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REVIEW ARTICLE

Transient leukemia of Down syndrome

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ABSTRACT

Childhood leukemia is mostly a "developmental accident" during fetal hematopoiesis and may require multiple prenatal and postnatal "hits". The World Health Organization defines transient leukemia of Down syndrome (DS) as increased peripheral blood blasts in neonates with DS and classifies this type of leukemia as a separate entity. Although it was shown that DS predisposes children to myeloid leukemia, neither the nature of the predisposition nor the associated genetic lesions have been defined. Acute myeloid leukemia of DS is a unique disease characterized by a long pre-leukemic, myelodysplastic phase, unusual chromosomal findings and a high cure rate. In the present manuscript, we present a comprehensive review of the literature about clinical and biological findings of transient leukemia of DS (TL-DS) and link them with the genetic discoveries in the field. We address the manuscript to the pediatric generalist and especially to the next generation of pediatric hematologists.

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Background on Down syndrome

In 2019, Down syndrome (DS) remains the most common chromosomal disorder. Each year in the United States (U.S.), approximately 6000 babies are born with DS, which is approximately one in every 700 babies born [1], with the prevalence increasing as the mother's age increases [2]. The birth prevalence is higher (i.e. 2–3 per 1000 live births) in middle- and low-income countries because of limited access to family planning, a high percentage of pregnant women of advanced maternal age (35 years or older) and deficient or absent prenatal screening, diagnosis, and associated services [3]. In high-resource countries, the population prevalence of DS is approaching 70% of its birth prevalence, although this is decreasing due to family planning, available information on age-related risk, antenatal screening, prenatal diagnosis, and selective abortion [4]. The disorder was initially described by John Langdon Down in 1866 [5]. In antiquity and the Middle Ages, infants with disabilities were either killed or abandoned [6]. At the beginning of the XX century, children with DS were institutionalized, few of the associated medical problems were properly treated and most died in infancy or early adult life. In the 1920s–1940s, with the rise of eugenics, 33 of the then 48 U.S. states and several countries began programs of forced sterilization of individuals with DS, whereas action T4 in Nazi Germany made public policy of a program of systematic involuntary euthanization [7,8]. With the discovery of karyotype in the 1950s, abnormalities of chromosomal number or shape were identified and correlated with genetic disorders including DS [9]. In 1959, Lejeune, Gautier, and Turpin described trisomy

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