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THE ROLE OF MONOCLONAL B-CELL LYMPHOCYTOSIS IN PREDICTING LYMPHOPROLIFERATIVE DISEASES: A LITERATURE REVIEW

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ABSTRACT

Relevance: *Monoclonal B-cell lymphocytosis (MBL), introduced by the World Health Organization in 2017 to classify certain types of blood diseases, opens up new perspectives in classification but also raises issues that require further study. MBCL studies are essential for improving diagnosis and monitoring, which can contribute to the early detection and prevention of chronic lymphocytic leukemia (CLL).*

The study aimed to *evaluate the immunophenotypic aspects of monoclonal B-cell lymphocytosis and the risk of progression to chronic lymphocytic leukemia.*

Methods: *A review of scientific publications examined the causes of MBL and its association with CLL, emphasizing immunophenotypic aspects of these conditions. The literature survey provided information on factors associated with the progression of MBL to CLL, including biomarkers and clinical characteristics, allowing a more comprehensive assessment of the risk of leukemia in patients with MBL.*

Results: *Numerous studies regarding the association between MBL and CLL were analyzed. The analysis showed that MBL often precedes the development of CLL, with MBL clones being detectable years before clinical diagnosis. This supports the hypothesis that MBL may be an early biomarker for detecting developmental risk.*

Various studies emphasize significant ethnic and geographic differences in the prevalence and progression of MBL and CLL. These differences may be related to epigenetic factors, immunoglobulin rearrangements, and other genetic features. Understanding these differences is essential for more accurate diagnostic and prognostic approaches that consider individual and patient population characteristics.

Conclusion: *The analysis shows that further investigation of the association between MBL and CLL and the introduction of screening programs for early detection of MBL can significantly improve the prognosis and health of patients in Kazakhstan.*

The review results emphasize the importance of early diagnosis and an individualized approach to treatment. This will help prevent MBL progression to CLL and improve our country's medical care quality.

Keywords: *monoclonal B-cell lymphocytosis (MBL), chronic lymphocytic leukemia, immunophenotype, risk of development, flow cytometry.*

Introduction: In recent years, the widespread use of 10 color (multicolor) blood cell measurement panels, thanks to advances in flow cytometry, has made it possible to detect in healthy individuals deficient levels of monoclonal B-lymphocytes in the blood that are immunophenotypically similar to chronic lymphocytic leukemia cells. As a result, general practitioners and even specialists who do not specialize in hematology may encounter patients who have a slight increase in the number of lymphocytes in the blood consisting of abnormal B-cell clones but who lack the diagnostic criteria for chronic lymphocytic leukemia (CLL) [1, 2].

The term 'monoclonal B-cell lymphocytosis (MBL)' was introduced by the World Health Organisation in 2017 to describe certain conditions in the field of oncohematology. It has improved understanding chronic lymphocytic leukemia (CLL) and raised new unanswered questions [3].

MBL is defined by peripheral blood monoclonal B-cell concentration of less than 5×109/L without evidence of lymphoproliferative diseases such as lymphadenopathy, organomegaly, or extramedullary lesions [4].

In approximately 75% of cases, the immunophenotypic profile of clonal B-cell expansion overlaps with the immunophenotypic profile of CLL with co-expression of CD19, CD5, CD23, and low levels (dim) of CD20 and surface immunoglobulins with light chain restriction ('CLL-like'). Other cases may co-express CD19 and CD5 but with bright CD20 and no CD23 ('atypical CLL-type'), while others are CD5-negative, with moderate

to bright expression of surface immunoglobulins ('non-CLL-type') [2-4].

In addition to the immunophenotypic profile, a key distinction is based on B-cell count, which further stratifies the category of MBL into low count ($<0.5\times10^9$/L) or high count ($\geq0.5\times10^9$/L) MBL. Data from a meta-analysis collecting information from MBL series worldwide clearly documented a bimodal distribution of MBL cases based on absolute B-cell count [5]. In cases detected in population-based screening studies, the number of clonal B cells ranged from 0.1 to 10 B cells per μL (with a median of 1 cell per μL), while in cases of MBL detected by routine examination for lymphocytosis, the mean number of B cells was 2.9×10^9/L and ranged from 0.5 to 5.0×10^9/L. Very few cases were intermediate, maintaining the threshold currently accepted.

This distinction is not trivial, given that the clinical and biological features and risk of progression to full-blown CLL significantly differ between the two conditions.

In general, MBL occurs more frequently with age. It was insignificant before age 40 and present in about 10% of all individuals over this age, reaching a maximum of >50% among those over 90 [6-8].

