Paris staging system for primary gastrointestinal lymphomas

Currently, much effort is put into the development of specific therapeutic approaches that are tailored to specific lymphoma entities. As a consequence, more specific information needs to be collected to support the choice of therapy. In gastric marginal zone B cell lymphoma of MALT-type, the need for specialised documentation of tumour extent in the organ wall has been stressed by the high predictive value for failure of response after Helicobacter pylori eradication, irrespective of the presence of the t(11;18) translocation. With new techniques such as endosonography, this infiltration depth can be assessed with improving accuracy. However, the information cannot be translated into the current staging systems. The dissemination patterns of extranodal lymphomas are also essentially different from primary nodal lymphomas. As tumour stage is one of the most important guidelines in the choice of local therapy (surgery, radiotherapy) and chemotherapy, adequate documentation of tumour localisation in the organ related lymph nodes and beyond is essential.

The Ann Arbor staging system, developed for and routinely used in nodal non-Hodgkin’s lymphoma, is not optimal for documentation of the specific relevant features of primary extranodal lymphoma in the gastrointestinal tract. Several modifications and alternatives have been proposed. However, neither differentiation of stage I (confined lymphoma to the mucosa and submucosa) from stage II (tumour extension beyond the submucosa according to Radaszkiewicz and colleagues) nor discrimination of patients for risk assessment and accumulation of good data for proper stratification will be possible without a modified TNM staging system, named after the first venue of the group in Paris. The staging system adequately records: (1) depth of tumour infiltration; (2) extent of nodal involvement; as well as (3) specific lymphoma spreading (table 1). It is adjusted to the gastrointestinal origin of the lymphoma, considering histopathological characteristics of extranodal B and T cell lymphomas. The use of this system in future studies will permit accurate comparison of the reported cohorts and should allow rapid accumulation of good data for proper stratification of patients for risk assessment and treatment options.

Table 1 Paris staging system for primary gastrointestinal lymphomas*

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Lymphoma extent not specified</td>
</tr>
<tr>
<td>TO</td>
<td>No evidence of lymphoma</td>
</tr>
<tr>
<td>T1</td>
<td>Lymphoma confined to the mucosa/submucosa</td>
</tr>
<tr>
<td>T1m</td>
<td>Lymphoma confined to mucosa</td>
</tr>
<tr>
<td>T1sm</td>
<td>Lymphoma confined to submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Lymphoma infiltrates muscularis propria or subserosa</td>
</tr>
<tr>
<td>T3</td>
<td>Lymphoma penetrates serosa (visceral peritoneum) without invasion of adjacent structures</td>
</tr>
<tr>
<td>T4</td>
<td>Lymphoma invades adjacent structures or organs</td>
</tr>
<tr>
<td>NX</td>
<td>Involvement of lymph nodes not assessed</td>
</tr>
<tr>
<td>NO</td>
<td>No evidence of lymph node involvement</td>
</tr>
<tr>
<td>N1</td>
<td>Involvement of regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Involvement of intra-abdominal lymph nodes beyond the regional area</td>
</tr>
<tr>
<td>N3</td>
<td>Spread to extra-abdominal lymph nodes</td>
</tr>
<tr>
<td>M1</td>
<td>Lymphoma invades bone marrow</td>
</tr>
<tr>
<td>M2</td>
<td>Non-contiguous involvement of separate site in gastrointestinal tract (eg, stomach and rectum)</td>
</tr>
<tr>
<td>M3</td>
<td>Limited involvement of separate site in gastrointestinal tract (eg, stomach and rectum)</td>
</tr>
<tr>
<td>M4</td>
<td>Extranodal involvement</td>
</tr>
</tbody>
</table>

*B: Lymphomatous infiltration of bone marrow

H: Histopathological staging: status of tumour, node, metastasis, bone marrow

The histological examination will ordinarily include 6 or more lymph nodes.

