Recent studies regarding somatic hypermutation of immunoglobulin genes show that both MALT lymphoma and Waldenström's macroglobulinemia are tumors of hypermutated post germinal center B lymphocytes that have undergone antigen selection.[1,7] All together, these data suggest a close relationship between these two entities from the perspective of cellular origin.

The maturation of small lymphoid cells into plasma cells, characteristic of Waldenström's macroglobulinemia, is also observed in 30–40% of low-grade MALT lymphomas. However, the appearance of a serum monoclonal component seems uncommon in MALT lymphoma. It has been reported in only one case of MALT lymphoma,[2] and seems much more common in the closely related nodal marginal zone B cell lymphomas.[6] The presence of a serum monoclonal component in MALT lymphoma might be due to extra-mucosal dissemination of the disease, especially in bone marrow, as illustrated in our first patient.

In conclusion, disseminated MALT lymphoma may mimick WM. Our observations suggest that some cases of MW with gastrointestinal involvement many in fact constitute disseminated forms of low-grade MALT lymphoma.

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Immunoglobulin lambda chain gene rearrangement in a case of acute nonlymphoblastic leukemia

TO THE EDITOR

Leukemic cells have been considered as the malignant counterpart of hematopoietic cells arrested at different stages of maturation. However, acute leukemias may occasionally display histochemical staining properties and/or cell surface antigens of more than one hematopoietic lineage and are considered hybrid leukemias.[1] This heterogeneity has been extended to the genomic level. Immunoglobulin heavy chain (*IGH*) genes have been found to be rearranged in T cell leukemias[2] and T cell antigen receptor α, β, γ and δ (*TCRA*, *TCRB*, *TCRG* and *TCRD*) gene rearrangements have been reported in B cell precursor leukemias.[3] Moreover, we and other groups have demonstrated the presence of gene rearrangement in case of ANLL (Ref. 4 and references therein). In this latter type of leukemias, the rearrangement of immunoglobulin (Ig) genes involves the *IGH* (10%) and Ig kappa light chain (*IGK*) (5%) genes whereas rearrangement of the Ig lambda gene (*IGL*) has never been reported.

In a series of 160 ANLL, we have systematically analyzed by Southern blot the genomic organization of the Ig and TCR genes and observed one patient that displayed rearranged *IGH* and *IGL* genes.[4] The patient, a 56-year-old male with a 2 week history of systemic symptoms, showed pallor without lymph node enlargement or hepato-splenomegaly in the physical examination. The blood count showed: Hb: 9.1 g/dl, platelets: 130×10^9/l, white blood cells: 2.9×10^9/l, with 43% granulocytes, 54% mature lymphocytes and 3% monocytes. No blast cells were observed in the peripheral blood. The bone marrow aspirate showed 60% of blasts cells displaying myeloid morphology and an increase of megaloblastic erythroid precursor with periodic acid Schiff (PAS) stain positivity (55%). A diagnosis of AML-M6 was established. Immunophenotypical studies showed that the blast cells expressed the myeloid antigen CD13 (80%) and a minor proportion the CD11b and CD71 antigens, while the CD14 antigen was negative, as well as markers for the megakaryocytic lineage (CD61 and CD41). Blast cells were negative for TdT and expressed neither B-lymphoid (CD19, CD20, CD10) nor T-lymphoid (CD3, CD7) antigens. Treatment with a conventional 3–7 day course of

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daunomycin and Ara-C was started but the patient died of septic shock during the aplastic phase of the first course.

Southern blot analysis of DNA with the probe pC76R51A, a 2.5 kb *Eco*RI–*Bgl*II genomic fragment containing the joining region of the *IGH* locus, demonstrated a single rearranged band after double and simple digestion (Figure 1). Hybridization with pBCk, a 2.5 kb *Eco*RI–*Eco*RI probe derived from the constant region of the *IGK* locus, failed to detect any rearranged band. However, the germline fragment was fainter in the patient than in the control DNA (Figure 1). Moreover, hybridization with the Kde probe, a 2.5 kb *Hin*dIII–*Bam*HI fragment derived from the kappa deleting element allowed us to demonstrate the presence of two rearranged bands, which suggest that both alleles might be deleted and that the faint germline band might correspond to contamination by residual non-leukemic cells (Figure 1). Analysis of the genomic organization of the *IGL* locus with HuλC2,C3, a 8 kb *Eco*RI–*Hin*dIII fragment that contains Cλ2 and Cλ3, demonstrated rearrangement of this gene after digestion with different restriction enzymes (Figure 1).