Therefore, these findings support the importance of studying MBL, as its prevalence increases with age and may indicate a pre-existing stage of serious diseases such as CLL. A more in-depth analysis of MBL can improve diagnostic and monitoring methods, leading to earlier detection and potential prevention of disease development. Also, a detailed study of the immunophenotypic characteristics of MBCL will give hematologists additional tools to effectively monitor patients' conditions, increasing the likelihood of accurate prediction and the development of targeted therapies.

The study aimed to evaluate the immunophenotypic aspects of monoclonal B-cell lymphocytosis and the risk of progression to chronic lymphocytic leukemia.

Materials and Methods: A review of scientific publications examined the causes of MBL and its association with CLL, emphasizing immunophenotypic aspects of these conditions. The review covered actual studies published in peer-reviewed scientific journals since 2010.

The review compared Immunophenotypic profiles of monoclonal B cells identified in patients with MBL and CLL using data from large meta-analyses and review studies conducted in different regions worldwide.

The literature survey provided information on factors associated with the progression of MBL to CLL, including biomarkers and clinical characteristics, allowing a more comprehensive assessment of the risk of leukemia in patients with MBL.

Source inclusion criteria:

– Publications containing empirical data on MBL and CLL.

– Articles published in peer-reviewed scientific journals since 2010.

– Work performed on hematological samples.

Source exclusion criteria:

– Research is based only on specific evidence or case reports without statistical analysis.

– Publications without access to the full text or published in journals without scientific peer review.

– Articles that are not in clinical medicine, immunology, or hematology.

Results: High-grade MBL has the highest prevalence among first-degree relatives of CLL patients and, unlike low-grade MBL, has IGHV mutations with a repertoire similar to CLL, indicating a biological link. However, in both types of MBL, cytogenetic changes associated with CLL are noted, including del (13q), +12, and del (17p), although at lower levels, suggesting that these changes occur early in clonal evolution and are not prognostically significant in the absence of B-cell lymphocytosis [9, 10]. We know that almost all clinical cases of CLL are preceded by the MBL phase. High-grade MBL progresses to CLL at a rate of 1-2% per year, with the number of clonal B-cells at presentation being the most significant risk factor. This is in contrast to MBL with low lymphocyte counts, which proceeds without overt lymphocytosis and does not require clinical monitoring of progression. In addition, there are cases of MBL with a different phenotype from CLL that are thought to be associated with marginal zone lymphoma. Given that CLL-like cells can be found in patients without lymph node enlargement (<1.5 cm) who have undergone lymphadenectomy for reasons not related to lymphoproliferative diseases, a third category has been proposed to describe this phenomenon – the 'nodal equivalent of MBL,' which is different from full-fledged small cystic lymphoma [11, 12].

Flow cytometry is the primary method to detect the MBL because it accurately identifies and differentiates phenotypes. MBL is classified into three phenotypes - CLL/SLL, atypical CLL/SLL, and non-CLL/SLL - based on specific markers on the surface of the cells. These markers include CD5, CD19, CD20, and CD23, as well as immunoglobulins, either light chains or complete chains (consisting of light and heavy chains). The distinction between these phenotypes is crucial since each can be associated with developing different types of malignant lymphocyte neoplasms [12-15].

Table 1 presents the markers for the three MBL phenotypes. Marker expression is indicated as follows: (+) for the presence of expression (weak, moderate, or bright), (–)

for its absence, and 'not allowed' for cases where the data are not applicable. Fluorescent probes determine expression by binding to marker proteins on cells. Flow cytometry, preferably using 6-8 different fluorescent probes, can detect this binding by analyzing about 5 million cells from the patient's blood. The table also shows the percentage of cases of each MBL phenotype that can progress to malignancies [4].

Table 1 – Markers of three MBL phenotypes on flow cytometry [4, 12-15]

MBL phenotype	CD5	CD19	CD20	CD23	Immunoglobulin light chains	Percentage with phenotype	Potential malignant complication
CLL / SLL MLB	+	+	+ (dim)	+	Ig with a light chain, either +, + (dim), or –	68-75%	CLL/ SLL
Atypical CLL / SLL MLB	+	+	+ (bright)	- or +	Full Ig, either + (moderate), or + (bright)	~15%	Mantle cell lymphoma, follicular lymphoma
Not- CLL/ SLL MLB	or – or + (dim)	+	+	N/A	Light chain Ig, ei-ther + (moderate) or + (bright)	~14%	Lymphoma of the mar-ginal zone of the spleen, lymphoma of the spleen/leukemia unclassified

Cases of non-CLL/SLL MBL where monoclonal B-cells do not express CD5, CD23, CD10, or CD103 but show high expression of CD79b and immunoglobulin light chains are generally classified as marginal zone monoclonal B-cell lymphocytosis (CBL-MZ). This designation applies because normal B cells in this area also express these markers. People with CBL-MZ often have very high levels of B-cells in their blood (>4.0x10^9/L, usually 3.0x10^9/L to 37.1x10^9/L) [13]. These cases constitute a significant proportion among non-CLL/non-SML MBL. These patients are also often found to have monoclonal IgM gammopathy, which means high levels of one type of IgM antibody. It is similar to Waldenstrom's macroglobulinemia and IgM monoclonal gammopathy, which are of uncertain significance. Such patients are more likely to develop malignant diseases, such as B-cell lymphomas of the marginal spleen zone, indeterminate lymphomas/leukemias of the spleen, hairy cell leukemia, and, possibly, Waldenstrom's macroglobulinemia [4, 12-15].

