Procedures and evolution in the diagnosis of ALL: A bibliographic review

https://doi.org/10.56238/sevened2023.006-043

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ABSTRACT
ALL is characterized as a malignant heterogeneous hematopoietic neoplasm in which an uncontrolled proliferation of blood cells occurs, resulting in the accumulation of young cells in the bone marrow. With the advances in diagnosis, the blood count is the first step in diagnosing ALL, with this immunophenotyping test also becoming effective. This immunophenotyping is performed using the flow cytometry technique, and has helped guide therapeutics. The present study aimed to understand the importance of laboratory evaluation for the early diagnosis of ALL, and the impact that a good evaluation can have on the diagnosis. This present work consisted of a qualitative bibliographic research on ALL diagnostic methods in Brazil. Analyzing the clinical perspective, there are several diagnostic methods for ALL, thus highlighting the importance of clinical diagnoses and the frequent improvement of methods.

Keywords: ALL, Diagnostic and blood count.

1 INTRODUCTION

According to the National Cancer Institute (INCA), 10,810 new cases of leukemia were diagnosed in Brazil per year during the 2020-2022 triennium (INCA, 2022).

Leukemia is distinguished by being a malignant disease that affects all etiological ages and occurs in the leukocyte series. There are more than 12 different types of leukemia, with the four main primary forms being: acute myeloid (AML), chronic myeloid (CML), acute lymphoctica (ALL), and chronic lymphoctica (CLL) (JUNQUEIRA, 2022).

ALL is characterized as a malignant heterogeneous hematopoietic neoplasm in which there is an uncontrolled proliferation of blood cells, resulting in the accumulation of young cells in the bone marrow. They are classified into 3 morphological subtypes, L1, L2 and L3. (CAVALCANTE, M. S, 2017)tag. L1- They are small and homogeneous lymphoid cells, with fine nuclear chromatin, and absence of nucleoli, and sparse cytoplasm and normal nuclear structure, L2- Large and heterogeneous cells, with foamy nuclear chromatin, which has the presence of nucleoli, and abundant cytoplasm and

irregularly shaped nucleus, L3- Large and uniform lymphoid cells with thin nuclear chromatin, and prominent nucleoli, strongly basophilic cytoplasm, and presence of vacuoles (WILLIG, 2021).

In 70% of cases, this disease affects children and is characterized by the presence of immature lymphocytes in the blood. To determine the severity of the cancer and determine whether it belongs to the L1, L2 or L3 subtypes, immunohistochemical tests and genetic research are performed (CAVALCANTE, M. S, 2017).

The pathophysiological process of acute lymphoblastic leukemia is understood as a disturbance in the maturation process of blood cells. In this way, there is a disorder in the production of lymphoid cells in the body, triggering a proliferation of blasts (young cells) in the bloodstream. In this sense, it is said that a dysfunction occurs in the bone marrow in which the processes of cell maturation are impaired (GUIMARAES, 2022).

Chronic myeloid leukemia (CML) is characterized by a progressive loss of cell differentiation. This disease is linked to a cytogenetic abnormality in the Philadelphia chromosomes (Ph). A CML occurs one to two times for every 100 million people, accounting for about 15% to 20% of all leukemias. It occurs more frequently in adults between 40 and 60 years of age, especially males. However, it can detect individuals of all etiological categories with less than 10% of patients in the younger 20 age group. Acute myeloid leukemia includes the three distinct phases of the clinical course known as: chronic, accelerated, and monetary crisis (DO LADO & SOSSELA, 2017).

Patients with acute lymphoblastic leukemia may also experience a variety of vague symptoms, such as: Weight loss; Tiredness; Weakness; Dizziness or lightheadedness; Shortness of breath; Fever; Severe or frequent infections; Bruising or bleeding (FONSECA, 2017).

With the advancement of diagnosis, the blood count is the first step in diagnosing ALL, so immunophenotyping also becomes effective. This immunophenotyping is performed by the flow cytometry technique, and has helped in therapeutic guidance, as it helps in the classification, diagnosis, prognosis, staging and follow-up of leukemias. Flow cytometry is a method that analyzes quantitative and qualitative data on antigen expression patterns (CD) in target cell tissues using fluorescently labeled monoclonal antibodies (MOREIRA et al, 2021).

Understand the importance of laboratory evaluation for the early diagnosis of ALL, and the impact that a good evaluation can have on the diagnosis. This article seeks to explicitly describe the procedures and evolution of diagnoses for Acute Lymphoblastic Leukemia. To conduct a survey on the advances in laboratory diagnostic techniques for Acute Lymphoblastic Leukemia. It also highlights the relationship between the diagnosis of ALL and the prognosis of each patient.

2 METHODOLOGY

This study consisted of a qualitative literature review on the methods of diagnosis of ALL in Brazil. We used the following platforms as a base, Google Scholar, Books, Scientific Electronic Library Online (SCIELO), PUBMED with information from the year 2017 to January 2023.

Throughout the data generation research, the following descriptors of the articles were used with the keywords "ALL", "Diagnosis of Acute Lymphocytic Leukemia" where they were prioritized for information collection. After data collection, this information was analyzed and filtered during a thorough review of the general aspects, the main diagnoses of acute lymphoblastic leukemia.

