ELSEVIER

Blood 142 (2023) 4023–4024

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

332.THROMBOSIS AND ANTICOAGULATION: CLINICAL AND EPIDEMIOLOGICAL

Identifying Novel Coagulation Biomarkers for Thrombosis in Patients with Lymphoma

Darko Antic[1,2], Vladimir Otasevic, MD[1], Olivera Mitrovic-Ajtic[3], Dragoslava Djikic[3], Emilija Zivkovic[3], Teodora Dragojevic[3], Jelena Ivanovic[1], Dejana Stanisavljevic[4], Natasa Milic[4], Milica Vukotic[3], Tijana Subotицki[3], Milos Diklic[3], Juan F. Santibanez[3], Vojin Vukovic[1,2], Sofija Kozarac[1], Andrej Pesic[1], Biljana Mihaljevic[1,2], Jawed Fareed[5], Vladan P. Cokic[6]

[1] Clinic for Hematology, University Clinical Center of Serbia, Belgrade, Serbia
[2] Faculty of Medicine, University of Belgrade, Belgrade, Serbia
[3] Department of molecular oncology, Institute for Medical Research, National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia
[4] Institute for Medical Statistics and Informatics, Faculty of Medicine, University of Belgrade, Belgrade, Serbia
[5] Loyola University Medical Center, Maywood, IL
[6] Department of molecular oncology, Institute for Medical Research, National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia

INTRODUCTION Thromboembolic events are a common complication of lymphoma, influenced by a number of factors, including status of the disease, patient characteristics and treatment modalities. Recent studies demonstrated presence of hemostatic dysregulation in lymphoma patients with the possible involvement of tissue factor (TF) in the development of thrombotic events; however, more data are needed to link coagulation biomarkers' levels with clinical data and increased thrombotic risk. TF initiates blood coagulation and expressed by nonvascular cells plays a major role in hemostasis, while TF expressed by vascular cells induces intravascular thrombosis. In this study, we aimed to profile coagulation biomarkers and determine the roles of neutrophils, monocytes, platelets and endothelial cells and their interactions in thrombus formation in patients with lymphoma.

METHODS Patients with newly diagnosed lymphoma were prospectively recruited and followed for all thromboembolic events from the time of diagnosis until 3 months after the last cycle of therapy. Peripheral blood samples were obtained before hematological treatment initiation from 127 patients with lymphoma. The coagulation factors profile (Fibrinogen, P-selectin, FVIII, Thrombin and TF) was measured by enzyme-linked immunosorbent assay (ELISA), while TF expression and monocyte-platelet aggregates were determined by flow cytometry. The isolation, quantification and flow cytometry profiling of extracellular vesicles (EVs) $\leq$1.0 μm have been done according to the protocol developed by Institute for Medical Research, Belgrade, Serbia. Thromboembolic events were diagnosed objectively based on clinical examination, radiographic studies and laboratory evaluation.

RESULTS The mean patients' age was 55±16 years (range, 18-86 years); 44.9% were males. Most patients (58.2%) had advanced stage disease (III/IV), and 35.4% had ECOG performance status $\geq$1. More than half of the patients had aggressive forms of lymphoma (64.6%), mostly diffuse large B-cell lymphoma (DLBCL). Thrombosis occurred in 14.3% of patients with lymphoma (18/127), predominantly in patients with aggressive (18.3%) vs. indolent forms (6.8%). Total number of thrombosis was 22 (4 patients had more than one thrombosis site), and venous thrombosis was the most prevalent (72.7%). ThroLy score $\geq$2 had 72.2% of patients with thrombosis, in contrast to 37% of patients without thrombosis. The median value of TF was higher in patients with thrombosis compared to those without thrombosis (224.41 [93.1-446.0] (median [IQR]) vs. 136.43 [109.4-193.4], p=0.036). The concentration of the other assessed coagulation related cells and biomarkers were not significantly different between patients who developed thrombosis during follow-up and those who did not. In multivariate regression analysis, ThroLy score $\geq$2 (OR=5.505, 95%CI 1.505–20.100, p=0.01), TF (OR=1.005, 95%CI 1.002–1.009, p=0.003), and aggressive form of lymphoma (OR=4.680, 95%CI 1.132–19.356, p=0.033), were independent prognostic factors for thrombosis occurrence. $CD11b^{+}CD16^{+}$ neutrophils were increased 8-fold in aggressive (DLBCL) compared to indolent form of lymphoma (p<0.001), as were 2-fold $CD61^{+}$ platelets and 3-fold $CD31^{+}$ endothelial cells labelled with TF ($CD142^{+}$, p<0.05) procoagulant EVs.

The monocyte-platelet aggregates ($CD14^+CD45^+CD41^+$) were increased 5-fold in DLBCL patients compared to the healthy controls ($p<0.001$).

CONCLUSION The presented results support the use of ThroLy score for differentiating the sub-groups of lymphoma patients who are at increased risk for thrombotic events, while profiling coagulation biomarkers in different lymphoma populations may aid in understanding the pathophysiologic mechanisms underlying the thromboembolic events. Special emphasis should be placed on the assessment of TF which might be used as a coagulation biomarker in addition to clinical prediction scores.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-185006