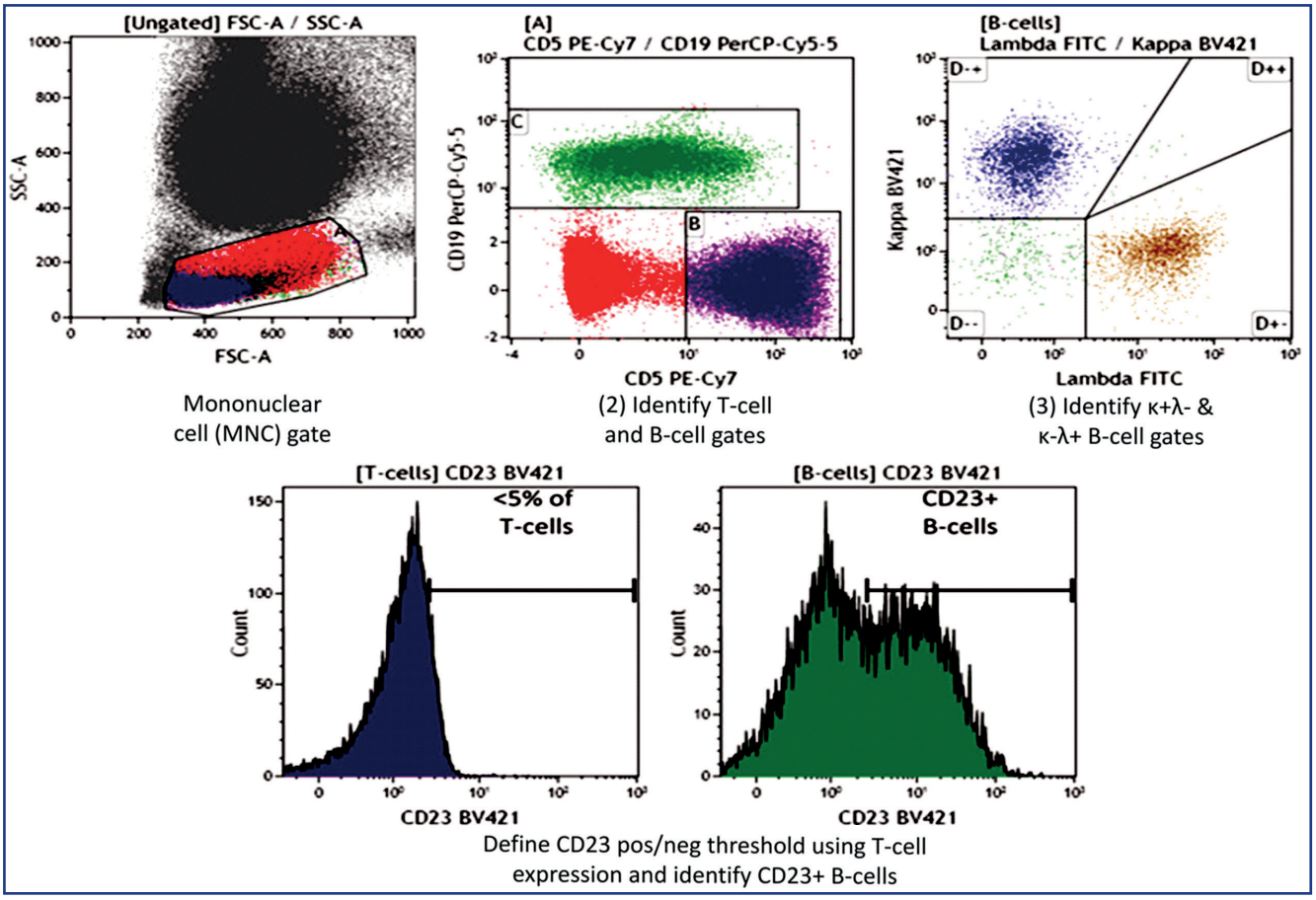

Figure 1 – Reproducible diagnosis of chronic lymphocytic leukemia using flow cytometry: European Research Initiative on CLL (ERIC) and European Society for Clinical Cell Analysis (ESCCA) Harmonization Project [19]

In 34 cases, the clinical, cytological, immunological, and genetic features of non-CLL MBL were described. As previously reported, the current cases have immunological and genetic similarities with marginal zone lymphoma (MZL). They may be associated with a new suspected condition, marginal zone clonal B-cell lymphocytosis (CBL-MZ). In addition, in some cases, similarities have been observed with diffuse lymphoma of the red pulp of the spleen (DLRPS). As a result, according to the literature, non-CLL MBL (associated with CBL-MZ) may be a precancerous condition leading to MZL and DLRPS [16, 17].

