

Clinical and Neurological Features of Patients with Chronic Lymphocytic Leukemia

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Abstract The prevalence of chronic lymphocytic leukemia in the Republic of Uzbekistan is 5.24 per 100,000 population. According to various literature data, damage to the nervous system in chronic lymphocytic leukemia, unlike other lymphoproliferative diseases, is diagnosed very rarely. Objective. To study the clinical and neurological characteristics of patients with chronic lymphocytic leukemia. Material and methods. 130 patients with chronic lymphocytic leukemia were examined at the Khorezm branch of the Republican Scientific Research Center of Hematology and Transfusiology of the Ministry of Health of the Republic of Uzbekistan (Khorezm branch of the Republican Scientific Research Center of Hematology and Transfusiology of the Ministry of Health of the Republic of Uzbekistan). The scientific research was based on the results of patients with CLL who were treated as inpatients from 2014 to 2023. Of these, 71 were men (54.6%) and 59 were women (45.4%). The ratio of men to women was 1.2:1. Results. All patients in the study underwent various courses of polychemotherapy. Patients underwent 3 courses of polychemotherapy during the follow-up period. Before the start of the study, patients had received an average of 4 courses of polychemotherapy (maximum 24 times and minimum 1 time). In our study, 29 patients underwent their first course of PCT. After 3 months, the average number of PCT courses patients had undergone was 7 (maximum 27 times and minimum 4 times) (Fig. 1). Patients with chronic lymphocytic leukemia mainly complained of general weakness, tremor and unsteadiness, hearing loss, dizziness, memory loss, and headache. Only 17 of 130 patients (13.08%) did not complain during the anamnesis collection. In 36 (26.67%) patients, no changes were found in the neurological examination. Vestibulo-atactic syndrome was the majority of neurological disorders in 57 (43.85%) patients. Sensory disturbances were observed in 7.69% of patients, including polyneuropathy in 5.38% and hemihypesthesia in 2.31%. Conclusion: The development of neurological syndromes is influenced not only by comorbidities, but also by the CLL disease itself and the complications of polychemotherapy. Neurological symptoms in patients do not appear as a result of true neurological pathology, but rather during treatment and as a result of CLL intoxication.

Keywords Chronic lympholeicosis, Neurological complications, Damage to the nervous system

1. Introduction

Lymphoproliferative diseases are malignant and benign neoplasms that develop from lymphoid cells at various stages of differentiation [1]. One of the most common diseases in this group is chronic lymphocytic leukemia (CLL). The prevalence of chronic lymphocytic leukemia in the Republic of Uzbekistan is 5.24 per 100,000 population [2,4]. According to various literature data, nervous system damage in chronic lymphocytic leukemia, unlike other lymphoproliferative diseases, is diagnosed very rarely and is noted in approximately 1% of cases [3,7]. However, there are reasons to believe that nervous system damage is more common. First, nervous system damage is underestimated, since their manifestation in chronic lymphocytic leukemia is not specific, and it is difficult for

specialists (neuropathologists and hematologists) to distinguish nervous system damage in CLL from other neurological diseases. Secondly, in most cases, damage to the nervous system in CLL is asymptomatic and is detected only at autopsy [5,6]. The diagnosis of neurological complications of CLL, especially in the early stages, is not given sufficient attention and is often diagnosed after the development of severe neurological focal complications, which leads to disability of patients. Neurological complications of CLL associated with polychemotherapy are the most studied in the world and local literature, and they usually affect the peripheral nervous system. Damage to the nervous system in CLL often occurs "hidden", which in turn can escape the attention of neurologists and other specialists. In patients with chronic lymphocytic leukemia, in addition to neurological disorders, the appearance of neuropsychological disorders (anxiety and depression) increases, leading to a decrease in

quality of life and a decrease in social adaptation [2,5]. The dynamic development of modern oncohematology has led to an increase in the survival rate of patients with chronic lymphocytic leukemia. All this determines the relevance and purpose of the study of issues related to the diagnosis and treatment of nervous system diseases in patients with chronic lymphocytic leukemia.

