benignas/provavelmente benignas, 58% como VUS ou não previamente descritas, e 0,5% como patogênicas/provavelmente patogênicas. Em média, 36 variantes foram detectadas por amostra, e variantes potencialmente relevantes foram observadas nos genes: VHL, EPAS1, HBB, HSF1 e HIF3A, incluindo 6 variantes novas. A variante patogênica encontrada em VHL foi confirmada como germinativa após análise de amostra de swab oral do mesmo paciente por sequenciamento de Sanger. O diagnóstico da eritrocitose representa um desafio devido às características clínicas associadas a diferentes etiologias. Neste trabalho, descrevemos características clínicas e moleculares de pacientes com PV, ESA e EI. Seis variantes novas e uma variante patogênica/provavelmente patogênica foram identificadas. O painel customizado de NGS desenvolvido surge como uma ferramenta valiosa para identificar variantes genéticas subjacentes à eritrocitose.

https://doi.org/10.1016/j.htct.2024.09.829

CHALLENGES IN INTERPRETING AVWS SCREENING IN POLYCYTHEMIA VERA: CORRELATIONS WITH CLINICAL AND LABORATORY FEATURES

V Weihermann, RCB Melo, A Kayano, CA Silva, TR Rocha, WF Silva, V Rocha, FS Seguro

Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), São Paulo, SP, Brasil

Background: The risk of thrombotic and hemorrhagic complications frequently coexists in myeloproliferative neoplasms (MPN), partly due to the occurrence of acquired von Willebrand syndrome (AVWS), particularly in essential thrombocythemia. However, the value of screening for AVWS in other MPNs is not so clear. Additionally, it is unknown whether laboratory-diagnosed AVWS correlates with clinical manifestations. Therefore, we aimed to investigate the connection between specific clinical and laboratory features and AVWS, and to determine if AVWS was associated with bleeding in our polycythemia vera (PV) cohort. **Methods:** This is a cross-sectional study involving adult PV patients followed at Hospital das Clínicas of the Faculty of Medicine, University of São Paulo, Brazil. Screening for AVWS was conducted using von Willebrand factor antigen (VWF Ag) and activity levels measured by the ristocetin cofactor assay (RCO). AVWS was defined as a VWF:RCo/Ag ratio < 0.6. Additionally, we collected data on thrombotic and bleeding complications. **Results:** We evaluated 46 of 597 patients (54% male, median age 62.5 years) diagnosed with polycythemia vera who were screened for AVWS from 2012 until 2023. In only three patients, the tests were ordered immediately after a bleeding event. At the moment of the screening, the median blood counts were: hematocrit 43% (IQR 38-51), leukocytes 11.7×10^9/L (8.0-16.8), platelets 572×10^9/L (IQR 307-952). Median VWF antigen was 146% (range 64-464), median VWF:RCo was 58% (range 1-159) and median function/antigen ratio (VWF:RCo/Ag) was 0.42 (range 0.01-0.78). Thirty-six patients (78%) had a screening test (VWF:RCO / Ag < 0.6) positive for AVWS, and this parameter was correlated to thrombosis ($p = 0.03$), but not to bleeding ($p = 0.58$). There were 12 bleeding events (26% of the cohort) and neither VWF antigen, VWF:RCo, hematocrit, leukocyte count, platelet count or risk group could be associated with these events. It was observed that VWF antigen was higher with higher platelet counts ($p = 0.02$). A reduced function/antigen ratio (VWF:RCo/Ag) showed a significant association with leukocytosis and thrombocytosis, but not with hematocrit above normal range. In nine patients, the AVWS screening tests were done on at least two occasions. We observed that the level of VWF:RCo increases when the patients achieve the target hematocrit level below 45%. However, the VWF:RCo/VWF ratio improved only when the platelets levels lowered after cytoreduction. **Conclusions:** : Most of the patients in our cohort (78%) had a positive screening for AVWS by the VWF:RCO / Ag ratio criteria. However, we did not show a correlation with bleeding events or blood count parameters. Despite the significant number of bleeding events, establishing the diagnosis of AVWS or a correlation with bleeding events is a challenge for patients with PV.

https://doi.org/10.1016/j.htct.2024.09.830

INTERFERENCE OF BCR::ABL1 SPLICING VARIANTS IN MANAGEMENT OF CHRONIC MYELOID LEUKEMIA PATIENTS

MCS Sousa [a], GT Stelzer [b], JB Costa [a], L Farias [a], DB Schaffel [a], LZ Renault [b], TF Padilha [a], I Zalcberg [a], B Sabioni [c], LM Gutiyama [a]

[a] *Divisão de Laboratórios Especializados, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil*
[b] *Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil*
[c] *Departamento de Hematologia, Hospital Universitário Clementino Fraga Filho (HUCFF), Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil*

Introduction: Chronic Myeloid Leukemia (CML) represents a paradigm in oncology, characterized by the hallmark Philadelphia chromosome resulting from the t(9;22) reciprocal translocation. This abnormal chromosome gives rise to the *BCR::ABL1* fusion gene, which encodes a constitutively active tyrosine kinase protein driving leukemogenesis. The use of tyrosine kinase inhibitors (TKI) have revolutionized CML treatment, demonstrating remarkable efficacy. However, TKI resistance, primarily attributed to point mutations within the *BCR::ABL1* kinase domain (KD) remains a significant clinical challenge, affecting approximately 20-30% of patients. The gold standard technique for monitoring mensurable residual disease in CML is the quantitative PCR (qPCR), while Sanger sequencing is utilized to identify KD mutations upon relapse. **Objective:** This study aims to address the specific challenges posed by two *BCR::ABL1* splicing variants — the deletion of exon 7 (Δ7) and the insertion of 35 base pairs between exons 8 and 9 (INS35) — in the molecular monitoring of CML patients. These splicing events occur frequently in CML, observed in approximately 20-25% of cases. Concurrent occurrence of alternative splicing variants with point mutations complicates the detection of low-frequency mutations, potentially leading to mislead or misinterpret