HEMATOLOGY

Late relapse or new disease?

Leukemia recurrence frequently appears as a consequence of the outgrowth of the original tumor cell population that was not completely eliminated during treatment. Relapse can occur during or shortly after therapy. Generally, recurrence during or immediately after the completion of treatment is associated with a less-favorable prognosis than recurrence occurring 2 years after treatment.

Jacques van Dongen and colleagues had previously found that in T-cell acute lymphoblastic leukemia (T-ALL), gene rearrangements in the T-cell receptor (TCR)—which are routinely used in leukemia to detect minimal residual disease—at first diagnosis and at relapse were remarkably similar. This led them to confirm that the relapse was in fact an evolved clone from the original leukemia. However, two of the 28 patients showed very different gene rearrangements. As these patients presented with recurrence

at least 2.5 years after treatment, which they called late T-ALL relapse, the investigators concluded that these patients might have developed a second and new disease, independent of the first one.

Using comparative TCR gene sequencing, the researchers analyzed bone marrow samples from first diagnosis and relapse from 22 patients with late T-ALL relapse. “This allowed us to firmly conclude that in eight out of 22 patients with late T-ALL disease recurrence, in fact, a second T-ALL had developed,” explains van Dongen. In these eight patients, TCR gene rearrangements and the pattern of mutations in *NOTCH1* were completely different at diagnosis than at second presentation.

The fact that two different T-ALLs might successively develop in one single patient suggests the possibility of a genetic predisposition to develop T-ALL; a possibility that was supported by the finding of a T-ALL related genetic

aberration in the DNA of non-leukemic cells in one patient. The researchers are now carrying out further studies in the other seven patients: “this is a unique finding because, so far, proven genetic predisposition has never been reported in acute leukemia,” van Dongen comments.

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Original article Szczepanski, T. *et al.* Late recurrence of childhood T-cell acute lymphoblastic leukemia frequently represents a second leukemia rather than a relapse: first evidence for genetic predisposition. *J. Clin. Oncol.* doi:10.1200/JCO.2010.30.2877