In modern oncohematology, polychemotherapy is the main and most successful method of treatment. Due to the increase in the average life expectancy of patients with CLL, when choosing a treatment strategy, it is necessary to take into account not only its effectiveness, but also delayed side effects.

Purpose. Study of clinical and neurological characteristics of patients with chronic lymphocytic leukemia.

2. Material and Methods

130 patients with chronic lymphocytic leukemia were examined at the Khorezm branch of the Republican Scientific Research Center of Hematology and Transfusiology of the Ministry of Health of the Republic of Uzbekistan (Khorezm branch of the Republican Scientific Research Center of Hematology and Transfusiology of the Ministry of Health of the Republic of Uzbekistan). The scientific research was based on the results of patients with CLL who were treated as inpatients from 2014 to 2023. Of these, 71 were men (54.6%) and 59 were women (45.4%). The ratio of men to women was 1.2:1.

were aged 46 to 86 years, including 13 patients (15.5%) aged 13 to 44 years, 25 patients (29.8%) aged 45 to 59 years, 37 patients (44.0%) aged 60 to 74 years, and 9 patients (10.7%) older than 75 years. The mean age of the patients was $64.07 \pm$

9.56 years ($p < 0.05$).

When the patients were studied according to the time of onset of the disease, the following situation was found: up to 6 months - 32 patients (24.62%), from 6 months to 1 year - 17 patients (13.08%), from 1 to 3 years - 31 patients (23.84%), from 3 to 5 years - 30 patients (23.08%), over 5 years - 20 patients (15.38%). 25.38% (33) of the patients have higher education, and the remaining 74.62% (97) have secondary and vocational secondary education.

3. Results

All 130 patients underwent clinical examinations by evaluating their anamnesis, complaints and neurological status.

All patients in the study underwent various courses of polychemotherapy. Patients underwent 3 courses of polychemotherapy during the follow-up period. Before the start of the study, patients had received an average of 4 courses of polychemotherapy (maximum 24 times and minimum 1 time) [2]. In our study, 29 patients underwent their first course of PCT. After 3 months, the average number of PCT courses patients had undergone was 7 [5] (maximum 27 times and minimum 4 times) (Figure 1).

Patients with chronic lymphocytic leukemia mainly received courses of polychemotherapy in the RFC regimen: (rituximab, fludarabine, cyclophosphamide), FC (fludarabine, cyclophosphamide), RCHOP (rituximab, cyclophosphamide, vincristine, doxorubicin, prednisolone), RB (rituximab, bendamustine), rarely RC (rituximab, cyclophosphamide), RD (rituximab, dexamethasone), RL (rituximab, leukeran), RCD (rituximab, cyclophosphamide, dexamethasone), COP (cyclophosphamide, vincristine, prednisolone) and leukeran monotherapy (Fig. 2).