MBL is defined by fewer than 5×9 clonal B-cells in the peripheral blood in the absence of lymphadenopathy, enlarged spleen or liver, and symptoms of B-CCL. These symptoms include unintentional weight loss, fatigue with a score of 2 or higher on the Eastern Cooperative Oncology Group (ECOG) scale, prolonged fever, and night sweats with no signs of infection. In contrast, CLL, the most common lymphoid malignant tumor, is diagnosed at a B-cell count greater than 5×10^9/L [18].

Table 1 shows that MBL can be classified into three types based on the immunophenotypic characteristics of abnormal peripheral lymphoid cells: *CLL, atypical CLL, and non-CLL type*. Advances in flow cytometry have made it possible to detect deficient levels of clonal B-cells, especially in healthy older adults.

For a more detailed understanding and clarification of the differences between these conditions, it is essential to consider the immunophenotypic characteristics of abnormal peripheral lymphoid cells for different types of MBL with specific biomarkers that will aid in diagnostics in clinical and diagnostic laboratories. *CLL* with immunophenotype CD19+, CD5+, CD23+, CD20dim (low expression), kappa or lambda surface immunoglobulins usually (+) (sIg), white blood cell count: marked elevation: $\geq5\times10^9$/L. CLL is a heterogeneous disease, and its course can range from long-term survival to rapid progression. This disease is associated with a pronounced clonic B-cell expansion [18].

Atypical CLL with immunophenotype CD19+, CD5+, CD23-/dim (low), CD20+ (bright expression), kappa or lambda surface immunoglobulins usually (moderate to bright expression), white blood cell count: significant increase, may range from 5×10^9/L to higher values. Atypical CLL shows altered immunophenotypic profiles compared to classic CLL, including bright CD20 expression and moderate to bright sIg expression [19].

