Editoriais / Editorials

Interaction of clinical, genetic and molecular features in chronic lymphocytic leukemia

Interação da clínica e dos aspectos genéticos e moleculares na leucemia linfóide crônica

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In recent years, the life expectancy of the Brazilian population has been increasing, leading to an increase in the incidence of chronic lymphocytic leukemia (CLL). This B-cell malignancy presents a wide range of clinical presentations as well as aggressiveness in its clinical course. According to reports from Brazil and other countries,[1-6] 2/3rd of patients have a low tumor burden at diagnosis and do not need up-front treatment. Many of these patients stay stable for long periods and probably will die from causes unrelated to CLL. Binet stage A, a low peripheral lymphocyte count and total tumor mass, a long lymphocyte doubling time, and a low proliferative rate as well as a high apoptotic rate of CLL cells in culture have been associated with these cases.[1-6]

Recent studies have better clarified the pathobiology of CLL, demonstrating several biologic and genetic features associated with its clinical diversity and the probability of progression. Thus, unmutated VH status, cytogenetic alterations such as del 11q or del 17p and expression of CD38 and ZAP-70 have been associated with a worse prognosis.[5-7] It has also been shown that the absence of ZAP-70 expression is strongly associated with the methylation of a highly conserved intronic region of its gene, suggesting that this is the mechanism of regulation of the expression of this protein in CLL cells.[8]

The interaction of several biological and clinical prognostic factors in CLL was examined by Nascimento MC et al.[9] (results published in this issue). Although the authors studied only 29 patients, precluding the finding of statistical significance for several possible associations, they observed a significantly higher frequency of unfavorable cytogenetic findings in women. A normal karyotype or del 13q14 was more often observed in patients aged < 60 years (although this association was not significant) and those not expressing CD38. Expression of ZAP-70 was not significantly associated with any specific karyotype.

New studies based on a larger number of cases are needed in order to better clarify the interaction between all these genetic and molecular features leading to an unfavorable phenotype and a more aggressive clinical course, especially in patients presenting a low tumor burden at diagnosis but having a high probability of progression, and permitting the early start of treatment and therefore prolonging the survival. This hypothesis however, has not been proven yet.[6,7] These patients should, at present, only be treated in well-designed randomized clinical trials. It has also been pointed out that chemotherapy could select resistant clones and therefore precipitate a bad outcome.[7] On the other hand, as these patients often present co-morbidities and have frequent complications after chemotherapy, it is important to detect the cases with a low chance to progress and therefore really do not need treatment.

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