doi: http://dx.doi.org/10.11606/issn.1679-9836.v100i2p189-192 Rev Med (São Paulo). 2021 March-April;100(2):189-92.

Case Report

Unusual case report of acute evolution of hairy cell leukemia in a young adult patient, *Amazônia*, Brazil.

Relato de caso incomum de leucemia de células pilosas de evolução aguda em paciente adulto jovem, Amazônia, Brasil

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Nascimento AL, Brito Junior LC. Unusual case report of acute evolution hairy cell leukemia in a young adult patient, *Amazônia*, Brazil / *Relato de caso incomum de leucemia de células pilosas de evolução aguda em paciente adulto jovem, Amazônia, Brasil.* Rev Med (São Paulo). 2021 March-April;100(2):189-92.

ABSTRACT: Hairy cell leukemia (HCL) is a rare disease of unknown origin and indolent course, which is detected in a complete blood count associated by pancytopenia and lymphocytes with cytoplasmic projections. This study presents a case report of a 31-year-old male patient, with pallor and no splenomegaly, who was admitted to the *Municipal Hospital* of *Rondon do Pará, Amazônia*, on December 31, 2018 to perform laboratory tests due to the worsening of his general condition. The complete blood count revealed: anemia (hemoglobin level of 7.5 g/dL and hematocrit level of 20%), thrombocytopenia (28,200/mm3) and hyperleukocytosis (179,000/mm3) while 88% of lymphocytes presented thin and elongated cytoplasmic projections suggestive of hairy cells. On January 7, 2019, the patient's condition worsened, resulting in death before the diagnostic confirmation of the immunophenotyping test, which revealed a clonal population of 68.3% of hairy cells that expressed antigens CD19, CD20, CD79b, CD23, IgM, CD200, CD38, FMC-7, CD25 and CD103. It was not possible to determine which factors were decisive to this situation.

Keywords: Hairy cell leukemia; Fatal outcome; Leukocytosis; Flow cytometry.

RESUMO: A Leucemia de Células Pilosas (LCP) é uma doença rara, de origem desconhecida, de curso indolente, e que se apresenta no hemograma associada a pancitopenia e linfócitos com projeções citoplasmáticas. No presente estudo apresentamos o relato de caso de um paciente de 31 anos, masculino, hipocorado, sem esplenomegalia, admitido no Hospital Municipal de Rondon do Pará, Amazônia, no dia 31.12.2018 para a realização de exames laboratoriais em função de rebaixamento do estado geral. O hemograma revelou: anemia (7.5g/dL de hemoglobina e 20% de hematócrito), plaquetopenia (28.200/mm^3) e hiperleucocitose (179.000/mm^3) as custas de 88% de linfócitos com projeções citoplasmáticas finas e alongadas sugestivas de células pilosas. No dia 07.01.2019 houve piora do quadro do paciente com evolução a óbito antes mesmo da confirmação diagnóstica pelo exame de imunofenotipagem que revelou tratava-se de população clonal de 68,3% de células pilosas com expressão dos antígenos: CD19, CD20, CD79b, CD23, IgM, CD200, CD38, FMC-7, CD25 e CD103. Não tendo sido possível a determinação de quais fatores foram determinantes para esse quadro.

Palavras-chave: Leucemia de células pilosas; Tricoleucemia; Evolução fatal; leucocitose; Citometria de fluxo.

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INTRODUCTION

Chronic lymphoproliferative disorders (CLDs) represent the most frequent group of blood cancers in the world among individuals 50 years old and older, with very different clinical presentations, evolutions and prognoses. Its initial diagnosis is suggested by the presence of persistent lymphocytosis, i.e., more than 5,000 lymphocytes/mm^3, in three consecutive complete blood counts (CBCs)[1,2]. The diagnosis must then be confirmed using complementary tests such as imaging tests; myelograms; bone marrow, skin, spleen or lymph node biopsies; analysis of neoplastic cells in body cavity or cerebrospinal liquids; serum tests; immunophenotyping or immunohistochemistry tests; and cytogenetic or molecular exams[1,3].

Among the various types of B-cell CLDs, hairy cell leukemia (HCL) stands out because of the morphological presentation of the lymphocytes. They contain round or oval nuclei, abundant cytoplasm with long and thin hair-like projections ("hairy cells") visible in the CBC, in bone marrow tests, and in the analysis of splenic red pulp[1,3,4].

Hairy cell leukemia is a rare disease of unknown origin with an incidence rate of 2% to 4% of all cases of lymphoid leukemias, although it has been associated by various authors with exposure to radiations, benzene, herbicides, and pesticides[1,4,5,6]. It affects mainly men (ratio of 5:1); white individuals (ratio of 3:1) in relation to those of other races, and the median age of patients is 55 years[7,8,9,10].

