Molecular analysis of fusion genes associated with acute lymphoblastic leukemia in pediatric patients in Pará state, Brazil

Fernando Augusto Rodrigues Mello Junior (Oncology Research Center, Federal University of Pará Brazil), Caroline de Fátima Aquino Moreira (Oncology Research Center, Federal University of Pará Brazil), Alayde Vieira Wanderley (Federal University of Pará, Brazil), Darlen Cardoso de Carvalho (Oncology Research Center, Federal University of Pará, Brazil), Amanda Marques de Sousa (Oncology Research Center, Federal University of Pará Brazil), Jéssica Almeida Batista (Oncology Research Center, Federal University of Pará Brazil), Laudreisa da Costa Pantoja (Ophir Loyola Hospital, Brazil), André Salim Khayat (Oncology Research Center, Federal University of Pará Brazil).

BACKGROUND: The pediatric cancer (0-19 years) corresponds between 1% and 3% of all malignant tumors in most populations. In Brazil, in 2016, was estimated to be 5,540 new cases of leukemia in men and 4,530 in women. Acute lymphoblastic leukemia (ALL) is the leading cancer affecting children and adolescents, representing 39% of cancer cases in the metropolitan region of Belém. Up to a quarter of patients with ALL still presents relapse, having association with recurrent genetic changes.

HYPOTHESIS: This study is justified by the fact that knowledge of molecular features, such as gene fusions, would be useful in determining a more accurate and early diagnosis, in collaboration with the most appropriate treatment guidance and prognostic assessments more consistent. This study aimed to investigate the major fusion genes (TCF3-PBX1, MLL-AF4, BCR-ABL, TEL-AML1 and SIL-TAL) associated with ALL in pediatric patients in the State of Pará.

METHODS: Therefore, 40 samples from patients were collected in the Ophir Loyola Hospital. Isolation of lymphocytes; RNA extraction; RT-PCR-multiplex; electrophoresis on an agarose gel, to allow visualization of amplified products, were performed showing the occurrence of fusion; and finally direct sequencing was performed to validate the findings.

RESULTS: It was observed that 50% of patients presented fusion gene, and of these, 65% were SIL-TAL, 20% BCR-ABL, 5% TEL-AML1, 5% TCF3-PBX1 and 5% TEL-AML1 and SIL-TAL simultaneously. These frequencies were not significantly associated with the clinical data, such as gender, age, and response to treatment, but were associated with the risk group stratification, noting that these changes are more frequent in patients classified as high-risk group, with the SIL-TAL fusion being more prevalent in this group. This finding makes it clear that fusion genes may be associated with a worse overall condition of the patient, requiring an intensification therapy. In addition, we succeeded in developing a multiplex RT-PCR test, which shows a quick, inexpensive and efficient tool for identifying fusion genes, which is of great use in aiding diagnosis, prognosis and treatment of patients with ALL.