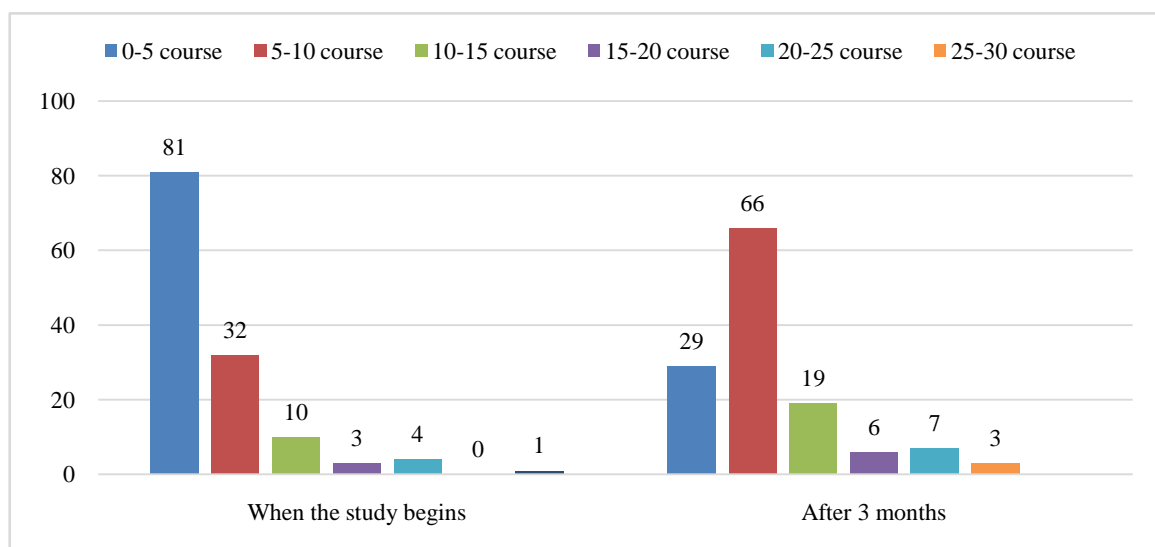


Figure 1. Distribution of patients receiving polychemotherapy treatment courses at baseline and 3 months later

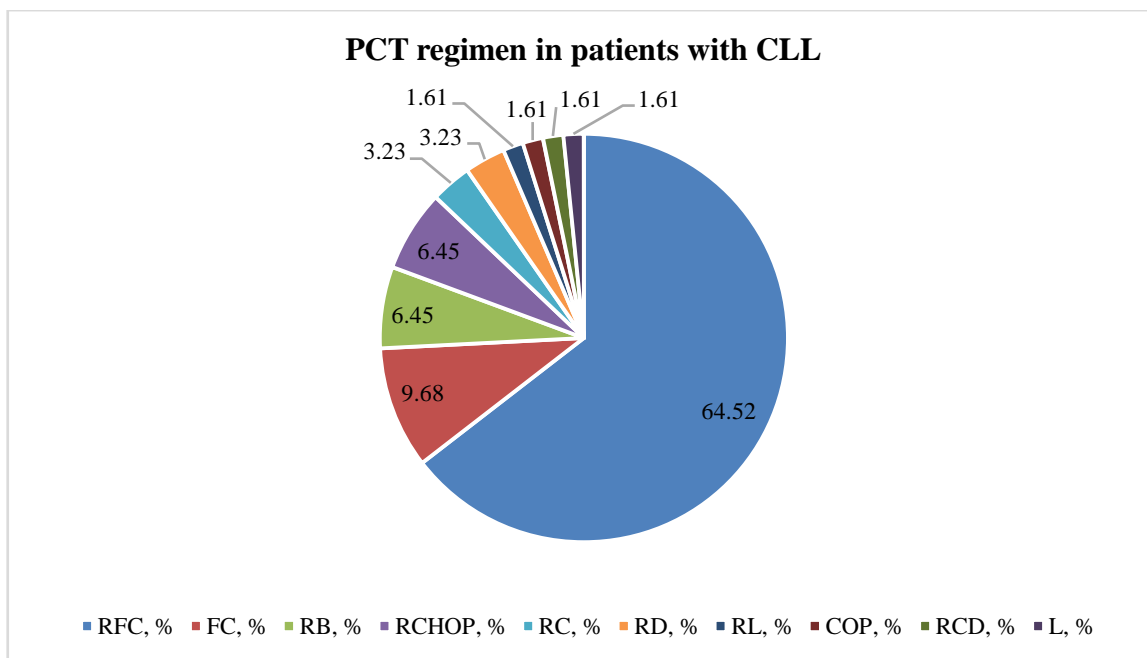


Figure 2. Distribution of polychemotherapy regimens in patients with chronic lymphocytic leukemia

We also analyzed the main complaints of patients, most of which were associated with intoxication syndrome and side effects of polychemotherapy against the background of the main disease. Out of 130 patients (13.08%), only 17 did not complain during the anamnesis (Table 1).

