G.K.Shakirova,
I.Z. Mirzaakhmedova,
M.I.Khamidova
Department of Hospital Therapy and Endocrinology
Andijan State Medical Institute
Andijan, Uzbekistan

COMPARISON OF THE COURSE OF CHRONIC LEUKEMIA IN MEN AND ELDERLY WOMEN

Resume. The patients were divided into 4 age groups: young, mature, elderly and senile. Based on the study of the duration of the disease from the moment of diagnosis verification to the establishment of stage III, the duration of the period before the start of chemotherapy, peripheral blood parameters, myelogram, the size of lymph nodes, liver, spleen, the dependence of the nature of the course of the disease on the age of patients was revealed. In young patients, a progressive course of the disease, a high frequency of tumor forms, and great preservation of erythron granulocytopoiesis were established. Patient of older age groups have a more favorable course, the presence of sluggish forms of the disease, frequent infectious complications.

Key words: B-cell chronic lymphocytic leukemia, age of patients, clinical and hematological features.

Г.К.Шокирова,
И.З. Мирзаахмедова,
М.И.Хамидова
Кафедра госпитальной терапии и эндокринологии
Андижанский государственный медицинский институт
Андижан, Узбекистан

СРАВНЕНИЕ ПО ТЕЧЕНИИ ХРОНИЧЕСКОГО ЛЕЙКОЗА У МУЖЧИН И У ЖЕНЩИН ПОЖИЛОГО ВОЗРАСТА

Резюме. Пациентов разделили на 4 возрастные группы: молодого, зрелого, пожилого и старческого возраста. На основании изучения длительности заболевания с момента верификации диагноза до установления III стадии, продолжительности периода до начала химиотерапии, показателей периферической крови, миелограммы, размеров лимфатических узлов, печени, селезенки выявлена зависимость характера течения заболевания от возраста больных. У пациентов молодого возраста установлено прогрессирующее течение болезни, высокая частота опухолевых форм, бóльшая сохранность эритрогранулоцитопоэза. У больных старших возрастных групп – более благоприятное течение, наличие вялотекущих форм заболевания, частые инфекционные осложнения.

Ключевые слова: В-клеточный хронический лимфолейкоз, возраст больных, клиникогематологические особенности.

Introduction. B-cell chronic lymphocytic leukemia (B-CLL) is the most common form of hemoblastosis, accounting for 30% of all types of leukemia [1, 2].One of the features of B-CLL is the predominance among the sick elderly people. In this regard, for a long time, chronic lymphocytic leukemia was considered a disease of the elderly. But in recent years, there has been a tendency to detect it in younger people, and now the occurrence of this disease in patients under the age of 35 is not uncommon [3].

B-CLL is heterogeneous, its clinical manifestations are very diverse, largely depending on the age of patients. In elderly and senile patients, the leukemic process develops on an involutional background, it is preceded by changes associated with aging. In such patients, various concomitant diseases, dysfunction of many organs, including the hematopoiesis system, are detected more often than in young patients [4]. These circumstances distinguish them from young and mature patients.

The clinical and hematological characteristics of B-CLL are presented in many manuals, reference books, journal articles on hematology. However, these publications mainly cover data concerning the general group of patients, without taking into account their age. At the same time, the authors note the variety of symptoms of the disease, the presence of clinical, morphological, prognostic differences, and different reactions of patients to therapy [5, 6]. A common symptom that determines the pathogenesis and

the main manifestations of the disease are leukemic infiltration mainly by small, mature, immunologically incompetent lymphocytes accumulating in the bone marrow, lymph nodes (LU), spleen, liver and other organs and causing a violation of their function, as well as detected in peripheral blood.

In some patients, the disease proceeds relatively calmly, they do not need specific treatment for a long time [7]. Other lei-

the treatment process, on the contrary, is difficult and they need an immediate appointment of intensive therapy [8]. One of the reasons for the variety of variants of the course of this disease is the age characteristics of patients, which determine the clinical and laboratory features of B-CLL in elderly and senile patients (atypicity, smoothness of clinical manifestations, violation of immune status, etc.) [9, 10].