Clinically, HCL evolves slowly and is associated with splenomegaly, susceptibility to bacterial infections, in addition to anemia and hemorrhages. In advanced stages, it can also manifest in association with adenomegaly, hepatomegaly, and significant skin manifestations [3,7,8,9,10,11].

Initial laboratory diagnosis of HCL requires the presence of pancytopenia followed by relative lymphocytosis, with the presence of "hairy cells", and monocytopenia in the CBC[1,3,4,7,8,11,12]. However, the definite diagnosis of the disease depends on biopsies, which will reveal the presence of bone marrow fibrosis, immunohistochemistry tests; and flow cytometry immunophenotyping tests using blood marrow or peripheral blood cells, which will express mature B-lymphocyte antigens CD19, CD20, CD22, CD79b, and surface immunoglobulins (IgM), in variable co-expression with antigens FMC-7, CD25, CD11c, and CD103. The same cells will also be negative for CD5, CD10, and CD23[1,3,4,8,12].

Thus, the objective of this study was to report a case of acute evolution of hairy cell leukemia in association with hyperleukocytosis and a fatal outcome in a young adult patient.

CASE DESCRIPTION

A 31-year-old male patient was admitted to the Rondon do Pará Municipal Hospital on December 31, 2018 with a fever, chest pain, asthenia and general malaise. In the general clinical evaluation, he was pale but presented normal blood pressure (120 x 80 mmHg) and normal physiological functions, with no enlarged organs, vesicular murmurs or abnormal auscultation findings. Because of the clinical complaint at admission, he was hospitalized to be monitored and receive complementary tests from the Regional Hemocenter of Marabá, state of Pará.

On January 4, 2019, the patient was referred to the Regional Hemocenter of Marabá for specialized care and to test for levels of serum iron (263µg/dL) and ferritin (2,262ng/mL) which were high; to perform serology for hepatitis B and C, human immunodeficiency virus (HIV I/II), human t-cell lymphotropic virus (HTLV), Chagas disease, and syphilis, all of which were non-reactive; and a CBC that revealed anemia (RBC - 2.01 million/mm^3, hemoglobin - 7.5g/dL, hematocrit - 20% and red cell distribution width (RDW) - 15.8%), thrombocytopenia (28,200/mm^3), and hyperleukocytosis (179,000/mm^3). The differential white blood cell (WBC) count performed by the equipment presented confusing results and alerted to the presence of immature granulocytes and/or blasts. Thus, the sample was sent to the Coordinating Hemocenter of Belém to carry out a morphological confirmation of the WBC differential count.

Using a common light microscope at the Coordinating Hemocenter of Belém, the peripheral blood smear analysis revealed the presence of 12,530 neutrophils/mm^3 (7%), 8,950 monocytes/mm^3 (5%) and 157,520 lymphocytes/mm^3 (88%) with specific cytomorphological abnormalities, such as long and thin cytoplasmatic projections, suggestive of hairy cells (Figure 1). Immediately after this analysis, the peripheral blood was sent for flow cytometry immunophenotyping in another specialized center in Belém, Pará, to confirm the diagnostic hypothesis.

On January 5, 2019, the patient's overall condition began to worsen, with epigastric pain that irradiated to the back, asthenia, and increased pallor. On January 7, 2019, new lab tests were conducted: glucose (60mg/dL); creatinine (1.10mg/dL); blood urea nitrogen (38mg/dL) and a CBC that revealed: bicytopenia of the red blood cells (erythrocytes – 1.66 million/mm^3; hemoglobin - 5.6g/dL; hematocrits - 16.30%) and of the platelets (9,000 platelets/mm^3); in addition to the maintenance of hyperleukocytosis (131,500 leukocytes/mm3) with 97% of WBC, whose morphology suggested HCL.

Still on January 6, 2019, the patient's condition deteriorated rapidly, resulting in death. The immunophenotyping test revealed a clonal population of 68.3% of cells that expressed mature B-lymphocyte antigens CD19, CD20, CD79b, CD23, IgM, and CD200, and a kappa/lambda ratio = 0.9; in addition to expressing cellular activation antigens CD38 and FMC-7; and antigens CD25 and CD103, which characterize the disease. Finally, the test was negative for both CD5 and CD10.

