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False macrocytosis in chronic lymphocytic leukemia and how we can correct it

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Abstract
Aim: To present a case report of CLL, with a false macrocytosis caused by an important lymphocytosis and to demonstrate how we were able to detect it and our action to correct it.
Methodology: When we have double population RBC histogram we have to use another parameter is the red blood cells most frequent volume (R-MFV) that defines the peak of the curve and fits the MCV in normal distribution.
Results: CBC revealed leucocytosis (60×10^9/L), moderate normochromic anaemia (haemoglobin of 11.9 g/dL, MCV of 125 fl, In our case R-MFV is of 107 fl. The macrocytosis is still present; but would not be expected to reach 125 fl. It is also necessary to recalculate the parameters which depend on the MCV. Liver laboratory tests are abnormal in relation to the liver failure. This explains the mild macrocytosis observed even after correction of MCV.
Conclusion: Pronounced leukocytosis can lead to overestimation of the MCV, especially in chronic lymphoid leukemia, therefore we must be careful when we interpret the parameters of complete blood count.

Keywords: CLL, macrocytosis**,** MCV, R-MFV

Introduction
Chronic lymphoid leukemia (CLL) is a very heterogeneous blood disease. It is the most frequent pathology of adult leukemia in the western world. It represents 25% of adult leukemia's and 25% of non-Hodgkin's lymphoma (NHL) [1, 2].
CLL is defined by an absolute value of monoclonal B lymphocytes CD5+/CD23+ at least 5×10^9/L in peripheral blood (PB) for more than three months [3, 4].
The great number of lymphocytes observed during CLL could disrupt the different parameters of Complete Blood Count (CBC), especially auto hematology analyze based on the principle of impedance.
In this case we present a newly diagnosed CLL, we present a patient whose CBC indicates a false macrocytosis caused by an important lymphocytosis, and we will describe how we were able to detect it and our action to correct it.

Case report
The patient was a 70 year-old who was diagnosed with CLL in 2018, the clinical history was significant for liver disease, and non-alcohol exposure.
On physical examination, the patient presents axillary lymphadenopathy, loss of appetite and vomiting.
CBC revealed leucocytosis (60×10^9/L), moderate normochromic anaemia (haemoglobin of 11.9 g/dL, MCV of 125 fl, Mean Corpuscular Haemoglobin (MCH) of 31 picogrammes), and mild thrombocytopenia (115×10^9/L) with double population in RBC histogram.
The peripheral blood smear showed 87% of lymphocytes (52, 20×10^9/L) with smudge cells 25%; 13% of polynuclear neutrophils (7, 8×10^9/L), without hyper segmentation. For red cells we can see a mild macrocysis, but don't fit to MCV of 125 fl; we can also see a spur cell, target cells without abnormalities of platelets.
According at his profile the patient was classified in stage A according the Binet classification and stage I according the RAI classification.
Flow cytometry revealed a population of B lymphocytes, which expressed CD19+, CD5+, CD23+, CD79b strong expression, FMC7-, and the surface lambda light chain. Chronic lymphocytic leukemia was then diagnosed and assigned to the Matutes score of 4.

Liver laboratory tests found Alanine aminotransferase (ALT) = 55 U/L, (Normal Range, NR 8-35 U/L); Gamma-glutamyl transferase (GGT) = 50 UI/L, (NR 6-28 U/L); Total bilirubin = 20 mg/L (NR ≤ 12 mg/L); Prothrombin time (PT) = 60% (NR = 70-100%).

Discussion

The red blood cell count (RBC) and the measurement of RBC size are realized in almost of auto hematology analyzer according to the coulter principle (impedance method). In chronic lymphocytic leukemia, the leucocytosis is often higher than 50 $\times 10^9$/L (52, 20×10^9/L in our case). The white blood cells and especially the lymphocytes can pass through the counting aperture of the red blood cell channel, and could be considerate as red blood cells. The number of red blood cells is slightly increased and does not influence the final red blood cell count. However the analyzer calculates mean corpuscular volume (MCV) based on the RBC histogram, and the lymphocytes that pass through the red blood cell channel falsely increase the MCV. The lymphocytes have an MCV of approximately between 150 and 200 fL), and the average MCV determined by the automated counter depends on the percentage of the lymphocytes that pass through the red blood cell [5].

In RBC histogram, whose x- coordinate represents the red cell volume (fl) and y- coordinate represents the number of the red blood cells; we can see double population: the first one corresponds to RBCs and the second one corresponds to the lymphocytes wish have passed in RBC channel .

When we have double population RBC histogram we have to use another parameter is the red blood cells most frequent volume (R-MFV) that defines the peak of the curve and fits the MCV in normal distribution [6]. In our case R-MFV is of 107 fl. The macrocytosis is still present; but would not be expected to reach 125 fl. It is also necessary to recalculate the parameters which depend on the MCV; which are haematocrit (HCT) and mean corpuscular haemoglobin concentration (MCHC).

Liver laboratory tests are abnormal in relation to the liver failure. This explains the mild macrocytosis observed even after correction of MCV. And the presence of macrocytosis, acanthocyte and target cell in peripheral blood smear this is due to the deposition of cholesterol at the level of the cytoplasmic membrane of the globules [7, 8].

Conclusion

Pronounced leukocytosis can lead to overestimation of the MCV, especially in chronic lymphoid leukemia, therefore we must be careful when we interpret the parameters of complete blood count. Some auto hematology analyzer proposes new parameters obtained by the optical method such as RBC-O, in parallel with the impedance method for RBC which minimizes the error rate and improves the management of disturbance of parameters of complete blood count [9].

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All authors disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work.

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