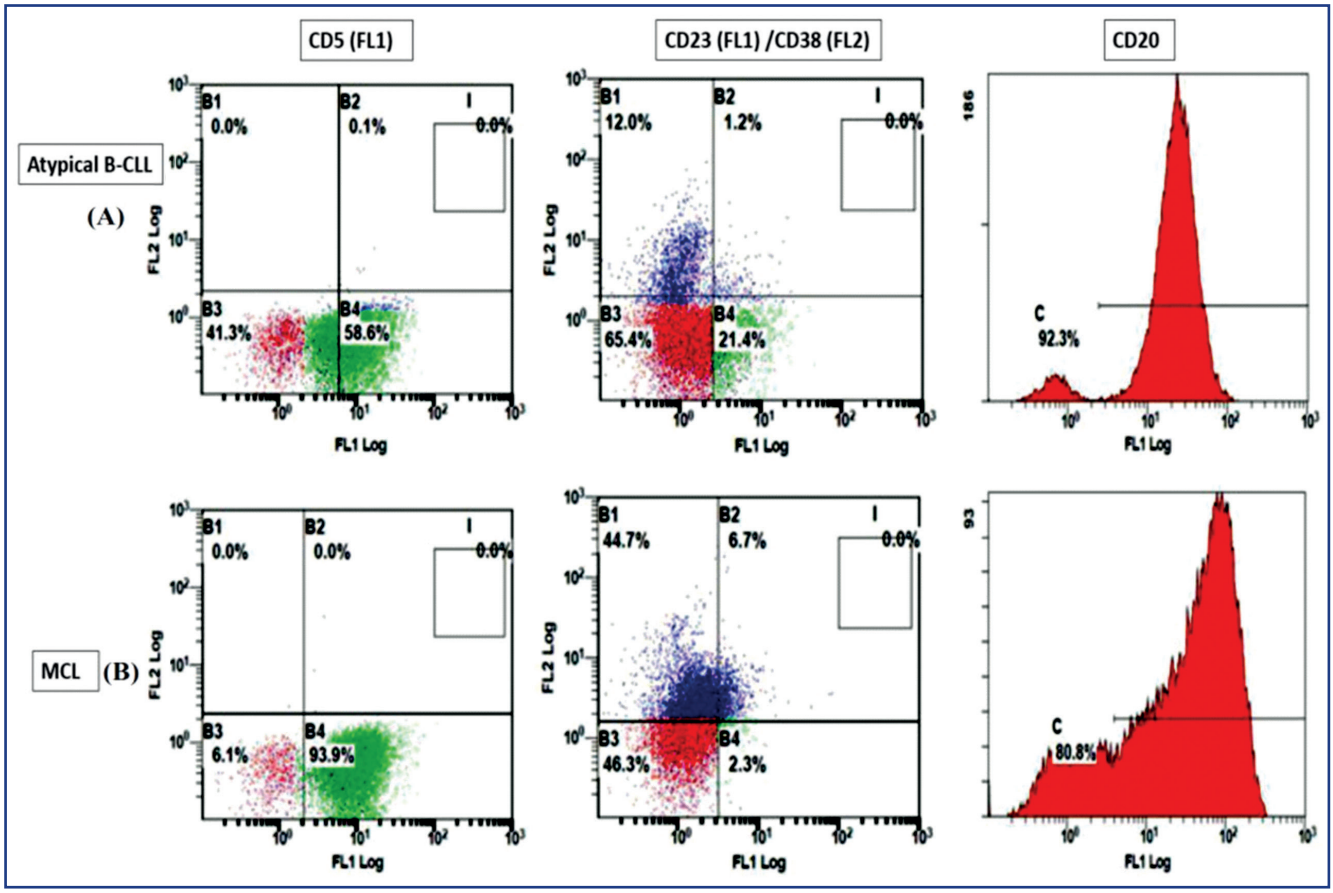

Figure 2 – Immunophenotypic assay for CD5, CD23, CD38 expression, and CD20 histogram in atypical (A) B-CLL and (B) MBL. Patients with MBL were found to have high expression of the CD5 marker, although patients with atypical B-CLL had lower levels of this marker. In patients with atypical B-CLL, CD23 expression was lower, but in patients with MBL, this marker was rarely expressed. In almost all patients with atypical B-CLL and MBL, CD38 expression was negative and positive, respectively. Both groups expressed CD20 without significant differences [20]

Non-CLL type with immunophenotype CD19+, CD5+, CD23-/dim (low), CD20+ (bright expression), kappa or lambda surface immunoglobulins (moderate to bright expression), white blood cell count may be normal or slightly elevated depending on the specific type of lymphoma or leukemia that is not CLL. This type includes various forms of lymphoma or leukemia that do not meet the criteria for CLL and may exhibit different immunophenotypic profiles [21].

In 2019, a team of scientists investigated the presence of CLL clones decades before a diagnostics of CLL, using the Copenhagen City Heart Study (CCHS) and the Copenhagen General Population Study (CGPS) to analyze pre-diagnostic peripheral blood samples obtained during visits between 1992 and 2014 from healthy individuals who were subsequently diagnosed with CLL between 2001 and 2019. They assessed clonal CLL DNA by minimal residual disease (MRD) analysis according to EuroMRD guidelines.4. A total of 247 individuals diagnosed with CLL, registered after participation in CCHS or CGPS between 1992 and 2014, were identified. A total of 22 of these patients underwent immunoglobulin heavy chain variable region (IGHV) mutational status analysis performed at the Department of Haematology at Rigshospitalet (Copenhagen, Denmark) from 2001 to 2017 at the time of CLL diagnosis and had a >5-year latency period from participation in CCHS or CGPS to CLL diagnostics. The study was manually supplemented with eight cases of individuals who either had an IGHV mutational status established at Rigshospitalet and a <5-year latency period (two cases) or IGHV mutational status established at Rigshospitalet in 2018 and 2019 and a >10-year latency period (six cases). A total of 10 patients were excluded either due to a lack of sufficient complete blood DNA material in the biobanks or due to misdiagnosis of CLL (patients with small lymphocytic lymphoma). In addition, three patients were excluded due to technically insufficient analysis. The final cohort consisted of samples from 17 patients [22, 23].

In another randomized trial, patients with CLL were divided into three epigenetic subtypes (epitypes) with high prognostic significance. These studies have shown that the intermediate epitype is particularly common in patients with rearrangements 3-21 and high-risk immunoglobulin lambdas variable (IGLVs), which affects their outcomes. This study used a combined strategy to create an epigenetic and light chain immunoglobulin (ELCLV3-21) signature to classify 219 individuals with MBL. The high-risk signature of ELCLV3-21 made it possible to identify individuals with MBL who had a high probability of disease progression (39.9% at 5 years and 71.1% at 10 years). ELCLV3-21 improved the accuracy of predicting time to treatment in patients with MBL compared to other established prognostic measures, including the International Prognostic Index for CLL (c-statistic 0.767 vs. 0.668). A comparison of ELCLV3-21 risk groups among patients with MBL and a cohort of 226 CLL patients showed that high-risk individuals with ELCLV3-21 and MBL had a significant reduction in time to treatment (P = 0.003) and a decrease in overall survival (P = 0.03) compared to low-risk ELCLV3-21 and CLL patients. These results highlight the effectiveness of the ELCLV3-21 approach in identifying patients with a high likelihood of an adverse clinical outcome. They may provide a more accurate classification of individuals with small B-cell clones [24].