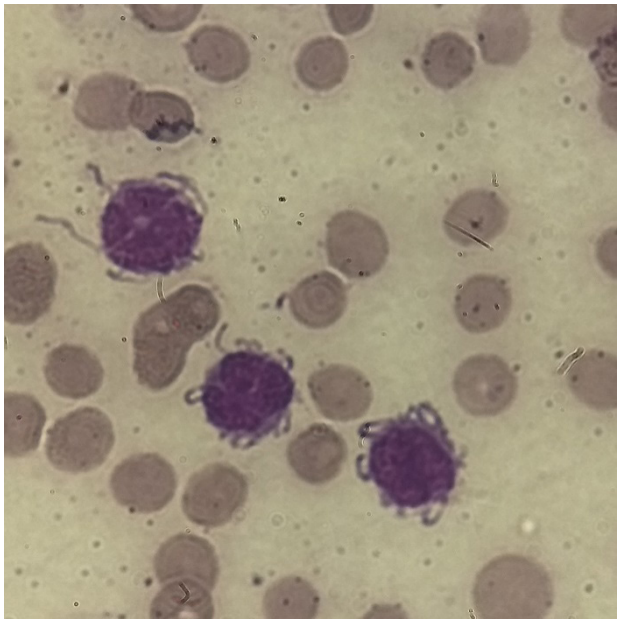

Figure 1: Lymphocytes with cytoplasmatic hair-like projections ("hairy cells").

DISCUSSION

According to the clinical laboratory and immunophenotypical criteria, the case presented in this article may refer to classic HCL that could have presented a good prognosis because of the absence of splenomegaly and the patient's young age. However, anemia, thrombocytopenia, high WBC count, the impossibility of investigating the *BRAFV600E* mutation that could better characterize the classic form of the disease, and the acute evolution of his condition possibly impaired the patient's prognosis, as has been well described in the literature[3,7,8,11,13,14].

Salam and Abdel-Wahab[8] have cited in their studies that in very rare cases, patients with classic HCL may present CBCs with WBC counts greater than 10,000 leukocytes/mm^3. Rudolf-Oliveira et al.[14], in turn, reported that leukocytosis is a more common finding in patients with HCL-variant. Several authors define that the classification of HCL into classic or variant can be based on criteria such as the patient's WBC count; therefore, according to this criterion, it is possible that the patient in question had classic HCL, however, with some genetic mutation that resulted in an increase in WBC count and consequently led to a fatal outcome[1,3,8].

Another factor that may have been crucial to the disease's acute evolution in this patient was the possible delay in seeking medical care, because the patient already presented significant anemia and thrombocytopenia when he was admitted. In their studies, Salam and Abdel-Wahab[8] suggest that anemia and thrombocytopenia are two of the main factors that limit the success of treatment for people with HCL. Secioso, Cardoso and Frazão[11] published a case report in which they assessed that the slow course of the disease and delays in diagnosing patients with HLC can produce serious infectious complications and culminate in the death of patients even before diagnosis.

Haouach et al.[15] presented a case report of a patient with HCL and tuberculosis and indicated that it is already common sense that patients with HCL have a special predisposition to mycobacterial infections in about 8% of cases. However, even though the patient in their study presented fever, chest pain, asthenia and general malaise, which are general symptoms in the course of HLC[1,8,11] and also tuberculosis, the hypothesis of tuberculosis or any other associated infection was not investigated during the patient's care because of the acute evolution of the disease.

The geographic origin of the patient in the present case study, Rondon do Pará, a predominantly rural town, reinforces the hypothesis that there may be an association between HCL and the use of pesticides in the Brazilian Amazon region, as has been recorded by our research group in other studies[2,4].

Barbosa et al.[5], for example, conducted an epidemiological study about cases of leukemia and lymphomas in the state of Pará between 2005 and 2011, and observed that the main occupation of 19.2% of patients was agriculture, and that the use of pesticides was a common practice in their daily routine.

In his studies about the use of pesticides in the Brazilian Amazon region, Waichman[6] showed that several factors contribute to the indiscriminate and incorrect use of these products in this part of the country. These include low education levels (illiteracy) of farmers who manipulate and apply the products; lack of preparation relative to the risks involved when using and disposing empty pesticide packages; lack of personal protection equipment; and free and indiscriminate sale of pesticides in the region. These factors contribute to an increased risk of contamination not only of farmers, but also of their family members and the environment.

CONCLUSION

Classic HCL is a chronic lymphoproliferative disorder that progresses slowly; however, as shown in this case report, there are patients with associated cases of hyperleukocytosis and fatal outcomes. It is essential that more studies be conducted to clarify which factors are associated with the emergence of the disease and these aggressive forms of HCL.

Author participation: *Aline Lira do Nascimento* - collected the data, performed the analysis, and drafted the paper. *Lacy Cardoso de Brito Junior* - performed the analysis and drafted the paper critically.

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Received: 2020, July 24
Accepted: 2021, January, 04