3 LITERATURE REVIEW

Acute lymphocytic leukemia (ALL) is diagnosed mainly based on symptoms that are easy to confuse with other diseases, such as a simple viral infection, bacterial infection, anemias of various degrees, among others common in this age group. As a result, ALL has a late diagnosis that can reduce its prognosis and curability. A simple blood test such as a blood count may suggest lymphocytic leukemia, but further investigation is needed. These tests include a myelogram followed by immunophenotyping and a karyotype to determine whether the leukemia is caused by T or B lymphocytes, the translocation of the Philadelphia chromosome, or another type of anemia. The diagnosis of acute leukemia is largely based on the morphological analysis of neoplastic cells. First, blood counts are performed with peripheral blood and myelogram and bone marrow, followed by complementary techniques of cytomorphology, immunophenotyping, and cytogenetics (RODRÍGUEZ, 2020).

3.1 CBC

Normally, the blood count is the first test to be requested to confirm the diseases, and presents the characteristics of the specific laboratory morphology of the disease, which is correlated with the condition of possible anemia, neutropenia, thrombocytopenia (SANCHEZ, 2020).

Pancytopenia and periblastic blasts suggest acute leukemia. The percentage of leukocytes in blasts in the surrounding areas can be as high as 90%. The differential diagnosis of severe pancytopenia should take into account aplastic anemia, viral infections such as mononucleosis infection, and vitamin B12 and folic acid deficiencies (SANCHEZ, 2020).

4 MYELOGRAM

Bone marrow examination is a breathy aspiration and orifice biopsy, which is performed daily. As with other types of malignancies, we categorize ALL according to the characteristics of the cells The Morphological Classification currently in use was developed by a group known as the French-

American-British (FAB), and is often used. According to the FAB, blasts have a low amount of cytoplasm and a variety of basophila. Explosions are divided into three distinct types (CAVALCANTE, M. S, 2017).

According to (SANTOS, 2019), the myelogram is a puncture of the bone marrow that is performed during the invasive examination known as myelogram. That is why the blood count is requested when significant hemographic changes occur, which indicate certain clinical situations, such as anemia, leukopenia, thrombocytopenia, unexplained elevations in the number of leukocytes, abnormal circulatory cells, clinical staging of the cancer, and unexplained hypercalcemia. The test allows the analysis and identification of markers in the membrane and cytoplasm of each leukocyte, allowing the differentiation of the disease subtype. The medulla in AML may exhibit hypercellularity originating from blasts; this morphology needs to be examined to distinguish the various cell types, such as myeloblasts with Auer's bast expression, promelocytes, monoblasts, and promonocytes in monocytic leukemia, and megakaryoblasts in megakaryocytic leukemia (SANTOS, 2019).

4.1 IMMUNOPHENOTYPING

One of the most important methods or tests for the B and T subtypes of ALL, and which indicates the level of leukemic differentiation is the immunophenotyping test that is performed with flow cytometry. Currently, flow cytometry immunophenotyping is the most effective method for determining the frequency of cell subpopulations within a heterogeneous assay set. It mainly allows the analysis of the molecular expression profile in cells, establishing the individual phenotype of these cells, through immunization with cell surface antigens or intracellular monoclonal antibodies labeled with fluorophores. These superficial ancestors are also known as cell differentiation clusters (DCs), and are divided into groups according to lineage (DE FRANÇA, 2020).

The leukemia of the B lineage is separated into 4 subtypes, each of which is related to a maturation of the progenitors that are common, B-mature. HLA-DR, Terminal Deoxynucleotide Transferase (TdT), CD34, CD19, and CD22 are all expressed by type B progenitor cells. A chain containing CD19, CD20, and CD10 is found in an ALL of pre-B cells. A mature B-type is distinguished by the expression of immunoglobulin chains in its superficial membrane (BORGES, 2020).

T-lineage leukemia, despite having a lower frequency, is divided into subgroups according to the various stages of T-cell maturation, which are pre-T, T-intermediate, and mature T-ALL. Cells within pre-T ALL release CD3 as well as CD7, CD2, CD5, and ToT. As the T intermediate progresses, cells become CD3c, CD2, CD1, and may present CD4 and CD8. The same markers are expressed by mature T-T and Pre-T (CAVALCANTE, M. S, 2017).

4.2 CYTOGENETICS

In the cytogenetic examination, the classical cytogenetic test has been considered a diagnostic tool of great importance in clinical medicine. On the other hand, molecular cytogenetics, such as fluorescence in situ hybridization (FISH) and comparative genomic hybridization (CGH), can elucidate complex rearrangements and submicroscopically detecting small alterations that escape the identification of routine karyotyping. Currently, the study of cytogenetics is a fundamental tool in the diagnosis, classification, and prognosis of acute leukemias (PINHEIRO, 2018).

4.3 CYTOCHEMISTRY

The cytochemical examination is responsible for the biochemical dyes, which stain the blood and bone marrow cells in a way that demonstrates their composition without significantly altering their morphology. Cytochemical dyes help in the diagnosis of other hematopathological conditions, as well as leukemias (ARAUJO, LUCIANE BITELO LUDWIG, 2019).

5 RESULTS AND DISCOURSES

Analyzing the clinical perspective, there are several diagnostic methods for ALL, and with this we highlight the importance of clinical diagnoses and the frequent improvement of methods. Therefore, there is a need for follow-up and advances in the diagnosis of leukemias. And laboratory tests help in diagnosis and pre- and post-treatment support, making the quality and commitment of the laboratory fundamental from the collection of the specimen to the release of the report, as well as the patient's commitment to the treatment.

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