Table 1. Distribution of baseline characteristics of non-complaint patients in SLL

Index	Distribution
Gender	Men - 82.35%, women - 17.65%
Young	59.17 ± 8.11
Concomitant diseases	No-64.71%, GB-32.55%, QD-5.88%, YIK-11.76%

This was observed mainly in patients with newly diagnosed CLL and those who considered themselves to be ill for many years: up to 6 months – 4 patients (23.53%), from 6 months to 1 year – 1 (5.89%), from 1 to 3 years – 2 (11.76%), from 3 to 5 years – 5 (29.41%), 5 years and more – 5 (29.41%).

The main complaints of patients are presented in Figure 3. Patients with chronic lymphocytic leukemia mainly complained of general weakness, tremors and unsteadiness, hearing loss, dizziness, memory loss, and headache.

All patients underwent neurological examination at the beginning of our study and after 3 months. In 36 of 130 (26.67%) patients, no changes were found in the neurological examination. These were mainly patients without comorbidities and were younger. One third of the patients (33.33%) did not have any complaints, and in most cases (66.67%) there were complaints related to the course of the SLL disease, as well as to the accompanying pathology (such as general weakness, headache, dizziness, back and bone pain, and increased blood pressure). The prevalence of neurological syndromes in patients is presented in Figure 4.

Among the neurological disorders of the patients, vestibulo-atactic syndrome accounted for the majority - in 57 (43.85%) patients, the main clinical symptoms of which were non-systemic dizziness, tremor, gait instability, difficulties in writing, problems with fine motor skills and coordination. Clinical symptoms ranged from mild to severe coordination disorders. The average age of patients in this group was almost 10 years older than that of the patients in the main sample - 68.3 ± 8.3 years, and 82.35% of patients had concomitant diseases. In 64.71% of these patients, cardiovascular diseases (arterial hypertension, ischemic heart disease, cerebrovascular diseases) were mainly observed. This group also included 10.69% of patients with traumatic brain injuries (cerebral contusions of varying degrees) and 5.89% with diabetes mellitus.

Sensation in 7.69% of patients disorders, including polyneuropathy in 5.38% and 2.31% hemihypesthesia observed. Hemihypesthesia patients who previously had an acute blood circulation disorder in the brain (lymphoproliferative disease from the beginning before) observed. And polyneuropathy developed as a complication of polychemotherapy. Damage to the paired cranial nerves was found in 5 patients (3.85%), 3 of them after a previous acute cerebrovascular accident, 1 of them after traumatic brain injury, and 1 of them as a result of intracranial plasmacytoma.

Rigid-akinetic syndrome was observed in 1 patient with Parkinson's disease and SLL. Hyperkinetic syndrome was observed in 1 patient with essential tremor and SLL. Pyramidal insufficiency was detected in 5 (3.85%) patients, 2 of whom were diagnosed after a previous acute cerebrovascular accident, and 3 with concomitant cerebrovascular disease and hypertension.

