* eradication may cause regression of the intestinal lesion. (Gut 2000;46:133–135)

Keywords: mucosa associated lymphoid tissue; colon; *Helicobacter pylori* eradication; lymphoma

The concept of lymphoma of the mucosa associated lymphoid tissue (MALT) type was introduced by Isaacson and Wright in 1983. Interestingly, MALT-type lymphomas usually arise in organs originally devoid of lymphoid tissue, which is acquired through chronic antigenic stimulation triggered by persistent infections and/or autoimmune processes. Most MALT-type lymphomas occur in the stomach, but they may arise at any site along the gastrointestinal tract and may also involve extragastrointestinal organs such as the salivary gland, thyroid gland, lung, ocular adnexa, bladder, and skin. Since the introduction of this clinicopathological entity, MALT-type lymphoma of the stomach has become a focus of interest for both pathologists and clinicians. The discovery of a definitive role of *Helicobacter pylori* in the pathogenesis of this disease along with the demonstration of complete regression of malignancy after successful eradication of *H pylori* has revolutionised treatment options for low grade gastric lymphoma of the MALT type. In a recently published study of 50 patients followed for a median time of two years, complete remission could be obtained after *H pylori* eradication in about 80% of patients, which confirms the results from other series. According to these findings, *H pylori* eradication seems to be the treatment of choice for patients with low grade gastric MALT type lymphoma. This benefit, however, appears to be restricted to patients with early stages of the disease—that is, involvement of mucosa and submucosa—while more advanced stages as well as patients with high grade disease do not appear to be responsive to removal of the antigenic stimulus provided by *H pylori*.

Scattered reports in the literature have claimed the propensity of MALT-type lymphoma to occur multifocally involving multiple sites of acquired MALT throughout the human body. In addition, late relapse of low grade gastric MALT-type lymphoma at gastrointestinal or extragastrointestinal MALT sites such as the lung has repeatedly been reported. Lesions arising outside the stomach, however, have not been linked to the presence of *H pylori*, and eradication of the bacteria has consequently not been tested as a therapeutic measure in such patients. We report the...
case of a 67 year old patient with low grade MALT-type lymphoma synchronously involving the stomach and colon, whose colonic lymphoma regressed completely after successful eradication of H pylori, whereas the gastric lymphoma, which was restricted to the mucosa and the submucosa, did not respond to antibiotic treatment.

Case report
A 67 year old man was referred to a general hospital with a four month history of persistent epigastric complaints refractory to treatment with H2 blocking agents. Upon gastroscopy, a single ulcer (3 cm in diameter) was discovered in the gastric corpus, and multiple biopsy specimens were taken from the ulcer as well as from the surrounding mucosa. Histological evaluation of the biopsy specimens obtained from the ulcer disclosed infiltration with small lymphoid cells invading and destroying the epithelium to form lymphoepithelial lesions. Immunophenotyping showed \( \kappa \) light chain restriction, indicating monoclonal B cell proliferation, and the lymphoid cells stained positive for CD20 and IgM, but were negative for CD5 and CD10. The proliferation rate was about 10% as assessed by staining with the MIB1 (Ki 67) antibody. Based on the characteristic histopathological and phenotypic features, the diagnosis of low grade B cell lymphoma of the MALT type was established. In addition to the diagnosis of low grade B cell lymphoma of the gastric lymphoma, the patient remains in complete remission 40 months after diagnosis and 26 months after initiation of treatment.

Discussion
Although MALT-type lymphoma may occur in a wide variety of organs, the stomach is the predominant localisation and constitutes about 70% of all cases. According to pioneering work published in the early 1990s, infection with H pylori provides the antigenic drive for development of low grade MALT-type lymphoma in the large majority of cases, and transformation to high grade malignancy in the course of the disease is a commonly observed phenomenon.

Follow up investigations were performed four months after initial diagnosis, and consisted of gastroscopy, endosonography, and colonoscopy. Endosonography showed no change in the gastric lymphoma, and histological evaluation of multiple biopsy specimens confirmed the presence of MALT-type lymphoma, but disclosed the absence of H pylori in the stomach with pronounced regression of the inflammatory infiltrate. Colonoscopy, however, showed complete disappearance of the colonic lymphoma both macroscopically and during histological examination of multiple biopsy samples obtained from the former site of the polyp. No response of the gastric lymphoma was shown on re-examination six, nine, and 14 months after initial diagnosis. The patient was therefore treated with oral cyclophosphamide (100 mg a day) resulting in a partial remission after seven months of continuous treatment, as judged by regular follow up with histological evaluation. Because of the presence of residual lymphoma, eradication of H pylori at a dose of 35 Gy was performed, which led to complete remission of the gastric lymphoma. The patient remains in complete remission 40 months after diagnosis and 26 months after initiation of treatment.
Hpylori eradication. Given the concept underlying the development of gastric MALT-type lymphoma, one would assume an Hpylori associated gastric lymphoma as the primary focus of disease in our patient, with secondary involvement of the colon. That this sequential order of dissemination is indeed the case has recently been confirmed by Du et al.15 Our histological, phenotypic, and genetic studies strongly suggest that the concurrent gastric and colonic lymphomas were derived from the same clone. Because of the postulated common mucosal immunity, an initially Hpylori associated lymphoma could theoretically remain dependent on Hpylori associated T cells for some time even after generalisation, which further underscores the potential gastric origin of the lesions encountered. Of interest, however, is the fact that the gastric lymphoma did not respond within a follow up period of 14 months, as confirmed by regular endoscopic and gastroscopic follow up with histological examination. One may speculate, however, that, with a longer follow up, a response in the gastric lesion would also have been observed. Nevertheless, this appears to be highly unlikely; although responses to successful Hpylori eradication have been observed after a prolonged period of time in some studies, the median time to remission in the most comprehensive series published so far was 5.5 months, and all responding patients showed at least some signs of regression endoscopically or histologically at an earlier time, which was clearly not the case in our patient. Nevertheless, we cannot offer a definite explanation for the dissociation of responses between the two localisations of the lymphoma. One hypothetical explanation is the presence of a high grade lymphoma component undetected by multiple forceps biopsies, as has been reported for patients with gastric MALT-type lymphoma not responding to Hpylori eradication.4 In the case of high grade transformation, however, one would expect at least some progression of the disease over the relatively long time of 14 months. Alternatively, responsiveness to Hpylori eradication has been shown to be an indicator for clonal evolution of the disease, as Hpylori induced stimuli appear necessary only at an early stage of malignancy; once genetic damage has accumulated to a certain “point of no return”, eradication of Hpylori does not cause a clinical response.1 In this context, one may postulate dissemination of Hpylori dependent gastric lymphoma to the colon at an early stage, with additional as yet undiscovered factors causing faster evolution in the gastric lesion as compared with the still responsive colonic lymphoma.

This report shows that, in the case of concurrent gastric and intestinal low grade MALT-type lymphoma, Hpylori eradication may cause regression of the intestinal lesion.

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