Critical Reviews in Oncology/Hematology 113 (2017) 304–317

Contents lists available at ScienceDirect

Critical Reviews in Oncology/Hematology

journal homepage: www.elsevier.com/locate/critrevonc

Lymphoblastic lymphoma

Sergio Cortelazzo[a,*], Andrés Ferreri[b], Dieter Hoelzer[c], Maurilio Ponzoni[b]

[a] Oncology Unit, Humanitas/Gavazzeni, Bergamo, Italy
[b] San Raffaele Scientific Institute, Milan, Italy
[c] Onkologikum, J.W. Goethe University, Frankfurt, Germany

Contents

* Corresponding author.
E-mail address: sergio.cortelazzo@gmail.com (S. Cortelazzo).

http://dx.doi.org/10.1016/j.critrevonc.2017.03.020

ARTICLE INFO

Article history:
Received 6 October 2016
Received in revised form 12 March 2017
Accepted 15 March 2017

Keywords:
Lymphoblastic lymphoma
Autologous stem-cell transplant
Allogeneic transplant
CNS prophylaxis

ABSTRACT

Lymphoblastic lymphoma (LBL) is a neoplasm of immature B cells committed to the B-(B-LBL) or T-cell lineage (T-LBL) that accounts for approximately 2% of all lymphomas. Although histological features are usually sufficient to distinguish lymphoblastic from mature B- or T-cell neoplasms, of greater importance for diagnosis is the characterization of immunophenotype by flow cytometry. LBL occurs more commonly in children than in adults, mostly in males. A bone marrow involvement <25% (or 20% according to WHO) formally distinguishes LBL from ALL. The prognosis of LBL has dramatically improved with the use of intensive ALL-type chemotherapy regimens, which includes intensive intrathecal chemotherapy prophylaxis and consolidation with mediastinal irradiation. Patients with adverse prognostic features assessed by postinduction CT/positron emission tomography scans (PET) and minimal residual disease analysis (MRD) should be considered for high-dose chemotherapy and stem cell transplantation. Further therapeutic progresses are expected from the introduction of new drugs and targeting agents.

1. General information

1.1. Epidemiology

1.1.1. Incidence

Lymphoblastic lymphoma (LBL) is a rare disease accounting for approximately 8% of all lymphoid malignancies (RARECAREnet, 2017). In Europe, incidence is estimated by the RARECAREnet project with LBL including the following ICD-O morphology codes 9687, 9727–9729, 9826, 9835–9837 and it is labelled as "Precursor B/T lymphoblastic leukaemia/lymphoblastic lymphoma (and Burkitt leukaemia/lymphoma)". The project estimated slightly more than 7000 new cases in 2013 in EU28.

Based on about European 22,800 cases, diagnosed during the period 2000–2007, the annual incidence rate was very low with a rate of 1.5 per 100,000 and with a significant increase of incidence: from 1.37 to 1.61 per 100,000 during the period 2000–2007. LBL is more frequent in males than females, with a male/female ratio of 1.4. The highest rate was in children (<15 years) with a rate of 3.6 per 100,000, then reduced to 0.8 in people aged 25–64 years aged and increased to 1.7 in the oldest age group of cases (65+ years). The disease was more frequent in Southern Europe (1.9) and low in Eastern European Countries (1.1) (RARECAREnet, 2017).

1.1.2. Survival

For European patients diagnosed 2000–2007, 5-year survival was bad in the oldest patients (65 years or more; 86%) and good in children (0–14 years; 90% (RARECAREnet, 2017; Reiter et al., 2000). Prognosis was intermediate in adolescents and young adults (15–24 years) and in adults (25–64 years): 5-year survival was 60% and 39%, respectively (RARECAREnet, 2017) In European adults, from 1997 to 1999 to 2006–2008 survival increased from 30% to 41% (Sant et al., 2014). However, improvements in survival were not homogeneous across Europe, which could be a result of persisting inequalities in the provision of care. Survival was significantly lower in Eastern and Southern Europe, and higher in Northern Europe in comparison with the UK (reference region) in a model adjusted for age, period, and year of follow-up (Sant et al., 2014). In European children affected by acute lymphoblastic leukaemia, most Central and Northern European Countries, the UK, Malta, and Italy had a 5-year survival (adjusted for age, sex, and period of diagnosis) higher than the European mean, whereas Bulgaria, Estonia, Latvia, Lithuania, and Slovakia had the lowest (<80%).Five-year survival increased with a risk of dying for childhood lymphoblastic leukaemia falling on average by 6% per year. The most notable improvements were in Eastern Europe, where 5-year survival rose from 65% in 1999–2001 to 70% in 2005–2007 (Gatta et al., 2014).

1.2. Risk factors

1.2.1. Ionizing radiation

The major studied risk factors for LBL is ionizing radiation during childhood and young adulthood. It is well established that exposure to high doses prenatally and early in life increases cancer rates in human and animals (Anderson et al., 2000) and that foetus and young children are more susceptible to the effect of ionizing radiation than adults. Evidence is based on studies about atomic bomb survivors who received high dose (up to 200 mSv) in an acute dosage (Preston et al., 1994) and from those foetuses who received X-rays in utero with much lower radiation dosages (Lightfoot and Roman, 2004). However, other sources such as diagnostic imaging during pregnancy contributes with a lower dosage.

1.2.2. Infections

Several viruses have been found to be involved as factor in the pathogenesis of haematological entities. They are the HTLV-I for acute T cell leukaemia/lymphoma, HIV and HHV-8 for the group of non Hodgkin lymphomas (NHLs). The first (HTLV-I) acts as a direct carcinogen in adult T cell leukaemia/lymphoma; the other viruses as indirect carcinogens. Adult T-cell leukaemia/lymphoma (ATLL) occurs almost exclusively in areas where HTLV-1 infection is endemic (South-Western Japan, the Caribbean, and parts of Africa and South America). The cumulative incidence of ATLL among HTLV-1 carriers was estimated 1%–5% in endemic areas (Murphy et al., 1989a; Proietti et al., 2005). ATLL occurs mostly in adults, at least 20–30 years after the onset of HTLV-1 infection; this infection mostly occurs during childhood. HTLV-1 can be transmitted from mother to child through breastfeeding and via transfusion of infected blood products or sharing of needles and syringes and via sexual intercourse (Manns et al., 1999). One per cent of all leukaemias is attributable to HTLV-1 (Pisani et al., 1997). The HIV type 1 operates with immunesoppression and greatly increased in immunosuppressed individuals. Indeed, infection with oncogenic viruses is much more common than the diseases that these viruses cause, and incidence and severity of these cancers is greatly increased by immunosuppression. HIV-1 is transmitted by sexual intercourse, blood contact, and from mother to infant. Globally, an estimated 35.3 million people were living with HIV (HIV-1 and HIV-2) in 2012. About 95% of new HIV infections occur in less developed regions. In 2012, the prevalence of HIV ranged from less than 0.5% in more developed regions to up to 26% in some Countries in the sub-Saharan Africa (UNAIDS, 2013). Also the Hepatitis C virus (HCV) can cause B-cell non Hodgkin lymphoma. The virus acts via chronic inflammation. HCV can be transmitted by transfusion of blood