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INHERITED THROMBOCYTOPENIA SYNDROMES MAY PREDISPOSE TO CHILDHOOD MALIGNANCIES – EXPERIENCES FROM POLISH COHORT

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INTRODUCTION

Inherited thrombocytopenia (IT) syndromes constitute a heterogeneous and continuously evolving group of diseases. The intensive development of molecular diagnostics has led to the recognition of close to 50 ITs. Apart from defects associated with isolated thrombocytopenia, particular attention is due to **variants predisposing to myelodysplastic syndrome, malignant transformation or severe bone marrow aplasia.**

AIM

The study aimed **to analyze the molecular background and clinical picture of IT** with a particular focus on syndromes predisposing for cancer.

METHODS

A cohort of **156 patients** (81 males and 75 females aged between 9 days and 68 years) with **childhood-onset chronic thrombocytopenia** was referred to the national reference laboratory for molecular diagnostics *Oncolab* in Lodz, Poland, from 2016 to 2023.

Each of them underwent targeted **next-generation sequencing** using a **panel of 750 genes**, focusing on those related to IT (according to the Thrombogenomics Project guidelines).

Clinical information about the patients was obtained through a **survey**.

RESULTS

The median **age** of patients included in the study was **8.99 years (2.37-14.77),** and pediatric patients accounted for 92% of the study group (n=144).

The molecular background of IT was **identified in 84 individuals (54%).** Among this group, **18 cases (21%)** were associated with **syndromes predisposing to cancerogenesis or bone marrow aplasia.** This population consisted of 17 pediatric patients (10 males and 7 females) and 1 adult female, with a median age of 3.82 years (1.10-6.18). The median **platelet count** upon referral was **44x10^9/L (25-75x10^9/L).** The most common cancer-predisposing defects were found in the ***WAS* gene (n=5), *RUNX1* gene (n=4), and *ETV6* gene (n=3).** The results of the genetic testing are presented on **Figure 1.**

During the median follow-up of 3.69 years, **three patients developed malignancies** (acute lymphoblastic leukemia or acute myeloid leukemia). One of them subsequently died of leukemia progression. The natural history of leukemia development in this patient is presented on **Figure 2.**

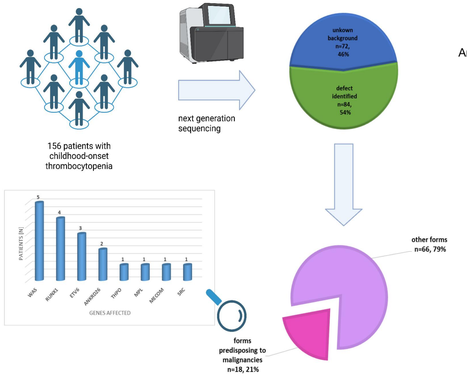


Figure 1. Algorithm of the study and results of molecular testing

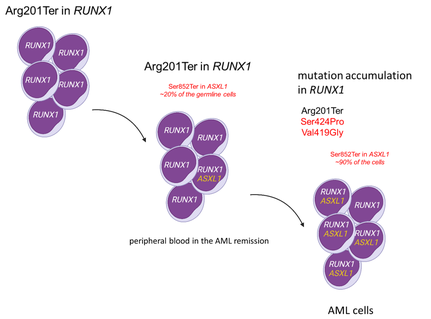


Figure 2. Natural course of leukemogenesis in one of the participants of the study. Acute myeloid leukemia developed as a consequence of somatic accumulation of additional mutations in the *RUNX1* and *ASXL1* genes

CONCLUSIONS

Inherited thrombocytopenia is **diagnosed in slightly over half of suspected patients.**

A significant group includes mutations predisposing to myelodysplastic syndrome and malignancies, primarily leukemias and lymphomas, such as **Wiskott-Aldrich syndrome or *RUNX1* familial platelet disorder.**

In our cohort, there is **a notable predominance of pediatric patients** with an early age of molecular evaluation, for whom **prompt diagnosis enables appropriate oncological surveillance and genetic counseling**, thereby acquiring crucial prognostic significance.

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INHERITED THROMBOCYTOPENIAS IN POLAND