Publications concerning the study of the features of the course of B-CLL relative to age are few. Basically, they reflect individual indicators characterizing the clinical features of CLL in elderly and senile patients, without comparison with younger patients, and limited to characterizing only individual clinical manifestations of the disease without a relationship between them and age [11, 12].

The aim of the study was to study the clinical and hematological features of B-CLL in patients of different age groups.assigned by Rai et al. The diagnosis of B-CLL was established taking into account clinical data, the results of peripheral blood examination, bone marrow punctate smears, histological examination of trepanobioptates, determination of the immunophenotype of cells circulating in peripheral blood.

Research methods. The group consisted of 72 men, 45 women (ratio 1.6:1). Taking into account the literature data [4], confirmed by our observations, the predominance of men with B-CLL can be regarded as one of the distinctive signs of the disease. The age of patients ranged from 33 to 83 years. The patients were divided according to the international classification into 4 groups depending on their age: 1st — young age (from 30 to 44 years), 2nd — mature (from 45 to 59 years), 3rd — elderly (from 60 to 74 years) and 4th — senile age (from 75 to 89 years old). The 1st group included 17 patients, the 2nd - 28, the 3rd — 50 and the 4th - 22 patients. Elderly people prevailed among the examined patients with B-CLL. Groups of elderly and senile age in some cases are combined, calling older age groups, and young and mature – young. In the future, this indicator reached 10-15% [9, 11]. These data and the results obtained (15% of young patients) confirm the emerging trend of CLL detection at a young age.

Results and their discussion. Due to the presence of anemia, complaints in patients were characteristic of anemic syndrome: general weakness, dizziness, headaches, shortness of breath, etc. Patients, mostly elderly and senile with cardiovascular, gastrointestinal diseases, noted other complaints corresponding to these diseases. The duration of the disease in patients of various age groups from the moment of diagnosis to the establishment of stage III and from the time of diagnosis of B-CLL before the start of therapy (the so-called latent period) is established on the basis of anamnesis data, medical documentation materials. Thus, it was found that the indicators of the duration of the disease from the moment of diagnosis to the development of stage III in the groups of elderly and senile patients were significantly higher compared to the young age group ($p < 0.05$). The older the patient, the later he started chemotherapy (CT). In young patients, the latency period is significantly less compared to patients of mature, elderly and senile age ($p < 0.05$). In addition, the reliability of differences in this indicator was determined in the mature age group compared with patients of older age groups ($p < 0.05$). As for the 3rd and 4th groups, there were no significant differences in this indicator ($p > 0.05$). Thus, young patients have the shortest duration of the disease, compared with elderly

and senile patients, and the shortest latency period, compared with patients of groups 2, 3 and 4 ($p < 0.05$).

The longest duration of the disease and the time before the onset of CT was established in elderly patients. In 11 of them, the so-called benign or smoldering form of B-CLL was detected, characterized by a calm course. The data obtained are consistent with the observations of other authors [1, 3] and indicate a faster progression of the leukemic process in young patients compared with senile and elderly patients. Almost all elderly and senile patients had the above-mentioned concomitant diseases complicating the course of B-CLL. In the same groups, a high frequency of inflammatory processes was noted: in 42% of elderly patients and in 40% – senile; most often – pneumonia, as well as bronchitis, pleurisy, cystitis, erysipelas, etc. In some patients, relapses of lung inflammation were noted twice during the year, which proceeded heavily, atypically, often without a temperature reaction, but with pronounced intoxication, difficult to treat.

