Transfusion and Apheresis Science 54 (2016) 80–84

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

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

Primary central nervous system lymphoma in daily practice and the role of autologous stem cell transplantation in relapsed disease: A retrospective multicenter study

Mehmet Ali Erkurt [a,*], Ilhami Berber [a], Emre Tekgündüz [b], Mehmet Hilmi Dogu [c], Serdal Korkmaz [d], Cengiz Demir [e], Mehmet Yilmaz [f], Olga Meltem Akay [g], Ciğdem Pala [h], Yusuf Bilen [i], Emin Kaya [a], Ismail Sari [c], Mehmet Sencan [j], Irfan Kuku [a], Fevzi Altuntaş [b,k], Mehmet Sinan Dal [b], Ismet Aydogdu [l]

[a] Department of Hematology, Inönü University Medical Faculty, Malatya, Turkey
[b] Hematology and HCT Clinic, Ankara Oncology Hospital, Ankara, Turkey
[c] Department of Hematology, Pamukkale University Medical Faculty, Denizli, Turkey
[d] Hematology Division, Kayseri Trainer and Research Hospital, Kayseri, Turkey
[e] Department of Hematology, Yüzüncü Yıl University Medical Faculty, Van, Turkey
[f] Department of Hematology, Antep University Medical Faculty, Gaziantep, Turkey
[g] Department of Hematology, Osmangazi University Medical Faculty, Eskişehir, Turkey
[h] Department of Hematology, Erciyes University Medical Faculty, Kayseri, Turkey
[i] Department of Hematology, Atatürk University Medical Faculty, Erzurum, Turkey
[j] Department of Hematology, Cumhuriyet University Medical Faculty, Sivas, Turkey
[k] Department of Internal Medicine, Division of Hematology, Yıldırım Beyazıt University Medical Faculty, Ankara, Turkey
[l] Department of Hematology, Celal Bayar University Medical Faculty, Manisa, Turkey

ARTICLE INFO

Keywords:
Autologous stem cell transplantation
CNS lymphoma
PCNSL
Methotrexate
High-dose chemotherapy

ABSTRACT

We investigated the course of 54 patients presenting with primary central nervous system lymphoma, who were treated in daily practice. The patients were treated with chemotherapy and/or radiotherapy and/or intrathecal chemotherapy. At a median follow-up period of 23 months (range 1–71), median relapse-free survival (RFS) and overall survival (OS) were not reached. Estimated 2-year RFS and OS rates were 42% and 48%, respectively. Ten relapsed PCNSL patients underwent ASCT. Complete remission rate of these patients was 40%, with 20% treatment-related mortality. Estimated 2-year RFS and OS rates were 37% and 40%, respectively. The prognosis of patients with PCNSL, who received off-study treatment, is still dismal.

1. Introduction

Primary central nervous system lymphoma (PCNSL) is an extranodal non-Hodgkin lymphoma, which is classified as a discrete entity in the classification of the WHO [1]. It is an aggressive malignancy that involves the brain parenchyma, spinal cord, eyes, cranial nerves and meninges [2,3]. The PCNSLs constitute about 1% of all non-Hodgkin lymphomas, 4% of intracranial lymphomas and 4–6% of extranodal lymphomas. The great majority (90%) of the PCNSLs are diffuse large B-cell lymphomas (DLBL), and the remaining cases are Burkitt lymphomas, other low-grade lymphomas and T-cell lymphomas [4]. PCNSL is a rare disease of increasing incidence mainly affecting the elderly. The major risk factor for PCNSL is immunodeficiency, especially the HIV infections [5].

* Corresponding author. Department of Hematology, Inönü University Medical Faculty, TR-44069 Malatya, Turkey. Tel.: +90 422 341 0660, ext. 4203; fax: +90 422 341 07 28.
E-mail address: erkurtali@hotmail.com (M.A. Erkurt).

http://dx.doi.org/10.1016/j.transci.2016.01.018
1473-0502/

The standard approach to PCNSL, that is high-dose methotrexate (HDMTX)-based chemotherapy followed by whole brain radiotherapy (WBRT), is associated with disappointing outcome. Moreover, this strategy is associated with increased risk of disabling neurotoxicity, especially in elderly patients. Several drugs and strategies have been investigated to improve results and neurotolerability. Among others, some investigators focused on the use of high-dose chemotherapy supported by autologous stem cells transplantation (HDC/ASCT) as consolidation after primary chemotherapy [6] and patient affected by relapsed/refractory PCNSL [7–9].

Current therapeutic knowledge in PCNSL management results from a limited number of single-arm phase II trials, meta-analyses and large retrospective series. The evaluation of new first-line chemotherapy combinations in non-randomized trials did not produce therapeutic progress because of the intrinsic limitations of comparison across series with heterogeneous patient populations. Thus, several questions like the optimum primary chemotherapy, the identification of new active drugs and the role of intrathecal chemotherapy, consolidation radiotherapy and HDC/ASCT remain unanswered. The latter is an important issue since preliminary evidence seems to suggest a central role for this strategy in PCNSL.

