Regression of a large gastric MALT lymphoma with antibiotic treatment to eradicate *Helicobacter pylori*

J Martin, S Boyle, M Jacyna

Summary

We report a case of a large low-grade gastric lymphoma of mucosa-associated lymphoid tissue (MALT), which regressed following the eradication of concurrent *Helicobacter pylori* infection. This case lends further support to a policy of *H pylori* eradication as a first line therapy for all these lesions, irrespective of size. The long-term prognosis of tumours treated in this way, however, needs further evaluation.

Keywords: *Helicobacter pylori*, MALT tumour

There is increasing evidence that *Helicobacter pylori* is causally linked to some types of gastric lymphoma and many reports have suggested that eradicating the organism may result in regression of some low-grade tumours.¹ We report the successful treatment of a large gastric low grade mucosa-associated lymphoid tissue (MALT) lymphoma with antibiotics to eradicate *H pylori*. This result supports previous evidence that even large tumours may be responsive to *H pylori* eradication therapy.

Case report

A 57-year-old man was referred for investigation of a two-month history of burning epigastric pain. He also described one episode of melaena, but no haematemesis. There was no previous history of dyspeptic symptoms, no weight loss, and he was not currently taking nonsteroidal anti-inflammatory drugs.

Examination was normal; he was not clinically anaemic, and there was no lymphadenopathy or hepatosplenomegaly. Routine biochemistry, liver function and full blood count were normal. An oesophago-gastroduodenoscopy revealed a large ulcer on the incisura with shouldering and rolled edges, highly suggestive of carcinoma (figure 1). Biopsies of the ulcer showed a population of lymphoid cells infiltrating, and destroying, the crypt epithelium. *H pylori* were seen in the specimen (figure 2). A diagnosis of MALT lymphoma was made and the patient was commenced on *H pylori* eradication therapy consisting of omeprazole 20 mg bid, amoxicillin 750 mg bid, and metronidazole 400 mg tid. Computed tomography of the abdomen, bone marrow aspirate and trephine were normal.

Figure 1 Initial endoscopic appearance of malignant ulcer on incisura

Figure 2 A mucosal infiltrate of lymphoid cells with destruction of gland epithelium

Figure 3 Endoscopic appearance of same area after four weeks treatment

Gastroenterology
Department,
Northwick Park and St
Marks' Hospital NHS
Trust, Harrow,
Middlesex HA1 3UJ,
UK

J Martin
S Boyle
M Jacyna

Accepted 17 April 1996

Four weeks later the patient was re-endoscoped and only a small superficial ulcer remained, with surrounding gastritis (figure 3). Histology demonstrated only small areas of residual lymphoma and no *H pylori*. The patient was treated with a further month of omeprazole 20 mg bid and amoxicillin 1 g bid. A further endoscopy following this treatment revealed only a small scar. Multiple biopsies of the area, as well as histological mapping of the stomach, showed only occasional lymphoid aggregates but no evidence of MALT lymphoma. The patient is presently well, off all medication and is negative for *H pylori* on histology and urea breath test.

Discussion

Lymphoid tissue is not present in normal gastric mucosa, but is present in the mucosa of all patients infected with *H pylori*.² *H pylori* is present in 92% of all patients with gastric lymphoma,³ and gastric lymphoma is significantly more common in areas where *H pylori* is prevalent.⁴ This circumstantial evidence suggests an association between *H pylori* and gastric lymphoma. Evidence for a causal relationship comes from Parsonnet,⁵ who demonstrated that people infected with *H pylori* were significantly more likely to develop gastric high grade, or MALT lymphoma, and that the infection precedes development of the malignancy.

If *H pylori* were the cause of gastric lymphoma then one would expect the tumour to regress when the organism is eradicated. There are now an increasing number of reports supporting this relationship for low grade MALT lymphoma,^{1,6} although eradication of *H pylori* in cases of high grade lymphoma appears to have no effect on the progress of the disease.⁷

MALT lymphomas are low-grade tumours consisting of a monoclonal proliferation of B-cells. It has been postulated that *H pylori* antigen activates non-neoplastic T-cells to produce IL-2, which in turn results in the B-

Learning points

- all gastric ulcers need to be biopsied and examined histologically
- *H pylori* eradication therapy is an acceptable first-line treatment for low-grade gastric MALT lymphomas, irrespective of size
- this approach is not suitable for high-grade lesions
- careful long-term follow-up of these patients is mandatory as the recurrence rate amongst apparently disease-free patients is not known

cell proliferation.⁸ However, the observation that not all low-grade tumours respond to *H pylori* eradication has led to the hypothesis that tumours which are initially *H pylori* dependent become *H pylori* independent and eventually, high-grade tumours. It is possible that these changes are mediated via translocations such as 1:14, trisomy 3, or alterations in the P53 protein.

The majority of tumours reported in the literature to have regressed following treatment of *H pylori* have been small, low volume lesions. Weber described the regression of a 10-cm ulcer,⁹ but otherwise evidence for treatment of large tumours is sparse. This report also concerns a large ulcer, and hence lends support to the view that the initial treatment for these malignancies should be *H pylori* eradication therapy. We would urge caution, however, as a proportion of these lesions will harbour high-grade malignancy or *H pylori* independent tissue, and hence will be unaffected by antibiotic treatment. As a result, regular follow-up to ensure endoscopic and histological improvement is mandatory. In Bayerdorffer's series there were no recurrences of disease in any of the responsive patients during a follow-up period of one year.⁶ As yet, no long-term studies exist to assess the long-term prognosis of MALT lymphomas treated in this way.

1 Wotherspoon AC, Doglioni C, Diss TC, *et al*. Regression of primary low-grade B-cell gastric lymphoma of mucosa-associated lymphoid tissue after eradication of *Helicobacter pylori*. *Lancet* 1993; **342**: 575–7.

2 Genta RM, Hamner HW, Graham DY. Gastric lymphoid follicles in *Helicobacter pylori* infection: frequency, distribution, and response to triple therapy. *Hum Pathol* 1993; **24**: 577–83.

3 Wotherspoon AC, Ortiz Hidalgo C, Falzon MR, Issacson PG. *Helicobacter pylori*-associated gastritis and primary B-cell gastric lymphoma. *Lancet* 1991; **338**: 1175–6.

4 Doglioni C, Wotherspoon AC, Moschini A, De Boni M, Issacson PG. High incidence of primary gastric lymphoma in northeastern Italy. *Lancet* 1992; **339**: 834–5.

5 Parsonnet J, Hansen S, Rodriguez L, *et al*. *Helicobacter pylori* infection and gastric lymphoma. *N Engl J Med* 1994; **330**: 1267–71.

6 Bayerdorffer E, Neubauer A, Rudolph B, *et al*. Regression of primary gastric lymphoma of mucosa-related lymphoid tissue after cure of *Helicobacter pylori* infection. *Lancet* 1995; **345**: 1591–4.

7 Pescatore P, Heine M, Manegold BC. Cure of gastric lymphoma with antibiotics. *Gastroenterology* 1995; **109**: 334–5.

8 Hussell T, Issacson PG, Crabtree JE, Spencer J. The response of cells from low-grade-B-cell gastric lymphomas of mucosa-associated lymphoid tissue to *Helicobacter pylori*. *Lancet* 1993; **342**: 571–4.

9 Weber D, Dimopoulos M, Anandu D, Pugh W, Steinbach G. Regression of gastric lymphoma of mucosa-associated lymphoid tissue with antibiotic therapy for *Helicobacter pylori*. *Gastroenterology* 1994; **107**: 1835–8.