Envoi SPECIALIST PATHOLOGISTS *inside insights*

Update No.13 - 2016 *Dr Mark Bettington*

Gastric MALT lymphoma

Definition: An extranodal lymphoma composed of marginal zone type small B-cells; i.e. marginal zone B-cell lymphoma of Mucosa Associated Lymphoid Tissue (MALT).

Epidemiology: Approximately 50% of MALT lymphomas occur in the GI tract and about 85% of these occur in the stomach. Around 50% of gastric lymphomas are MALT lymphomas.

Aetiology: Helicobacter pylori is the major cause of gastric MALT lymphoma and is present in 75-90% of cases. Organisms begin to disappear as the disease becomes more established and, as such, serological testing for Helicobacter should be performed in all cases that are histologically negative.

Histology: In mucosal biopsies, gastric MALT lymphoma is characterised by a monotonous infiltrate of monocytoid B-cells that expand and replace the normal structures of the lamina propria (Fig. 1). Malignant infiltration of the gastric glands in the form of lymphoepithelial lesions is a characteristic feature (Fig. 2). The presence of larger, more irregular or more proliferative cells raises the possibility of transformation to diffuse large B cell lymphoma.

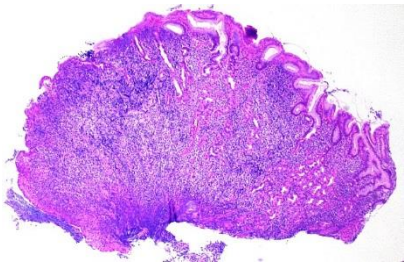

Fig. 1 MALT lymphoma – replacement of the lamina propria by a dense lymphoid infiltrate

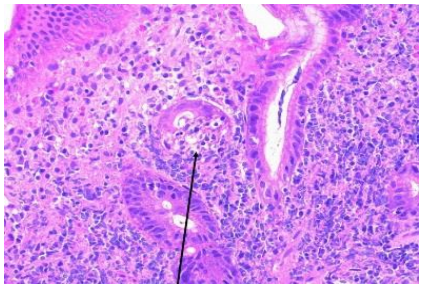

Fig. 2 Lymphoepithelial lesion

Differential diagnosis: The major differential diagnosis is with a florid Helicobacter-associated gastritis. This distinction can be impossible in some cases. The Wotherspoon histological criteria are useful to quantify the degree of uncertainty surrounding a diagnosis and use features such as the intensity of the cellular infiltrate and the presence or absence of lymphoepithelial lesions.

Prognostic and predictive factors: Gastric MALT lymphoma is an indolent disease. Even when bone marrow and multiple extranodal sites are involved the disease still tends to progress slowly. Adverse prognostic factors include older age, H.pylori negative at diagnosis and advanced stage.

Factors that predict a lack of response of gastric MALT lymphoma to Helicobacter eradication:

- Helicobacter negative at diagnosis
- presence of *t(11;18)*
- male gender
- invasion into or beyond submucosa (as assessed by endoscopic ultrasound)
- proximal or generalised disease

Transformation to diffuse large B cell lymphoma (DLBCL) can occur and must be carefully excluded at diagnosis and at any subsequent biopsy. DLBCL is more likely to present with macroscopic lesions and as such all macroscopic lesions must be generously biopsied.

Treatment: Helicobacter eradication is the first-line therapy regardless of Helicobacter status. The majority of patients enter a sustained remission after Helicobacter eradication and many will not require any further treatment. When required, local radiation therapy or chemotherapy are highly effective second line treatment options.

Follow-up:

- ***Disease regression*** post Helicobacter eradication usually takes 3-6 months. Re-biopsy during this time will usually show some residual disease. Rarely, lymphoma resolution can take up to two years or more post treatment.
- The optimal surveillance program is not clear. Upper endoscopy with biopsies should be performed at least every 6 months until two consecutive biopsies show a complete clinical response (see table – complete histological response, **CR** or probably minimal residual disease, **pMRD**). Biopsies should be taken from all macroscopic lesions, along with random biopsies from normal appearing body and antral mucosa.
- Subsequent surveillance is less clear, however yearly or two-yearly endoscopy is reasonable. This is to 1) ensure that the MALT lymphoma has not recurred and 2) assess for gastric adenocarcinoma. There is a six-fold increased risk for gastric adenocarcinoma in patients who have had gastric MALT lymphoma.
- Patients with ***progressive disease*** require oncological treatment.
- Patients showing ***no change*** after Helicobacter eradication therapy are more controversial. If there are no adverse features such as macroscopic lesions, suspected nodal involvement, initial Helicobacter negative status or *t(11;18),* a 'watch and wait' strategy can be employed for up to two years.
- Patients with ***persistent responding residual disease*** also represent a difficult group, the management should be individually tailored, but a 'watch and wait' strategy similar to that described above can be employed and potentially extended beyond two years.

The histological categories of disease response post Helicobacter eradication are as follows:

GELA category	Histology	Clinical significance
Complete histological response **(CR)**	No residual atypical lymphoid infiltrate. Regressive changes can be seen.	Complete response
Probable minimal residual disease **(pMRD)**	Small residual lymphoid aggregates are present.	Complete response
Responding residual disease **(rRD)**	Overt residual lymphoma with a nodular or diffuse pattern but also evidence of regression (lamina propria fibrosis and 'empty' lamina propria)	Partial remission
No change **(NC)**	Persistent lymphoma similar to the pre-treatment biopsies and without evidence of regression	Stable disease or progressive disease

GELA – Groupe d'Etude des Lymphomes de l'Adulte

Further reading:

A Ruskone-Fourmestraux, W Fischbach, B M P Aleman, et al. EGILs consensus report: Gastric extranodal marginal zone B-cell lymphoma of MALT. Gut 2011; 60:747-758

Shotaro Nakamura, Toshiro Sugiyama, Takayuki Matsumoto, et al. Long-term clinical outcome of gastric MALT lymphoma after eradication of Helicobacter pylori: a multicentre cohort follow-up study of 420 patients in Japan. Gut 2012; 61:507-513