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Original research article

Central nervous involvement by chronic lymphocytic leukaemia

Dariusz Szczepanek [a], Ewa Wąsik-Szczepanek [b], Agnieszka Szymczyk [b,c,*], Małgorzata Wach [b], Maria Cioch [b], Monika Podhorecka [b], Ewelina Grywalska [d], Marek Hus [b]

[a] Department of Neurosurgery and Paediatric Neurosurgery, Medical University of Lublin, Poland
[b] Department of Haematooncology and Bone Marrow Transplantation, Medical University of Lublin, Poland
[c] Independent Clinical Transplantology Unit, Medical University of Lublin, Poland
[d] Department of Clinical Immunology, Medical University of Lublin, Poland

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ABSTRACT

Inclusion of the central nervous system (CNS) in the course of chronic lymphocytic leukaemia (CLL) is rare. At the moment no risk factors or proven treatment methods are known. The disease is described both in its early phase and during its acceleration period, thus it has been suggested that there might be independent mechanisms influencing the development of this condition. As there are no unified diagnostic procedure algorithms each patient needs to be assessed individually. CLL can manifest mostly in elderly people, for whom a possibility of development of neurological disorders with their aetiology different from leukaemia, should also be taken into consideration. The thesis presents a group of seven patients with CLL with CNS infiltration. Patients with prolymphocytic leukaemia, Richter's transformation and the original location of leukemic infiltration within the eye socket constitute an especially interesting case.

1. Introduction

Chronic lymphocytic leukaemia (CLL) is a disease that is characterised by a clonal proliferation and accumulation of mature B lymphocytes in peripheral blood, bone marrow and lymphoid tissues [1]. A different location is very rare and is usually connected with the skin and central nervous system (CNS) [2]. Despite that fact, CLL belongs to the type of proliferation in which the central nervous system involvement (CNSi) is seldom considered, contrary to infective, immunological complications or transformation of Richter syndrome (RS) [3]. At the moment no CNSi risk factors or unified proven treatment methods are determined. It results mainly from a small group of patients with such condition (in the last 40 years fewer than 100 cases of CLL and CNSi have been

* *Corresponding author at*: Department of Haematooncology and Bone Marrow Transplantation, Independent Clinical Transplantology Unit Medical, Medical University of Lublin, Staszica 11 Str., 20-081 Lublin, Poland.
E-mail address: agnieszka.szymczyk.med@wp.pl (A. Szymczyk).
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described) [3]. The most often described patients had CLL with meninges and cranial nerve, but extremely rarely with the brain and spinal cord. What is characteristic is a highly diverse clinical manifestation, although the neurological symptoms can be observed in a small number of patients, and in case of histologically confirmed affection of meninges, it concerns only 1% of the examined [4,5]. Thus, we can probably talk about a significant underestimation of the number of patients with this illness.

1.1. *Objective*

The objective of this research paper is a retrospective analysis of patients with CLL/SLL and CNS infiltration.

2. Materials and methods

The analysis included patients with CLL/SLL diagnosed in the years 2007–2016. In this timeframe, 223 CLL/SLL patients were treated. Apart from patients with inclusion of the CNS in the course of CLL, 102 women and 114 men at a median age 64.9 years (34–87 years), Rai stage 0–4 and Ann Arbor II-IV clinical stage, has been observed or treated.

Based on a retrospective analysis we have conducted an assessment of the clinical, biological and radiological parameters (magnetic resonance imaging; MRI, computed tomography; CT) of the patients with CLL and CNSi, in the period from February 2007 to March 2015. Five patients had lumbar puncture done with the collection of cerebrospinal fluid (CSF). The CSF tests included the cytological, biochemical, cytometric and microbiological evaluation. In three cases material for histopathological tests was also collected. Clinical, immunophenotyping and genetic parameters of the CLL patients at the moment of diagnosis of CNSi are shown in Table 1.

3. Results

Seven patients with CLL, who were diagnosed with CNSi were analysed. They were four men and three women aged between 43 and 76 years old. They were in the stadium 0–3 according to Rai et al. classification. The CNSi diagnosis was determined based on the flow cytometric analysis of the CSF in five patients and histopathological examination in three patients (in two patients, based on the autopsy: patient nos. 3 and 5). Three patients received intrathecal treatment, one had a neurosurgical procedure (total resection of the tumour) followed by radiotherapy. Three patients due to their serious general condition did not receive the cytostatic treatment. All patients were radiologically diagnosed (MRI/CT) and they manifested diverse neurological symptoms. Neurological disorders, radiological image, received treatment of patients with CLL and CNSi and test results of the cerebrospinal fluid are shown in Tables 2 and 3 and Figs. 1 and 2.

4. Discussion

Affecting the CNS in the course of non-Hodgkin's lymphomas (NHL) is observed in approx. 8% of patients [6,7]. It is mostly observed in case of the most aggressive histopathological types, such as e.g. Burkitt lymphoma or lymphomas of specific locations (testicular lymphoma, lymphoma around the paranasal sinuses) [8,9]. There are several hypotheses attempting to explain the mechanisms leading to affecting the CNS in the course of CLL. One of them indicates a possibility of the

Table 1 – Clinical characteristics, immunological and genetic parameters of patients with CLL at the time of CNSi diagnosis.

	Patient 1	Patient 2 (CLL/PLL)	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age (year)/sex	63/M	43/M	54/M	70/F	76/K	56/M	70/K
Rai clinical stage	0	2	2	2	2	0	3
Stage of disease during CNSi	Stable disease	Progression		(transformation into PLL)	Progression (Richter's transformation)	Progression	Stable disease
Stable disease	Stable disease						
Prior therapy for CLL	0	0	COP, CHOP, FC, F,	ofatumumab + idelalisib	B, BR	0	0
0							
Genetic aberrations	Not found	Not done	Not found	del11q	Not found	Not found	Not found
ZAP-70/CD38	ZAP-70−/CD38+	Not done	ZAP-70−/ CD38+	ZAP-70−/CD38−	ZAP-70−/CD38−	ZAP-70−/CD38+	ZAP-70+/CD38+
Time between CLL and CNSi diagnosis (month)	3	2	71	27	0	0	0
Follow up (month)	38	3	1	2	1	126	3
Status at last follow up	Alive	Death	Death	Death	Death	Alive	Death

C – cyclofosfamide; O – vincristine; H – doxorubicin; P – prednisone; F – fludarabine; B – bendamustin; R – rituximab.

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