In this report we retrospectively analyzed the outcome of patients with PCNSL.

2. Materials and method

A total of 54 consecutive patients from 12 centers with biopsy-proven PCNSL between 2007 and 2015 were included. The data of the patients were retrospectively obtained from hospital records. Seven patients (12.9%) were in poor physical condition with a WHO performance status (PS) of 3–4. The histopathological types were diagnosed according to the WHO lymphoma classification [1]. Systemic lymphoma had to be excluded by bone marrow examination, thoracic and abdominal computed tomography (CT) as minimal requirements. Positron emission tomography scans were done for some patients. Pretreatment evaluation included a lumbar puncture (cerebrospinal fluid cytology), ophthalmologic examination, and HIV-1 antibody titers in the majority of patients. The protocol was reviewed and approved by the local institutional review board of Inonu University. All patients gave written informed consents for all aspects of therapy and HDC/ASCT. Response to treatment was determined according to established guidelines [10]. Neuroimaging evaluations were obtained before administration of corticosteroids, before each step of chemotherapy and radiation, and after completion of all treatment.

Treatment options were grouped as chemotherapy only (Chemo), radiotherapy only (RT), chemotherapy plus radiotherapy (Chemo/RT), chemotherapy plus radiotherapy and intrathecal therapy (Chemo/RT/ITT).

2.1. Statistical analysis

The numerical data were presented as median–range, and categorical data were presented as frequency–percentage in the descriptive tables. Comparisons of numerical data between the independent groups were performed with Mann–Whitney-U statistics, and categorical data were compared with chi-square test. The survival analyses were performed using the Kaplan–Meier method, and survival times were compared between independent factors by log–rank test. A p value <0.05 was considered significant. IBM SPSS 21 was used for the analyses.

3. Results

The study included a total of 54 patients. The demographic and clinical characteristics of the study cohort were summarized in Table 1. None of the patients had HIV infection, immunodeficiency, immunosuppressive treatment, and transplantation history. Forty-nine, 2 and 3 patients were diagnosed with diffuse large B-cell lymphoma (DLBCL), B-cell lymphoblastic lymphoma, Burkitt lymphoma, respectively. None of the patients had lymphadenopathy and organomegaly. All patients had normal cerebrospinal fluid analyses. Two, 8, 20 and 24 patients received RT, Chemo, Chemo/RT and Chemo/RT/ITT, respectively. Among patients who received chemotherapy as part of induction, 22 (40.8%) patients were treated with HDMTX only, while 30 (59.2%) patients received HDMTX plus high-dose cytarabine-based combination chemotherapy (HDMTX/HDARA-C) protocols. The patients received median 3 cycles of chemotherapy. None of the patients received upfront HDC/ASCT as part of consolidation. At least one adverse event related to chemotherapy was positive in 68.5% of the patients. Most common grades III/IV adverse events related to the chemotherapy were neutropenia 46.2%, fever 22.2%, thrombocytopenia 18.5%, acute renal failure 11.1%, and pancytopenia 5.5%.

Following induction treatment 20 (37%) and 18 (33.6%) achieved complete and partial response, respectively. Sixteen

Table 1
The demographic and clinical characteristics of patients at diagnosis.

Parameter	Result
Age (years) (median; range)	53 (19–82)
Gender (n; %) (female/male)	18 (33.3%)/36 (66.7%)
Family history of cancer (n; %)	8 (14.8%)
Leptomeningeal involvement (n; %)	10 (18.5%)
Spinal cord/nerve root compression or extradural disease (n; %)	4 (7.4%)
Intracranial mass (n, %)	52 (96.2%)
B symptoms (n; %)	24 (44.4%)
Extremity weakness (n; %)	36 (66.7%)
Paresis or paralysis (n; %)	31 (57.4%)
Cranial nerve involvement (n; %)	11 (20.3%)
Impaired vision (n; %)	10 (18.5%)
Pathological signs in ophthalmologic examination (n; %)	7 (12.9%)
Headache (n; %)	43 (79.6%)
Lethargy (n; %)	18 (33.3%)
Papilledema (n; %)	6 (11.1%)
Seizures (n; %)	11 (20.3%)
Ataxia (n; %)	6 (11.1%)
Hearing loss (n; %)	2 (3.7%)
Aphasia (n; %)	2 (3.7%)
Deep venous thrombosis (n; %)	2 (3.7%)
Peripheral neuropathy (n; %)	12 (22.2%)
Multifocal CNS mass lesion (n; %)	12 (22.2%)
Solitary CNS mass lesion (n; %)	42 (77.8%)

CNS: central nervous system.