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The Cancer Control Challenge:
Better Understanding It to Better Face It

KMT2A::AFF1 Fusion in Adolescent ALL: Atypical Age-Related Genetic Profile and Clinical Implications

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Introduction: Leukemia is among the most common types of hematologic cancer worldwide, with approximately 474,000 new cases diagnosed each year. Within this context, acute lymphoblastic leukemia (ALL) stands out as the most common childhood cancer, accounting for 25% to 30% of all pediatric tumors and about 75% of leukemias diagnosed in children. The highest incidence occurs between the ages of 2 and 5, which is considered the peak age range for the disease. ALL is often associated with specific genetic alterations, with gene fusions being among the most relevant in terms of diagnosis and prognosis. Among these alterations, the *KMT2A::AFF1* t(4;11) fusion is notable for its association with poorer responses to conventional chemotherapy and, consequently, a worse prognosis compared to other genetic subtypes of the disease. It is commonly observed in neonatal patients under one year of age, typically diagnosed within the first few months of life, suggesting that the mutation may arise in utero. Reports of this fusion in adolescents are quite rare, accounting for approximately 1% to 2% of ALL cases. Still, when they do occur, they can offer new insights into the disease, revealing unique biological features of this leukemia subtype. **Objectives:** To describe a case of acute lymphoblastic leukemia in a 15-year-old adolescent with *KMT2A::AFF1* fusion, a genetic alteration typically observed in neonates, and to discuss its clinical and prognostic implications. **Case Description:** Patient, sex male, mixed race, 15 years old, presented with fever associated with marked leukocytosis. The patient was diagnosed with B-cell acute lymphoblastic leukemia (B-ALL) through immunophenotyping analysis. The biochemical data revealed glucose at 120 mg/dL, creatinine at 0.69 mg/dL, urea at 28 mg/dL and the lactate dehydrogenase at 1189 mg/dL, triglyceride levels of 124 mg/dL, bilirubin levels of 0,43 mg/dL, and alanine aminotransferase (ALT/TGP) levels of 19 U/L.". The patient presented with a leukocyte count of 531,300/µL, with 64% blasts, a platelet count of 39,000/µL, and a hemoglobin level of 7,8 g/dL. Molecular biology analysis was performed using the Nested PCR technique, which detected the *KMT2A::AFF1* fusion transcript through agarose gel electrophoresis. Additionally, Sanger sequencing was

carried out, confirming the results obtained by PCR. According to the criteria established by the National Cancer Institute (NCI), patients presenting with a leukocyte count greater than 50,000/μL and age over 10 years are classified as having an unfavorable prognosis for the disease. **Conclusion:** The identification of the *KMT2A::AFF1* fusion in an adolescent patient highlights that genetic alterations traditionally associated with neonates can also occur outside the usual age range, requiring special attention during diagnostic evaluation. Although it is typically described as a neonatal abnormality, its occurrence in adolescents, although rare, underscores the biological heterogeneity of the disease and the need for specific therapeutic approaches. Early detection of these alterations may contribute to guiding more effective treatment strategies and to a better understanding of the mechanisms involved in leukemogenesis across different ages.

Keywords: Acute lymphoblastic leukemia (ALL); KMT2A::AFF1 fusion; prognosis.