

Commentary

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Choosing the right MALT

Up to 40% of non-Hodgkin's lymphomas occur at extranodal sites. Most of these arise in the gastrointestinal tract with the stomach as the commonest location. However gastric lymphoma makes up only 2-8% of all gastric malignancies and so, although the incidence is reported to be rising, these are relatively rare tumours. A conservative estimate would suggest that only 600 gastric lymphomas are diagnosed in Britain each year. Since the recognition by Isaacson and Wright¹ that most low grade gastric lymphomas are distinct from nodal type lymphomas and that their morphology, architecture, and immunophenotype indicate an origin from mucosa associated lymphoid tissue (MALT) our knowledge of the pathobiology of these tumours has increased rapidly. Most investigators would now accept that the initial step on the road to primary gastric lymphoma involves the acquisition of organised lymphoid tissue in the form of MALT² and that this is most frequently seen in response to infection by *Helicobacter pylori*.³ There follows a series of genetic events that are distinct from those involved in the pathogenesis of nodal-type lymphoma leading to the development of an overt lymphoma, which probably arises from the marginal zone B cell population. There are some morphological features of low grade MALT lymphoma including the presence of follicular colonisation and plasma cell differentiation of tumour cells that suggest that the neoplastic cells are proliferating in response to antigenic stimuli. In vitro studies have shown this to be the case. The stimulus is T cell dependent and associated with the presence of *H pylori*.⁴ Treatment of early low grade MALT lymphoma by eradication of the organism has led to regression of the lymphoma in a proportion of cases,^{5,6} although longterm follow up of these cases is still awaited. The rarity of gastric lymphoma and the absence of large clinical studies have resulted in many gaps in our knowledge of the clinical behaviour and appropriate treatment of these tumours.

In this issue of the journal Taal *et al* consider some of these areas. In particular they have studied the relation of the histological grade to clinical presentation, endoscopic appearances, and prognosis. Of 114 patients studied 51 were considered low grade MALT lymphoma, 16 high grade MALT lymphoma, and 47 pure primary high grade gastric lymphoma. Although weight loss was more common in the high grade lesions there were no clinical features to predict the diagnosis. The endoscopic patterns (ulceration, polypoid mass or diffuse infiltration) were not related to the grade reinforcing an earlier study from the same group that reached the same conclusion.⁷ The macroscopic interpretation of the endoscopic findings was correct in only 15% of cases. Low grade lymphoma mimicked a benign lesion while high grade lymphoma was more frequently thought by the endoscopist to be carcinoma. Histological evaluation of the biopsy material gave a correct diagnosis in 75% of low grade tumours and 79% in cases that were high grade. This study has further

confirmed other studies that have suggested that high grade lymphoma with or without features of MALT are more aggressive tumours with more presenting at stage II and with a worse overall and disease free survival than low grade lesions.^{8,9} However the current study is different from other clinical studies of gastric lymphoma in the near uniformity of stomach conserving therapy in this series in which most patients received radiotherapy with additional chemotherapy for stage II₂ disease.

There are two areas that are not tackled in this paper and will therefore continue to be a source of debate. Firstly, is the exclusion of lymphomas of stage III and IV. This will obviously confer a better prognosis to gastric lymphoma as a whole. Although this can probably be justified in cases of primary pure high grade lymphoma, which lack specific morphological features to distinguish a nodal versus extranodal origin low grade MALT lymphoma has a sufficiently distinctive architecture, morphology, immunophenotype, and genotype to allow a diagnosis on a gastric biopsy specimen even in the presence of more widespread dissemination. The second contentious point will be familiar to histopathologists and concerns the criteria for the assessment of grade. Taal *et al* consider a high grade tumour to be 'dominated by large blast cells' but there are no defined criteria for 'domination'. Isaacson and Norton consider high grade transformation to be present where there are 'clusters or sheets of transformed cells' - but what constitutes a cluster or sheet is not stated.¹⁰ They also exclude the presence of activated or transformed cells in the follicle centres of some MALT lymphoma showing follicular colonisation when the diffuse infiltrate is typically low grade.

Within this context Taal *et al* have advanced our knowledge a little further. The diagnosis of lymphoma remains difficult as low grade lymphomas show subtle features and mimic reactive conditions while high grade lymphomas mimic carcinoma. Diagnosis of lymphoma at first biopsy is improving with increased awareness of the pathological features and wider sampling. The response of lymphoma to radiotherapy and subsequent survival is significantly worse in high grade lymphomas irrespective of the presence of MALT-type features.

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- 1 Isaacson PG, Wright DH. Malignant lymphoma of mucosa associated lymphoid tissue. A distinctive type of B-cell lymphoma. *Cancer* 1983; 52: 1410-6.
- 2 Wotherspoon AC, Ortiz-Hildago C, Falzon MR, Isaacson PG. Helicobacter pylori-associated gastritis and primary B-cell gastric lymphoma. *Lancet* 1991; 338: 1175-6.
- 3 Genta RM, Hamner HW, Graham DY. Gastric lymphoid follicles in Helicobacter pylori infection: frequency, distribution and response to triple therapy. *Hum Pathol* 1993; 24: 577-8.

- 4 Hussell T, Isaacson 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.
- 5 Wotherspoon AC, Doglioni C, Diss TC, Pan L, Moschini A, de Boni M, *et al*. Regression of low-grade B-cell gastric lymphoma of mucosa-associated lymphoid tissue type after eradication of *Helicobacter pylori*. *Lancet* 1993; **342**: 575–7.
- 6 Bayerdorffer E, Neubauer A, Rudolph B, Thiede C, Lehn N, Eidt S, *et al*. Regression of primary gastric lymphoma of mucosa-associated lymphoid tissue type after cure of *Helicobacter pylori* infection. *Lancet* 1995; **345**: 1591–4.
- 7 Taal BG, den Hartog XX, Jager FCA, Tytgat GNJ. The endoscopic spectrum of primary non-Hodgkin's lymphoma of the stomach. *Endoscopy* 1987; **19**: 190–2.
- 8 Cogliatti SB, Schmid U, Schumacher U, Eckert F, Hansmann ML, Hedderich J, *et al*. Primary B-cell gastric lymphoma: a clinicopathological study of 145 patients. *Gastroenterology* 1991; **101**: 1159–70.
- 9 Radaszkiewicz T, Dragosics B, Bauer P. Gastrointestinal malignant lymphomas of the mucosa-associated lymphoid tissue: factors relevant to prognosis. *Gastroenterology* 1992; **102**: 1628–38.
- 10 Isaacson PG, Norton AJ. *Extranodal lymphomas*. Edinburgh: Churchill Livingstone, 1994: 39–41.