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# ОСТРЫЙ МИЕЛОИДНЫЙ ЛЕЙКОЗ У БОЛЬНОГО ХРОНИЧЕСКИМ ЛИМФОЦИТАРНЫМ ЛЕЙКОЗОМ: ТРУДНОСТИ ДИАГНОСТИКИ (КЛИНИЧЕСКИЙ СЛУЧАЙ)

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О сосуществовании хронического лимфоцитарного лейкоза (ХЛЛ) и острого миелоидного лейкоза (ОМЛ) у одного и того же пациента сообщалось редко, чаще как результат лечения химиотерапевтическими препаратами. Изменения показателей крови у онкологических больных могут быть интерпретированы как прогрессирование заболевания или ятрогенные эффекты, связанные с агрессивным лечением, приводя к несвоевременной диагностике. В нашей статье мы хотим обратить внимание на возможность развития ОМЛ у больных ХЛЛ и сопутствующие трудности диагностики.

***Ключевые слова:*** *хронический лимфоцитарный лейкоз; острый миелоидный лейкоз; гематологические анализаторы; флаги; мазок периферической крови; разрушенные клетки; бласты.*

## ACUTE MYELOID LEUKEMIA IN A CHRONIC LYMPHOCYTIC LEUKEMIA PATIENT: DIAGNOSTIC CHALLENGE (CLINICAL CASE)

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Chronic lymphocytic leukemia (CLL) and acute myeloid leukemia (AML) coexistence in the same patient has been rarely reported, more frequently due to treatment with chemotherapeutic agents. Blood parameter changes in cancer patients may be interpreted as disease progression or iatrogenic effects related to aggressive treatment, leading to delayed diagnosis. In our article, we call attention to the possibility of AML development in CLL patients and its diagnostic challenge.

***Keywords:*** *chronic lymphocytic leukemia; acute myeloid leukemia; hematology analyzers; flags; peripheral blood smear; smudge cells; blasts.*

Chronic lymphocytic leukemia (CLL) is known to be associated with the increased risk of second hematological malignancies [1]. The coexistence of CLL and acute myeloid leukemia (AML) in the same patient has been rarely reported. Most cases were the result of treatment with chemotherapeutic agents for CLL [2]. Few cases describe CLL patients who developed AML two weeks to four years after treatment. In addition, cases without previous treatment are extremely rare [3].

Modern automated blood count analyzers enable quantitative and identification analyses and flagging tangible blood components with electrical impedance, laser light scattering, and dye bonding (flow cytometry). Different

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groups of detected components are presented numerically and displayed on scattergrams. Automated hematology analyzers perform complete blood count (CBC), generate algorithms-based pathology flags for all three lineages (erythrocytes, leukocytes, and platelets) to alert the clinical pathologist. As for leukocyte differentiation alterations and other morphologic abnormalities, Sysmex (Kobe, Japan) analyzers detect pathologic patterns and generate messages (flags): «Blast?» (Sysmex XE-5000) or «Blasts/Abnormal Lymphocytes?» (Sysmex XN with improved detection performance). These flags appear in acute and chronic leukemias of myeloid and lymphoid origin, myelodysplastic syndrome, plasma cell myeloma, lymphomas, left shift in granulocyte maturation, pseudo-Pelger-Huët anomaly, and in newborn children. The examination of the peripheral blood (PB) smear is routinely used as a basic step to evaluate hematological conditions and diseases suspected on analyzers flags [4-6].

In this letter, we intend to raise awareness of the possibility of AML development in CLL patients and its diagnostic challenge.

***Case description.*** An 80-year-old man presented to the Emergency Department in November 2019 with an acute-onset of right knee pain and edema, general weakness, and fever. His physical examination revealed skin pallor and hepatosplenomegaly.

His recent medical history included prostate cancer diagnosed in January 2018 and treated with leuprolide; clear cell renal cell carcinoma diagnosed in June 2018 with subsequent nephrectomy; small lymphocytic lymphoma diagnosed in June 2018 and treated with six cycles of complex chemotherapy (*rituximab* + *cyclophosphamide* + *vincristine* + *prednisolone*). While his initial response was positive, the patient progressed to CLL in October 2018 and started *Ibrutinib* with a favorable response.