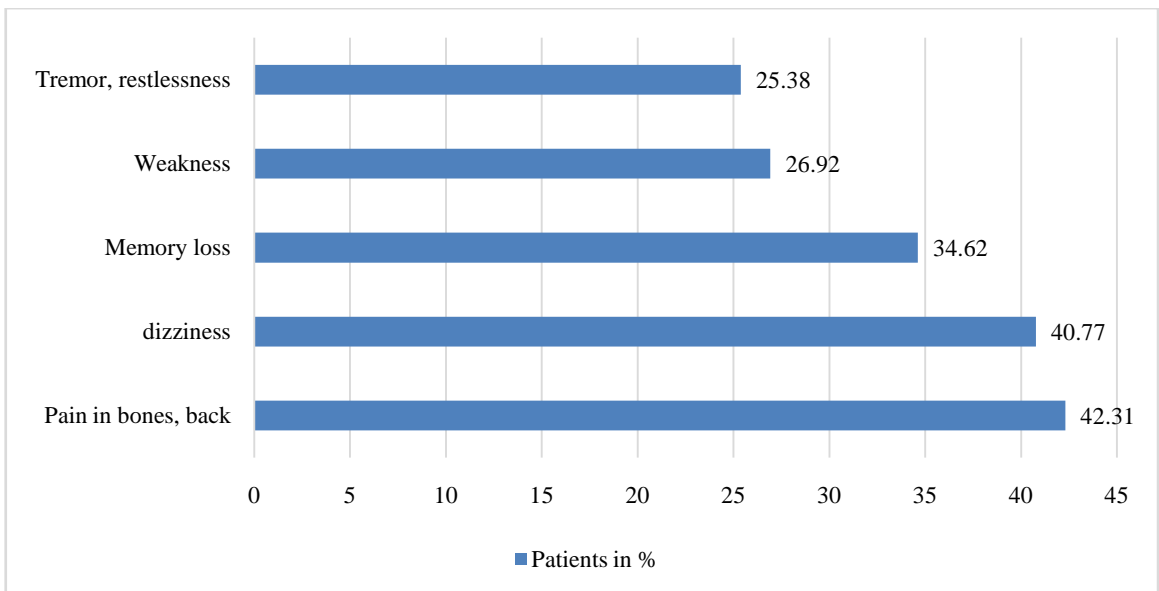


Figure 3. Patient's main complaints (n =130)

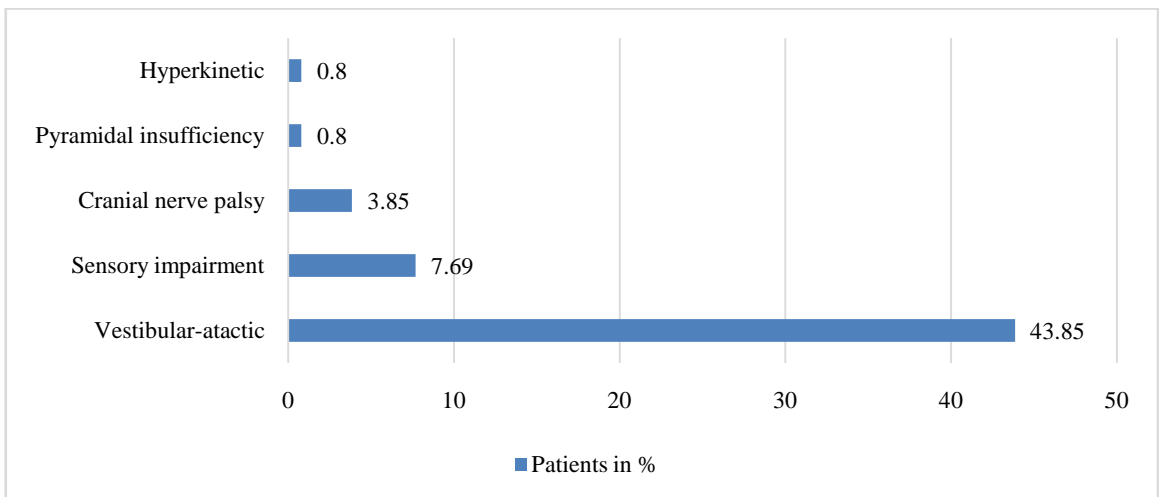


Figure 4. Prevalence of neurological syndrome in patients (n=130)

4. Conclusions

The development of neurological syndromes is influenced not only by concomitant diseases, but also by the CLL disease itself and the complications of polychemotherapy. Complaints such as dizziness, general weakness, headache, hearing loss, tremor, memory loss and headache in patients do not arise as a result of a true neurological pathology, but rather arise during treatment and as a result of CLL intoxication. The development of sensory disturbances in our patients occurred after the acute cerebral circulation disorder (before the onset of lymphoproliferative disease), as well as polyneuropathy as a complication of polychemotherapy.

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