In a cross-sectional study, A.C. Rawstron et al. studied individuals at least 45 years of age who were HIV-1 seronegative from an established cohort of Ugandan populations from whom whole blood samples were taken. Also, in the UK, blood samples were collected from people of the same age and sex who did not have cancer and had average blood test results. Flow cytometry was used to determine the presence of MBL in the specimens, according to standard diagnostic criteria. Comparisons were made between the proportion of cases with an MBL phenotype characteristic of CLL and CD5-negative MBL and differences in the absolute number of monoclonal B-cells between the two cohorts. Between January 15 and December 18, 2012, samples were collected from 302 volunteers from Uganda and 302 from the United Kingdom, matching age and gender. The overall prevalence of MBL was higher in participants from Uganda (42 cases, 14%) than in the UK cohort (25 cases, 8%; p=0.038). The CLL MBL phenotype was identified in three (1%) participants from Uganda and 21 (7%) participants from the United Kingdom (p=0.00021). All three participants from Uganda had absolute monoclonal B-cell counts below one cell per μL. In comparison, 21 participants from the UK had an average absolute number of circulating tumor cells of 4.6 (interquartile range 2 - 12) cells per μL. The prevalence of CD5-negative MBL was higher in the Ugandan cohort (41 cases (14%), of which two (5%) also had the MBL phenotype, CLL) than in the UK cohort (six cases (2%), of which two (33%) also had the MBL phenotype, CLL; p<0.0001). However, the median absolute number of B-cells was similar (227 cells per μL (interquartile range 152-345) in the Ugandan cohort versus 135 cells per μL (interquartile range 105-177) in the UK cohort; p=0.13) [25].

CLL is much less common in Asians than in Caucasians. In the previous stage of CLL development, known as the MBL phenotype CLL (CLL-like MBL), the likelihood of progression to CLL is low. MBL is classified as high or low based on the number of clonal B-cells in the peripheral blood. Patients with high levels of MBL have a higher risk of progression to CLL than patients with low MBL.

Unlike Caucasian populations, in which MBL is quite common, Asian populations, including Japanese, have a lower incidence of MBL. The exact reasons for the ethnic differences in the prevalence of CLL and MBL remain unknown but may be related to the lower incidence of MBL and the slower progression of CLL-like MBL in Asians.

Therefore, studying the prevalence of MBL among Asian populations may help to understand these ethnic differences and the mechanisms of CLL development.

This study was conducted among descendants of Japanese immigrants living abroad, including the city of São Paulo in Brazil. It involved 258 healthy Japanese adults over 40, mostly without racial mixing. The study used highly sensitive multiparametric flow cytometry (MFC) to analyze clonal B-cells in peripheral blood. The study found a low incidence of MBL, which precedes CLL, among the descendants of Japanese immigrants living abroad. Patients with high MBL levels were rare; low MBL levels were more common, but the risk of progression to CLL was low. This supports the assumption of a lower incidence of MBL and a slow progression to CLL in the descendants of Japanese immigrants living abroad. These results may help to understand better ethnic differences in the development of CLL and its previous conditions, as well as shed light on the mechanisms of the development of this type of leukemia [26].

This review considers research on MBL and its relationship to CLL. Studies conducted in different populations have shown significant differences in the prevalence and progression of MBL and chronic lymphocytic leukemia (CLL). These differences are revealed not only between ethnic groups but also between patients with different epigenetic profiles. In particular, a combined strategy to create an epigenetic and light chain immunoglobulin (ELCLV3-21) signature has demonstrated high prognostic significance. It allows you to identify people with MBL who have a high probability of disease progression, which improves the accuracy of predicting the time to therapy compared to other prognostic indicators.

A study in Uganda and the United Kingdom found significant differences in the prevalence of MBL between the two populations. These results highlight the importance of considering ethnic and geographic factors when studying MBL and CLL, as they can significantly influence the prevalence and phenotypic characteristics of the disease.

Discussion:

This review examines modern approaches to diagnostics and classification of MBL in detail, emphasizing the importance of flow cytometry in identifying and differentiating its phenotypes.