†Valid for lymphomas originating from the gastro-oesophageal junction to the anus (as defined by identical histomorphological structure).

Tumour staging of epithelial origin has also been proposed as an alternative in gastrointestinal lymphoma to describe localised disease. The “T” part of this system pertains to the anatomical structure of the organs and sufficiently fulfills the requirements for staging of local extent of the disease.

The European Gastro-Intestinal Lymphoma Study Group (EGLS) is a multidisciplinary group of investigators, including clinical investigators such as gastroenterologists, medical oncologists, radiotherapists, and pathologists, as well as basic researchers such as cellular and molecular biologists. Several groups from the UK, France, Germany, the Netherlands, Spain, and Austria now take part and have come together regularly since 1999 to discuss and study subjects in epidemiology and molecular and cellular biology of gastrointestinal lymphoma. Clinical protocols and trials have been developed and performed as a collaborative effort. As a result of discussions on staging protocols and reporting systems over the past years, we would like to propose a modified TNM staging system, named after the first venue of the group in Paris. The staging system adequately records: (1) depth of tumour infiltration; (2) extent of nodal involvement; as well as (3) specific lymphoma spreading (table 1). It is adjusted to the gastrointestinal origin of the lymphoma, considering histopathological characteristics of extranodal B and T cell lymphomas. The use of this system in future studies will permit accurate comparison of the reported cohorts and should allow rapid accumulation of good data for proper stratification of patients for risk assessment and treatment options.

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A new cause for CA19.9 elevation: heavy tea consumption

A 52 year old woman was referred to our unit with heavy tea consumption. The regression of gastric MALT lymphoma after eradication of Helicobacter pylori is predicted by endosonographic staging. The regression of gastric MALT lymphoma after eradication of Helicobacter pylori is predicted by endosonographic staging.

CA19.9 is a reliable tumour marker of gastric lymphomas compared with lymph node lymphomas in a population-based registry differ in stage distribution and survival. A new cause for CA19.9 elevation: heavy tea consumption. A new cause for CA19.9 elevation: heavy tea consumption.

**Table 1**

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Mild elevation (&lt;200 U/ml)</th>
<th>High levels (&gt;1000 U/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive jaundice</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Acute liver failure and acute hepatitis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Alcoholic liver disease</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Non-alcoholic liver disease</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Acute</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chronic</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Intestinal pulmonary disease</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Collagen vascular diseases</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Anecdotally reports: hydrenephrosis,13 endometriosis,14 splenic cyst,15 bronchogenic cyst,16 sigmoid diverticulitis,17 and hypothyroidism.18

In this case, the usual causes of CA19.9 elevation were ruled out before a link with the tea beverage was suspected. After tea consumption withdrawal, a diagnostic endoscopy occurred and the patient became symptom free, suggesting the diagnosis of tea intoxication. At the same time, serum CA19.9 levels dropped and a positive rechallenge test proved the relationship between tea overconsumption and raised levels of CA19.9.

To our knowledge, this is the first reported case of markedly raised levels of CA19.9 associated with heavy tea consumption. The mechanism of this relation remains unclear. In addition, the epithelial tissue target involved in CA19.9 secretion by tea overuse is unknown. Individual susceptibility to abnormal CA19.9 secretion triggered by tea overconsumption could not be excluded.

**References**


A 52 year old woman was referred to our unit with heavy tea consumption. A new cause for CA19.9 elevation: heavy tea consumption.

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Non-alcoholic steatohepatitis and hepatic steatosis in patients with adult onset growth hormone deficiency

Adult onset growth hormone (GH) deficiency closely resembles syndrome X. Patients with syndrome X often suffer from obesity, dyslipidaemia, insulin resistance, and hypertension, and hepatic steatosis and non-alcoholic steatohepatitis (NASH) have also been characterised as symptoms of syndrome X. However, the relationship of GH deficiency to hepatic steatosis and NASH remains unclear.