As an example, a brief extract from the medical history No. 28616 of patient K., 80 years old (senile age group) is given. She was admitted to the hematology clinic in October 2001 . The diagnosis of B-CLL was established in 1996. She periodically took chlorambucil. On examination, there was an increase in all groups of peripheral LU up to 1 cm in diameter, the liver protruded from under the edge of the costal arch by 2 cm, the spleen – by 5 cm. The hemoglobin content in peripheral blood was 108 g/l, erythrocytes – 3.32 T/l, platelets – 72.2 G/l, the number of leukocytes — 100.9 G/l, lymphocytes – 95%; in the bone marrow of lymphocytes – 88%. In the trepanobioptate of the iliac bone marrow, foci of diffuse lymphoid infiltration were determined. In 1999, the patient was treated for erysipelas-

the lower right leg. Over the past two years, pneumonia has been diagnosed three times. The disease was atypical. With significant symptoms of intoxication, cough, shortness of breath, auscultative data were expressed insignificantly, while during X-ray examination, pneumonia was established, sometimes bilateral lower lobe. Despite active antibiotic therapy, the relief of the inflammatory process was delayed for a long time (3-4 weeks). In patients of young and mature age,

inflammatory diseases were detected less frequently than in patients of older age groups, in 22% of young people and in 18% of mature age, respectively.

The clinical picture of B-CLL during the examination of patients is characteristic of this form of leukemia. Hyperplasia of peripheral LU and an increase in the size of the spleen and liver were noted in patients of all age groups. However, the severity of these symptoms varied depending on the age of the patients. The largest LU sizes were observed in young patients ($p < 0.05$), the smallest – in senile ($p < 0.05$). depending on age, they were elastic, mobile, painless, with the exception of dense bags of LU in one young patient, in whom B-CLL evolved into Richter syndrome. Abdominal and retroperitoneal hyperplasia, more often diagnosed in patients of a young age group, was found in 36.3% of patients. Comparison of the size of the spleen in patients of different age groups established its moderate increase in young patients and significant splenomegaly in mature, elderly and senile individuals, in whom, according to the results of palpation, percussion and ultrasound, the spleen protruded from under the edge of the costal arch by 4-6 cm and was characterized by high density due to leukemic infiltration, as well as possibly due to scarring due to past heart attacks. In some patients (the preponderance reached a huge value, descending into the pelvis. The absence of a relationship between the degree of enlargement of the LU and the spleen, observed in all patients with B-CLL, can be explained primarily by the unequal degree of leukemic infiltration of these organs in patients of different ages. In the young, infiltration by tumor cells of the LU prevailed, in the older age groups – the spleen. There were no differences in liver size in patients in different age groups. In 5 patients (29%) of young age, the value of LU significantly exceeded the average values established in this group. The sizes of cervical, axillary, as well as intra- and retroperitoneal LU reached 4-5 cm in diameter, some of them were conglomerates. Such a clinical picture was regarded as a tumor variant of the disease.

When analyzing the materials in Table 3, significant differences in the hemoglobin content were found in young and senile patients, higher rates in young. The number of erythrocytes in young patients is also higher compared to senile and

elderly people ($p < 0.05$). There were no differences in the content of reticulocytes. The number of leukocytes was significantly higher in young patients compared with patients of mature, elderly and senile age. The same ratio was noted when assessing the number of blood platelets in patients of different age groups: the number of platelets is higher in young people compared with patients of other age groups ($p < 0.05$). There was no statistically significant difference in the percentage of lymphocytes between the compared groups of patients. However, the absolute number of lymphocytes in 1 ml of blood is significant in patients of other age groups ($p < 0.05$). Mature, small, narrow-plasma forms prevailed among lymphocytes. In elderly and senile patients, single broad-plasma lymphocytes with abundant azurophilic granularity were detected more often than in young patients. In all patients, prolymphocytes (2-3%) were detected in the hemogram, in some – single (1-2%) lymphoblasts, as well as Botkin —Gumprecht cells in different amounts.

The above, concerning the assessment of peripheral blood parameters, indicates more pronounced violations of normal erythro- and thrombocytopoiesis in senile and elderly patients compared with young patients.

High indicators of the total number of leukocytes and the absolute number of lymphocytes in young patients, exceeding those in individuals mature, elderly and senile, indicate a more pronounced degree of leukemia, high activity of the tumor process at a young age. This can explain the rapid progression of the disease in these patients. The analysis of the data in Table 4 showed that the content of erythro- and normoblasts, pronormocytes and granulocytes in young patients was significantly higher compared to patients of mature, elderly and senile age ($p < 0.05$), which indicated greater preservation of erythro- and granulocytopoiesis in them. There was no significant difference in the number of myelocaryocytes in patients of different age groups.