Studies of MBL and its progression to CLL and other lymphoproliferative diseases suggest that different biomarkers and phenotypes play a crucial role in predicting risk. The review presents data from the MBL, demonstrating heterogeneity with different profiles. The number of clonal B-cells in the peripheral blood is one of the most significant risk factors. A low MBL level, at which the number of clonal B-cells is less than 0.5×10^9/L, can remain stable for a long time. At the same time, high-grade (HC) CLL type MBL (>0.5×10^9/L clonal B-cells) can progress from a precancerous state to true CLL [11]. The prediction of lymphoproliferative diseases such as CLL is based on analyzing these clonal populations and their characteristics. MBL is defined as a circulating population of monoclonal B-cells below 5×10^9/L (5,000/μL) persisting for at least three months in otherwise asymptomatic individuals [9, 10].

MBL phenotypes, as determined by flow cytometry, also play an essential role in predicting the risk of progression to CLL and other lymphoproliferative diseases. There are three types of MBCL: CLL-type, atypical CLL-type and non-CLL-type. Each of these types has its own unique immunological and clinical characteristics. The expression of the CD5, CD19, CD20, and CD23 markers characterizes the CLL-like phenotype. This phenotype has the most significant risk of progression to CLL, an atypical CLL-like phenotype expressing CD5, CD19, and CD20 markers but not CD23. The risk of progression to CLL is lower than that of the CLL-like phenotype but higher than that of the non-CLL phenotype; the non-CLL phenotype does not express the CD5 marker but expresses CD19 and CD20. Associated with marginal zone lymphoma and has the lowest risk of progression to CLL. Determination of immunoglobulin light and heavy chains on the surface of B-cells may help in predicting the risk of progression. Kappa and lambda light chains and their ratio and expression level may indicate clonality and possible disease progression [13-15, 18-21].

Mutations in the Immunoglobulin Heavy Variable (IGHV) genes are an essential prognostic factor in MBL. The presence of mutated or unmutated IGHV genes may indicate a different risk of progression to CLL. Unmutated IGHV genes are associated with a more aggressive course of the disease and a higher risk of progression [18, 19].

Cytogenetic changes such as del(13q), +12, and del(17p) are often found in patients with MBL and may be significant for prognosis. The detection of del(13q) is usually associated with a favorable prognosis, del+12 may be associated with an intermediate prognosis, del(17p) is associated with a more aggressive course of the disease and a worse prognosis and is often found in patients with CLL [9, 11].

Conclusion: The present study confirms the importance of different types of MBL differentiation for accurate diagnostics and prognosis. High-grade MBL, which has a higher probability of progression to CLL, requires closer monitoring. The detection of cytogenetic alterations such as del(13q), +12, del(11q), and del(17p) early in clonal evolution emphasizes the need for early detection and surveillance.

In contrast, MBL with low lymphocyte content proceeds more benignly and does not require as intensive monitoring as MBL with high content. Differences in the expression of surface markers between MBL phenotypes, such as CD5, CD23, CD10, CD103, CD79b, and immunoglobulin light chains, are critical to their classification and determination of progression risk.

The next stage of our study will be to examine archival material from the last 15 years. We plan to determine the number of patients with CLL, identify cases of genetic predisposition and MBL, and estimate clonality. Our experience will also show how many patients with CLL had MBL and what types of clonality were found.

Further studies are needed to understand better the molecular mechanisms underlying the progression of MBL to CLL and to develop better strategies to predict and prevent this progression. Clinicians must be aware of the differences between types of MBL and utilize appropriate diagnostic and monitoring techniques to ensure the best patient outcomes.

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АҢДАТПА

ЛИМФОПРОЛИФЕРАТИВТІ АУРУЛАРДЫ БОЛЖАУДАҒЫ МОНОКЛОНАЛДЫ В ЖАСУШАЛЫ ЛИМФОЦИТОЗДЫҢ РӨЛІ: ӘДЕБИЕТКЕ ШОЛУ

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Өзектілігі: *Дүниежүзілік денсаулық сақтау ұйымы 2017 жылы қан ауруларының кейбір түрлерін жіктеу үшін енгізген моноклоналды в-жасушалы лимфоцитоз (МБКЛ) жіктеудің жаңа перспективаларын ашады, сонымен қатар қосымша зерттеуді қажет ететін мәселелерді көтереді. МБКЛ зерттеулері диагностика мен бақылауды жақсарту үшін өте маңызды, бұл созылмалы лимфоцитарлық лейкемияны (ХЛЛ) ерте анықтауға және алдын алуға көмектеседі.*

Зерттеудің мақсаты: *моноклоналды В жасушалы лимфоцитоздың иммунофенотиптік аспектілерін және созылмалы лимфоцитарлы лейкозға айналу қаупін бағалау.*

Әдістері: *Ғылыми жарияланымдарды талдау барысында MBL себептері және оның cll-мен байланысы қарастырылып, осы жағдайлардың иммунофенотиптік аспектілеріне назар аударылды. Әдеби деректерді зерттеу MBL-дің CLL-ге өтуіне байланысты факторлар, соның ішінде биомаркерлер Мен клиникалық сипаттамалар туралы ақпарат берді, бұл MBL бар науқастарда лейкоздың даму қаупін толық бағалауға мүмкіндік берді.*