We looked for the presence of hepatic steatosis using computer tomography (CT) in a study of 18 patients with adult onset anterior lobe pituitary hormone deficiency, with or without GH deficiency. We also performed a liver biopsy in one patient with adult onset GH deficiency. None of the patients was positive for hepatitis B surface antigen, hepatitis C virus antibody, antinuclear antibody, or antimitochondrial antibody. The criterion used for diagnosing hepatic steatosis was a ratio for the liver/spleen CT value of less than 0.9. In 15 patients with GH deficiency, seven showed hepatic steatosis (53.8%) while in five patients without GH deficiency no hepatic steatosis was present (p = 0.035). Body mass index (BMI kg/m²), serum triglyceride level (TG mg/dl), and serum total cholesterol (T-ch mg/dl) were analysed using an unpaired Student’s t test. BMI, TG, and T-ch were analysed using an unpaired Student’s t test.

The male patient on whom we performed a liver biopsy was diagnosed with GH deficiency at 58 years old. He showed hepatic steatosis, measured by CT, at 64 years. Serum aspartate aminotransferase level fluctuated from 20 to 80 U/l. The patient did not have a history of alcohol abuse but was slightly obese (BMI 30 kg/m²). Liver biopsy was performed when the patient was 72 years old, and this showed the presence of NASH (fig 1).

We have demonstrated that hepatic steatosis is more frequently observed in patients with GH deficiency than in those without GH deficiency. Furthermore, by liver biopsy, we showed that a patient with GH deficiency also had NASH. These results indicate that adult onset GH deficiency is a possible risk factor for hepatic steatosis and NASH.

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References


Expression of thiopurine methyltransferase in South Asians

Azathioprine and its metabolite 6-mercaptopurine (6-MP) are widely used in the treatment of Crohn’s disease, ulcerative colitis, autoimmune hepatitis, and a range of other inflammatory and autoimmune diseases, as well as for prevention of transplant rejection. Thiopurine methyltransferase (TPMT) converts 6-MP to 6-methylIMPDH and its expression predisposes treated patients to bone marrow depression; it may also enhance the efficacy of thiopurines by increasing their metabolism to 6-thioguanine nucleotides. Previous reports in Caucasians have shown that approximately 0.3% are homozygously and 10% heterozygously deficient in TPMT. One study
suggests that the frequency of individuals with the mutant TPMT allele, TPMT*3A, is lower in Southwestern Asians than in Caucasians; variant allele causes reduced enzyme activity in vitro. However, there are no data on the phenotypic expression of TPMT in South Asian populations.

We have compared expression of TPMT in South Asian and Caucasian patients attending gastroenterology, renal, rheumatology, and dermatology clinics who were being considered for treatment with thiopurines. TPMT activity was assayed by tandem mass spectrometry for 6-methylMP (assays kindly provided by Purine Research Laboratory, Guy’s Hospital, London SE1 9RT, UK). Homozygous deficiency of TPMT was defined as a level <10, heterozygous as 10–25, and normal as >25 pmol/h/mg haemoglobin.

Of 83 Caucasian patients, one (1.3%) was homozygously deficient, 10 (12%) were heterozygous, and 72 (86.7%) had normal expression of TPMT. The corresponding values in 77 South Asian patients were 0.7 (9%), and 70 (91%), respectively. The prevalence of deficiency of expression of TPMT in South Asian patients resembles that in Caucasians. Use and monitoring of azathioprine and 6-MP should therefore follow similar principles in both ethnic groups.

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References

Fatigue is associated with high circulating leptin levels in chronic hepatitis C

We read with great interest the recent paper from Piche and colleagues (Gut 2002;51:434–9) relating leptin levels to fatigue in chronic hepatitis C patients. On the surface, their findings are very intriguing, they may have significant limitations. Some of us have argued previously that there is only one way forward. All bodies funding prospective therapeutic studies in colorectal cancer should insist that a panel of molecular markers are measured and recorded in all patients using a standardised technique, even if they are not included as an end point, and make these results readily available for subsequent analysis. Studies in which end points are performed prospectively carry the least risk of methodological flaws.

