

Review / Revisão

T-lymphoblastic lymphoma in adults

Linfoma linfoblástico-T em adultos

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In this short opinion review we discuss recent aspects of T-lymphoma lymphoblastic adults, like the evolution of the knowledge of classification, prognostic factors and the patients management. Rev. Bras. Hematol. Hemoter. 2009;31(Supl. 2):19-20.

Key Words: *Lymphoma lymphoblastic; classification; prognostic factors; treatment.*

Introduction

Adult lymphoblastic lymphoma (LBL) is a rare disease which represents less than 2% of all non-Hodgkin's lymphomas (NHL). More than 80% of adult LBL, which is more common in adolescents and young patients, have a T-cell phenotype.¹ T-cell lymphoblastic lymphoma (T-LBL) is an aggressive disease with frequent mediastinal involvement at diagnosis, but also with frequent involvement of extranodal sites such as bone marrow (BM) and central nervous system (CNS). At presentation the disease is often in Stage IV. T-LBL cells show morphological and phenotypic aspects similar to acute T-lymphoblastic leukemia (T-ALL), even though T-ALL cells are mainly pre-thymic and T-LBL cells mostly originate from the cortex and medulla of the thymus.

Evolution, classification and prognostic factors

Due to the rarity of the disease, several management issues must still be defined.

In the 1980s, following a series of disappointing results, the adoption of sequential intensified and prolonged chemo/radiotherapy associated with CNS prophylaxis dramatically improved outcomes in adult LBL patients with complete remission (CR) rates ranging from 75% to 95%. However, in spite of these initial stimulating results, the majority of patients relapsed during and after the completion of treatment, lasting from one to three years. The 3-year progression-free survival and overall survival (OS) of these

patients appeared to be about 20%.² A variety of clinical features were indicated as being responsible for relapse, such as age, advanced stage, B symptoms, LDH elevation and BM or CNS involvement. However, only small series of patients were analyzed in single reports and the "negative factors" defining a "prognostic model" were very variable and no risk factors for relapse could be identified.

In the 1990s, the high CR rate and subsequently, the high relapse rate, determined the rationale for the use of high-dose therapy and autologous stem cell transplantation (ASCT) for adult LBL in first CR. Results reported by several studies showed that, in this subset of patients, a long-term disease-free survival (DFS) of about 60%-75% could be achieved.³ These data compared favorably with results observed with conventional chemotherapy, but the problem of the real usefulness of ASCT in first CR remained to be established. The randomized study of the European Group for Blood and Marrow Transplantation and the United Kingdom Lymphoma Group, comparing conventional CT and ASCT in adult LBL in first CR, showed a statistical trend in terms of DFS in favor of ASCT with a similar overall survival.⁴ Once again, no risk factors were detected. Allogeneic SCT in first CR adult LBL patients is characterized by a DFS similar to that obtained with ASCT: a higher relapse rate occurs in the ASCT setting while a higher toxicity and mortality rate is observed in the allogeneic setting.⁵ More recent studies did not modify the previously reported data and the dilemma of which patients may benefit from high-dose therapy and SCT remains.

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At the beginning of the third millennium, the German, the American and the French Groups report excellent results in adult T-LBL using different approaches. These include aggressive induction-consolidation therapies, intrathecal CT prophylaxis, mediastinal irradiation, and maintenance with or without re-induction therapy. In these studies, more than 90% of the patients achieve CR, the relapse rate is about 30%-35% and 50%-60% of the patients are long-term survivors.^{6,7} These results are very similar to those observed with the use of HDT plus SCT. Bone marrow and CNS involvement seem to be risk factors predicting a poor outcome.

No biological data, including correlation between T-phenotype differentiation and outcome, are available. In T-LBL, T-cell receptor genes almost invariably show monoclonal re-arrangement detectable with the PCR technique. Monitoring of minimal residual disease (MRD) has been shown to be highly predictive in childhood T-ALL and this approach should also be predictive in adult T-LBL. However, similar studies have still not been performed in adult T-LBL. More recently, analysis of gene expression profile (GEP) studies involving the use of DNA microarrays were able to detect some signatures corresponding to specific maturation stages observed during the development of normal thymocytes.⁸ A number of other GEP based studies have identified several gene prognostic factors. Nevertheless, the majority of such studies were carried out on pediatric patients while no studies have involved adult T-LBL.

Conclusion

In conclusion, up to now, prognostic models, based either on clinical or molecular biology data to judge the risk of adult T-LBL patients and to choose the best therapeutic option are not available. Therefore, future prospects for improvement of treatment results in adult T-LBL patients include intensified CT, definition of prognostic factors, study of minimal residual disease and study of the biological properties of the disease.

Following all these considerations, in Italy an "observational clinical and biological study on adult T-LBL patients" has been designed. The principal end-point is to collect a large number of clinical and biological data on LBL. This national study is now requesting a large international participation in order to overcome the natural problems of a truly rare disease such is adult T-LBL. The "Associazione Italo-Brasileira di Ematologia" (AIBE) which has brought Italian and Brazilian hematologists together is very enthusiastic about this study. We hope that many countries accept our invitation to participate in order to answer so many unresolved questions.

Resumo

Nesta breve revisão os autores apresentam diversos aspectos de evolução dos conhecimentos na classificação e no manuseio dos pacientes portadores de linfoma linfoblástico-T em adultos. Rev. Bras. Hematol. Hemoter. 2009;31(Supl. 2):19-20.

Key words: Linfoma linfoblástico; classificação; fatores de prognóstico; tratamento.

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O tema apresentado foi proposto pela Organização do 8º Simpósio da Associação Ítalo-Brasileira de Hematologia, realizado durante o XIII Congresso de Transplante de Medula Óssea. Publicado após concordância do editor.

Conflito de interesse: sem conflito de interesse

Recebido: 07/07/2009

Aceito: 16/07/2009