Нәтижелері: *MBL мен CLL арасындағы байланысқа қатысты көптеген зерттеулер талданды. Талдау көрсеткендей, MBL көбінесе CLL дамуынан бұрын пайда болады, MBL клондары клиникалық диагноздан бірнеше жыл бұрын анықталуы мүмкін. Бұл MBL даму қаупін анықтау үшін ерте биомаркер бола алады деген гипотезаны қолдайды.*

Әр түрлі зерттеулер MBL және CLL таралуы мен дамуындағы айтарлықтай этникалық және географиялық айырмашылықтарды көрсетеді. Бұл айырмашылықтар эпигенетикалық факторларға, иммуноглобулиннің өзгеруіне және басқа генетикалық ерекшеліктерге байланысты болуы мүмкін. Бұл айырмашылықтарды түсіну пациенттердің жеке және популяциялық ерекшеліктерін ескеретін дәлірек диагностикалық және болжамды тәсілдерді әзірлеу үшін маңызды.

Қорытынды: *Жүргізілген талдау MBL мен CL арасындағы байланысты одан әрі зерделеу, сондай-ақ MBL ерте анықтау үшін скринингтік бағдарламаларды енгізу Қазақстандағы пациенттердің болжамы мен денсаулығын айтарлықтай жақсарта алатынын көрсетеді.*

Шолу нәтижелері ерте диагностиканың және емдеуге жеке көзқарастың маңыздылығын көрсетеді. Бұл MBL-дің CLL-ге өтуіне жол бермейді және біздің елдегі денсаулық сақтау сапасын жақсартады.

Түйін сөздер: *Моноклоналды в жасушалы лимфоцитоз, созылмалы лимфоцитарлық лейкемия, иммунофенотип, даму қаупі, ағындық цитометрия.*

АННОТАЦИЯ

РОЛЬ МОНОКЛОНАЛЬНОГО В-КЛЕТОЧНОГО ЛИМФОЦИТОЗА В ПРОГНОЗИРОВАНИИ ЛИМФОПРОЛИФЕРАТИВНЫХ ЗАБОЛЕВАНИЙ: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: *Моноклональный В-клеточный лимфоцитоз (МБКЛ), введенный Всемирной организацией здравоохранения в 2017 году для классификации некоторых видов заболеваний крови, открывает новые перспективы в классификации, но также поднимает вопросы, требующие дальнейшего изучения. Исследования МБКЛ имеют важное значение для улучшения диагностики и мониторинга, что может способствовать раннему выявлению и предотвращению развития хронического лимфоцитарного лейкоза (ХЛЛ).*

Цель исследования *– оценить иммунофенотипические аспекты моноклонального В-клеточного лимфоцитоза и риск прогрессирования в хронический лимфоцитарный лейкоз.*

Методы: *В ходе анализа научных публикаций были рассмотрены причины возникновения МБКЛ и его связь с ХЛЛ, акцентируя внимание на иммунофенотипических аспектах данных состояний. Исследование литературных данных предоставило информацию о факторах, связанных с прогрессированием МБКЛ в ХЛЛ, включая биомаркеры и клинические характеристики, что позволило более полно оценить риск развития лейкоза у пациентов с МБКЛ.*

Результаты: *Были проанализированы многочисленные исследования, касающиеся связи между МБКЛ и ХЛЛ. Анализ показал, что МБКЛ часто предшествует развитию ХЛЛ, причем клоны МБКЛ могут быть обнаружены за годы до клинического*

диагноза. Это подтверждает гипотезу о том, что МБКЛ может служить ранним биомаркером для выявления риска развития.

Различные исследования подчеркивают значительные этнические и географические различия в распространенности и прогрессировании МБКЛ и ХЛЛ. Эти различия могут быть связаны с эпигенетическими факторами, иммуноглобулиновыми перестройками и другими генетическими особенностями. Понимание этих различий важно для разработки более точных диагностических и прогностических подходов, которые учитывают индивидуальные и популяционные особенности пациентов.

***Заключение:** Проведенный анализ показывает, что дальнейшее изучение связи между МБКЛ и ХЛЛ, а также внедрение программ скрининга для раннего выявления МБКЛ могут существенно улучшить прогноз и здоровье пациентов в Казахстане.*

Результаты обзора подчеркивают важность ранней диагностики и индивидуального подхода к лечению. Это поможет предотвратить прогрессирование МБКЛ в ХЛЛ и повысить качество медицинского обслуживания в нашей стране.

***Ключевые слова:** моноклональный В-клеточный лимфоцитоз, хронический лимфоцитарный лейкоз, иммунофенотип, риск развития, проточная цитометрия.*

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