Award Lectures

FECS Clinical Research Award

1

The clinicopathological and molecular features of MALT lymphoma

P.G. Isaacson. *University College London Medical School, Department of Hematology, London, United Kingdom*

A distinctive type of extranodal B-cell lymphoma recapitulates the cytomorphological features of mucosa associated lymphoid tissue (MALT). Typically, these MALT lymphomas occur in tissues normally devoid of lymphoid tissue but are preceded by chronic inflammatory, usually autoimmune disorders that result in the accumulation of MALT. MALT lymphomas arise at a wide variety of extranodal sites the commonest of which is the stomach. Gastric MALT lymphomas arise in the setting of *H. pylori*, infection that is associated with accumulation of gastric MALT; eradication of *H. pylori* results in regression of 75% of these lymphomas. Curiously, idiotypic immunoglobulin (Ig) from MALT lymphoma B-cells shows specificity for auto-antigens rather than *H. pylori;* it is the reactive infiltrating T-cells that are *H. pylori* specific and, by providing contact help for the proliferation of the lymphoma B-cells, drive the growth of the lymphoma. Identification of those cases that do not respond to eradication of *H. pylori* is of some importance since it would save the multiple repeated endoscopies and gastric biopsies required for the follow-up and the non-responders could be offered conventional lymphoma therapy up-front. While it has been recognised that more deeply invasive lymphoma tend not to be unresponsive to antibiotics, there is no certainty which of those confined to the mucosa, which constitute the majority, will respond. In this context the genetic abnormalities associated with MALT lymphoma have been extensively investigated. Three different translocations, t(1;14)(p22;q32), t(11;18)(q21;q21) and t(14;18)(q32;q21) have been identified in MALT lymphomas. T(1;14) results in fusion of a novel gene, bcl10 with the Ig heavy chain (IgH) gene and causes aberrant intense nuclear expression of BCL10. T(11;18) results in a chimeric fusion between the API2 gene, an apoptosis inhibitor and the MALT1 gene, and is also associated with nuclear expression of bcl10 albeit at much weaker intensity. T(11;18) is present in approximately 20% of gastric MALT lymphomas and is associated with failure to respond to eradication of *H. pylori*. This can be exploited clinically using an RT-PCR strategy to identify the translocation that is applicable to paraffin embedded tissue. T(14;18) results in fusion of the IgH and MALT1 genes but has, as yet, not been found in gastric MALT lymphomas. All three translocations can be shown to activate NFκ B which is the common pathway that characterises MALT lymphomas. It is hoped that current micro-array studies, comparing lymphomas with and without these translocations and the different translocations with each other, will help more precisely to identify the exact molecular pathways in MALT lymphoma leading to more treatment strategies.

References

[1] Isaacson PG & Spencer J. Malignant lymphoma of mucosa-associated lymphoid tissue. Histopathol 1987; **11**: 445-462.
[2] Wotherspoon AC, Doglioni C, Diss TC, Pan LX, Moschini A, de Boni M, Isaacson PG. Regression of primary low-grade B-cell gastric lymphoma of mucosa-associated lymphoid tissue after eradication of *Helicobacter pylori*. Lancet 1993; **342**: 575-577.
[3] 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**: 571-574.
[4] Sackmann M, Morgner A, Rudolph B, *et al.* Regression of gastric MALT lymphoma after eradication of Helicobacter pylori is predicted by endosonographic staging. MALT Lymphoma Study Group. Gastroenterology 1997; **113**:1087-90
[5] Willis TG, Jadayel DM, Du Mq *et al.* Bcl10 is involved in t(1;14)9p22;q32)) of MALT B cell lymphoma and mutated in multiple tumor types. Cell 1999; 96: 35-45.
[6] Dierlamm J, Baens M, Wlodarska I *et al.* The apoptosis inhibitor gene API2 and a novel 18q gene, MLT, are recurrently rearranged in the t(11;18)(q21;q21)p6ssociated with mucosa-associated lymphoid tissue lymphomas. Blood 1999;**93**:3601-3609
[7] Liu H, Ye H, Ruskone-Fourmestraux A, et al T(11;18) is a marker for all stage gastric MALT lymphomas that will not respond to H. pylori eradication. Gastroenterology 2002;**122**:1286-1294
[8] Streubel B, Lamprecht A, Dierlamm J *et al.* T(14;18)(q32;q21) involving IgH and MALT1 is a frequent chromosomal aberration in MALT lymphoma. Blood 2003;**101**:2335-2339

Pezcoller Foundation/FECS Award

2

Supportive care in cancer – the ultimate challenge in modern multiprofessional oncology

H. Senn. *Zentrum für Tumordiagnostik und Prävention, St. Gallen, Switzerland*

Clinical, especially medical oncology, has greatly changed the prognostic outcome of many neoplastic diseases during the last 25 years: "incurable" types and stages of cancers have become "curable" and others have been "stabilized" for years with acceptable quality of life for the respective patients. However, despite remarkable progress and contrary to pediatric oncology, the outlook for the great majority of adult cancer patients, once the disease has come to a metastatic spread, is rather limited. In addition, modern "curative" oncology with its increased survival chances, imposes increasing toxicities with temporary inflictions on qualitiy of life on respective patients. It is on this background, that – as a consequence of increasing medical progress and failure – that supportive care in cancer (SCC) has evolved during the last 15 years as a "silent paradigm-shift" in modern oncology, where the holistic view of the patient's wellbeing –despite of his transient or ultimately fatal neoplastic illness – represents an important, independent outcome of care. SCC is not identical to palliative care: it is the total umbrella of rational medical, surgical, nursing, rehabilitative, psychosocial and spiritual supportive measures, which are necessary for a cancer patient to either better tolerate his active cancer therapies or to support him effectively, when tumor-directed treatments come to an end and symptom-relief and terminal care become the greatest challenge for the effective management of his condition. In this ultimate challenge of realistic SCC, a truely multiprofessional approach, uniting physicians of various specialities, experienced oncology nurses, psycho-oncologists and other cancer-directed health-professionals is inevitable. The medical profession ows great tribute to its nursing oncology colleagues and other non-medical health-professionals, having forced us to accept and cultivate this paradigm-shift "from cure to care", having also stimulated great efforts of clinical research in SCC during the last decade of the former century. It is extremely important, to integrate this multiprofessional way of assessing the patient's real needs and caring for his preponderant problems in common, multi-professional educational curricula at the international as well as national level, especially also within the boundaries of respective multinational societies, journals and quality-of-life oriented workshops. And above all: while the complexity of SCC definitely needs a global view, it has still to remain based at the national and regional level, respecting the various socio-cultural barriers prevailing in a historically divergent continent such as Europe.