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BARBARIUM TO ULTRASOUND, CT, AND MAGNETIC RESONANCE (MR), ETC., STILL MEANS THAT IT PROVIDES A DIAGNOSTIC CHALLENGE.

How does Radiological Imaging of the Small Intestine help? The answer is enormously, as it presents an encyclopaedic review of all of the small bowel abnormalities with their attendant investigative techniques. The only problem (and it is one which affects all radiological texts) is the question of whether to go for chapters which reflect technique or for those which reflect pathological conditions. In this case the editor has gone for both and while this results in a superlative volume, there is bound to be some repetition. For example, reference to Crohn’s disease or small bowel tumours will appear both in their own section as well as under CT/MR, etc. However, as all of these chapters are written by different authors with their own experiences, this can prove to be an advantage enabling the reader a “second bite of the cherry.”

Is there competition in the market place and how does this book hold up? The inevitable comparison has to be made to Classic Imaging of the Small Intestine by Herlinger, Maglinte, and Birnbaum, interestingly also published by Springer. This is the more mature book, now in its second edition, having been originally published in 1989. Its authorship is primarily North American with two European contributors whereas Radiological Imaging is primarily a European work with some distinguished North American contributors. Indeed, two of the editors of Classic Imaging are authors. Both books go for the same layout—that is, chapters which are technique based followed by those on pathological states. Both are totally comprehensive and although Classic Imaging is slightly larger (576 pp versus 477 pp) it is less expensive ($164 versus $214). This price differential is most likely to be due to the inclusion of 141 beautiful colour illustrations of both endoscopic views and pathology specimens in Radiological Imaging. This is also the most recent publication (2002 versus 1999) and in areas where there is rapid technical change—typically MR imaging—the reader can appreciate the difference. It has to be said that both books fulfil their remit extremely well but your reviewer, if he had to choose, would opt for spending the extra Euros.

Professor Gourtsoyiannis and his team have to be congratulated on producing a superb book that graces the swelling ranks of medical radiology. A must for every radiology department and a continuing source of information for any radiologist with an interest in the gastrointestinal system

A H Freeman

NOTICES

New In Vivo Imaging Modalities for Molecular Biology, Cell Biology and Physiology

This Jacques Monod conference will be held on 31 May–4 June 2003 in Roscoff, France. Further information: Bertrand Tavitian, IN- SERM M10103, Service Hospitalier Frédéric Joliot, CEA Direction des Sciences du Vivant, Direction de la Recherche Médicale, 4 place du Général Leclerc, 91401 Orsay Cedex, France. Tel: +33 1 696 779 77; fax: +33 1 696 879 33; email: tavitian@slhf.cca.fr

Prague Hepatology Meeting

To be held on 5–7 June 2003 in Prague, Czech Republic. Leading speakers from Europe and the USA will present new ideas and suggestions on pathophysiology, diagnostics, and therapy of liver diseases in ten programmes. Further details: Ms Veronika Revicka. Tel: +420 241 445 759; fax: +420 241 445 806; email: veronika@congressprague.cz

8th International Liver Symposium

This symposium will be held on 13 June 2003 in Manchester, UK. Leading speakers from the USA and Europe will present state of the art reviews on recent advances in hepatology. Further details: Professor TW Warnes, Department of Gastroenterology, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, UK. Tel: +44 (0)161 276 4316; fax: +44 (0)161 276 8779; email: judith.harroo@cmmc.nhs.uk.
Fatigue is associated with high circulating leptin levels in chronic hepatitis C

M Romero-Gómez, D Sánchez-Muñoz and M Cruz

Gut 2003 52: 915
doi: 10.1136/gut.52.6.915

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