His automated PB count revealed bicytopenia and leukocytosis (hemoglobin: 5.2 g/dL, platelets: $75\times10^9$/L, white blood cells: $93.73\times10^9$/L). The Sysmex XE-5000 analyzer reported a flag «blasts?» that was already present in all the patient´s CBCs since his CLL diagnosis. While anemia, leukocytosis, and thrombocytopenia could be interpreted as CLL relapse, the scattergram cytoDIFF was suspicious for the presence of blasts and required further examination (Figure 1).

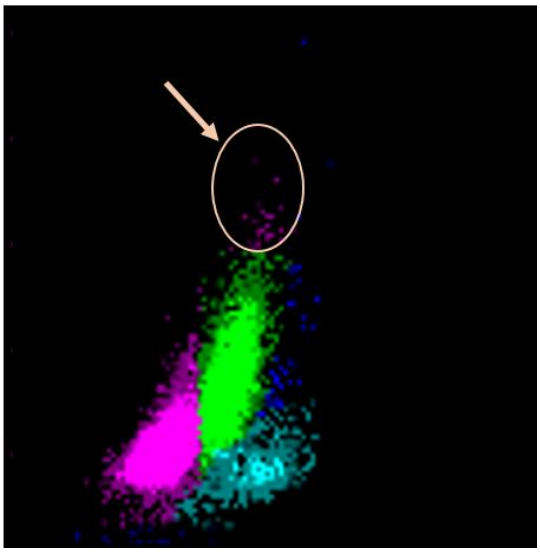

Fig. 1. Sysmex 5000 – Scattergram cytoDIFF

The PB smear microscopic examination showed two distinct populations suggesting an abnormality: small cells corresponding to mature lymphocytes (83%) with smudge cells

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and large cells corresponding to *blast cells* (13%, Figure 2). In four weeks, the blast cells proportion increased to 37%.

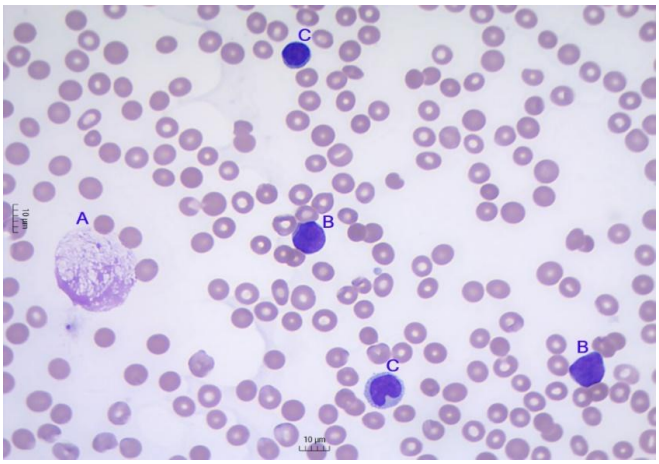


Fig. 2. PB Smear (May-Grunwald-Giemsa staining) microscopy (500×):
A – Smudge cell, B – Blast cells, C – Lymphocytes

PB immunophenotypic analysis confirmed morphological findings. CLL diagnosis was confirmed by demonstrating the expression of mature B-cell markers (CD19+, CD20dim), CD5+, and CD10-. Blast cells expressed myeloid markers (CD33+, MPO+), and «AML not otherwise specified» was diagnosed.

## Conclusions

Bicytopenia development in cancer patients may be interpreted as disease progression or iatrogenic effects related to aggressive treatment, leading to delayed diagnosis. The present case highlights the *need for careful PB smear revision, especially in CLL patients* where the automatic analyzers routinely produce abnormal leucocytes presence alerts. Awareness of the possible development of AML in CLL patients is the key to its timely and accurate diagnosis.

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**Дополнительная информация [Additional Info]**

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