Rearrangement of the *IGH* genes has been previously reported to ocur in around 10% of cases of ANLL and a minority of these cases also show concomitant rearrangement at the *IGK* locus (Ref. 4 and references therein). Rearrangement of the *IGL* locus only occurs when kappa light chain gene rearrangement fails to generate a productive rearrangement what makes this rearrangement the ultimate to occur during B-lymphocyte differentiation. The absence of cases displaying isolated Ig light chain gene rearrangements in ANLL supports the notion that rearrangement of the Ig light chain locus requires previous *IGH* gene rearrangement[5] and that the leukemic cells maintain the normal hierarchy of gene rearrangement. Moreover, *IGL* gene rearrangement has only been described in leukemias of the B cell lineage probably due to the fact that it is an event that occurs late during B-lymphocyte development.

The present study illustrates a case displaying morphological and immunological criteria of ANLL that showed a rearrangement of the *IGL* locus. Although the use of cytoplasmic CD22 or CD79a would be of additional value to rule out a B-lineage origin, cells were not available for these additional tests. Nevertheless, the negativity for TdT, CD19, CD20 and CD10 are clearly against a B cell origin.

To the best of our knowledge, this is the first reported case of ANLL rearranging the *IGL* locus. The detection of a biallelic deletion at the *IGK* locus suggests that the leukemic clone is derived from a cell in which the hierarchy of Ig gene rearrangements has been maintained. The nature of this lineage infidelity is unclear. As recently proposed[6] these leukemias could result from a transformational event occurring at an early stage of normal hematopoietic development in a bipotential cell with the genetic program of both lymphoid and myeloid cells. Alternatively, myeloid leukemic cells displaying Ig gene rearrangement might represent a lymphoid cell whose differentiation program has gone astray, leading to inappropriate expression of genes from the wrong lineage. Another plausible explanation for cross-lineage Ig locus rearrangement in AML is the aberrant activity of the recombinase enzyme system in a myeloid precursor cell resulting in an otherwise 'normal' hierarchical Ig gene rearrangement pattern.

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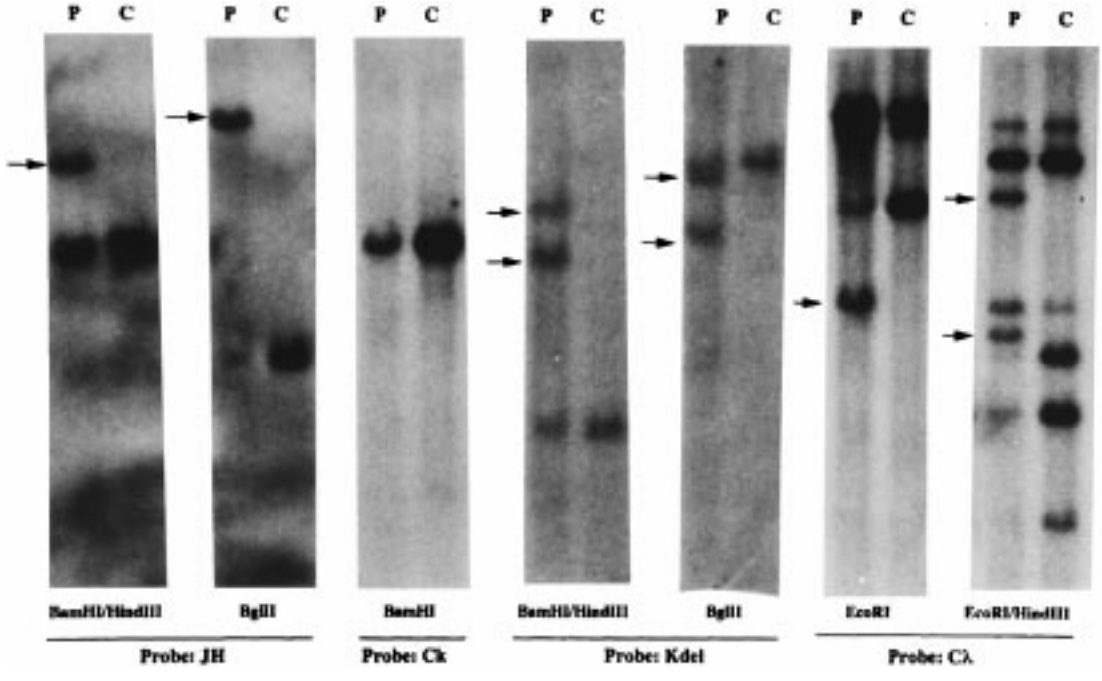

Figure 1 Southern blot analysis of the *IGH*, *IGK* and *IGL* genes. (P, DNA from the patient; C, DNA from a control). The arrows point to the rearranged fragments.

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