The leuko-erythroid ratio (L : E) was determined, normally equal to 3 (4): 1. In young patients, this ratio was 26.7 ± 3.1, in mature — 42.4 ± 4.9, in elderly — 43.6 ± 4.0 and senile — 40.7 ± 4.6.As an example, brief extracts from the histories are given diseases of patients with B-CLL. He was admitted to the hematology

department in May 2001 (sixth hospitalization). In July of the same year, they began to increase progressively. The diagnosis of B-CLL was established in August 2000. based on the data of peripheral blood examination, myelogram, results of cytochemical studies, immunophenotyping of lymphocytes, histological examination of bone marrow trepanobiopts and LU biopsies. The patient was prescribed courses of polychemotherapy according to the schemes of SOR, ASOR (cyclophosphamide — 400 mg per day intramuscularly for 5 days, vincristine – 2 mg, doxorubicin – 30 mg intravenously once, prednisolone – 50 mg per day for 9 days with a further dose reduction), as well as interferon alpha-2b for 3 million – 10 injections. The CT performed gave only a short-term effect (after 2-3 weeks, the LU increased again). Upon examination of the patient, enlarged cervical LU were noted, merging into conglomerates. Enlarged axillary and inguinal LUS from 2 to 4 cm in diameter were also palpated. In the abdominal cavity, with the help of ultrasound, enlarged LU with dimensions of 3.2–4 cm were revealed. An overview X-ray of the thoracic cavity organs in the roots of both lungs also revealed enlarged LU. The liver protruded 2 cm from under the edge of the costal arch, the spleen - 1 cm. Blood test: ge contentmoglobin – 124 g / l, the number of erythrocytes – 4.5 T / l, platelets – 225.5 G / l, leukocytes – 28.7 G / l, lymphocytes – 67%. In the myelogram, lymphocytosis is up to 81%. Bone marrow trepanobioptate was characterized by high cellularity due to pronounced (diffuse) infiltration by lymphoid elements. The features of the disease in this patient were young age, rapidly progressing course of the leukemic process, a short period from the time of diagnosis of the disease to the beginning of CT, tumor form. Patient K., 68 years old, medical history No. 1679 (elderly group). She was admitted to the clinic in February 2002 with complaints of weakness, dizziness, dry mouth, and a decrease in body weight by 45 kg.

She has been ill with B-CLL since 1988. For a long time, the disease proceeded calmly, peripheral LU with dimensions of 0.5–1.5 cm in diameter were palpated. The content of hemoglobin and erythrocytes remained within the normal range (128 g/l and 3.6 T/l, respectively), the number of leukocytes fluctuated in thedose ranges from 15 to 30 G / l, platelets — 230 G / l. Specific therapy

(chlorambucil – 4-6 mg / day) began to be received only 11 years after the diagnosis of leukemia due to the progression of the disease, the continued increase in peripheral LU and the development of splenomegaly. When the patient was admitted, the hemoglobin content of 104 g / l was determined in the peripheral blood analysis, erythrocytes – 3.12 T / l, the number of leukocytes increased to 190 G / l, lymphocytes – up to 94%. Lymphocytosis was observed in the bone marrow – up to 85%. Focal diffuse lymphoid infiltration was determined in the trepanobioptate of the iliac bone marrow. In this elderly patient, the disease was characterized by a long, calm course, a long period before the onset of CT, moderate LU hyperplasia.

Conclusions

1. The data presented in the article, based on the examination of 117 patients with stage III B-CLL, indicate the dependence of the nature of the course of the disease, hematological parameters on the age of the patients.

2. In young people, a progressive course of the disease was established, a high frequency of tumor forms, a large preservation of erythro granulocytopoiesis was noted.

3. Patients of older age groups have a more favorable course, the presence of sluggish forms of the disease, frequent infectious complications.

4. The conducted studies confirm the validity of the opinion of a number of authors who noted a clear tendency to diagnose CLL in younger people.

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