Detection of ICAM-1, ICAM-2, ICAM-3, PECAM-1 and VCAM-1, evaluation of hypercoagulable state and platelet aggregation in hemoglobinopathy patients with erythroblasts

The aim of this report is to describe the presence of adhesion molecules on the surface of various peripheral blood cells, included erythroblasts, from hemoglobinopathy patients (thalassemia intermedia and thalassemia major). The results of this analysis, together with the alterations of other coagulation parameters, might contribute to explaining the hypercoagulable state of these patients.

A high prevalence of thromboembolic phenomena has been described in patients with thalassemia intermedia (TI); venus thromboembolism is also associated with various other chronic pathologies (cardiopathy, diabetes, hepatic dysfunction, hypothyroidism).[1] Some authors have highlighted the role of erythroblasts and/or damaged erythrocytes in determining a hypercoagulable state in splenectomized patients with TI because of the abnormal exposure of phosphatidylserine on the cells' surface:[2,3] this phenomenon is absent in healthy individuals who have been splenectomized for trauma.[6]

We evaluated the presence of adhesion molecules ICAM-1 (normally present on monocytes) ICAM-2 (normally present on lymphocytes and monocytes), ICAM-3 (normally present on leukocytes), PECAM (normally present on monocytes and neutrophils) and VCAM-1 (normally present on macrophages and dendritic cells) on the surface of erythroblasts, lymphocytes, neutrophils, and monocytes.[5] These molecules were bound to monoclonal antibodies (Becton Dickinson, Franklin Lakes, NJ, USA), and detected by direct flow cytometry (FACSCalibur, Becton Dickinson)

Erythroblasts were identified using two monoclonal antibodies simultaneously: one for glycophorin A (present on red blood cells) and one for the specific molecule of adhesion.

We evaluated 25 patients divided into 5 groups according to transfusion therapy and the presence or absence of erythroblasts (Table 1).

Platelet aggregation, factors V and VII, proteins C and S, antithrombin III, D-dimer, and activated protein C resistance were evaluated in all patients.[4]

Table 1. Patients' characteristics.

	GROUP A	GROUP B	GROUP C	GROUP D	GROUP E
Number of patients	2	4	6	7	6
Age (mean)	32	29	13	43	32
Gender (M/F)	0/2	1/3	4/2	4/3	4/2
Pathology	TI	TI	TI	TI	TM
Splenectomized	0/2	4/4	0/6	7/7	6/6
Transfusion therapy	No	No	Yes	Yes	Yes
Erythroblasts	Absent	Present	Absent	Present	Present

TI=thalassemia intermedia, TM=thalassemia major.

Platelet aggregation, factors V and VII, proteins C and S, and activated protein C resistance were normal in all patients. Two patients from group D had abnormal values of antithrombin IIIa (58% and 44%, normal values: 80-120%) Almost half the patients had abnormal values of D-dimer without any distinction between the groups, but all patients with altered values had a high number of erythroblasts (>50% of nucleated cells). None of our patients has ever suffered from thrombotic events.

The distribution results of the adhesion molecules are displayed in Table 2.

The data from our study are preliminary, but in our opinion this is the first study that takes into account the presence of adhesion molecules on the various peripheral blood cells, particularly on the erythroblasts, in patients with hemoglobinopathies. The presence of a large number of circulating erythroblasts in the blood of patients with thalassemia might contribute to explaining the hypercoagulable status of these patients[7-10] because their erythroblasts carry ICAM-2 and PECAM-1 molecules.

Giovanni Garozzo, Roberto Distefano, Alessandra Miceli, Piero Bonomo

Immunohematology and Transfusional Medicine Service, Center of Diagnosis and Therapy of Thalassemias and Hemoglobinopathies, Azienda Ospedaliera "Civile-M.P. Arezzo", Ragusa, Italy

Table 2. Distribution of adhesion molecules on the surface of various types of cell (percentage of positive cells): subdivision by group.

GROUP A				GROUP B				GROUP C				GROUP D				GROUP E			
E	L	M	N	E	L	M	N	E	L	M	N	E	L	M	N	E	L	M	N
ICAM-1 (CD54)																			
0	0	89	0	1	0	80	0	1	0	88	0	0	0	84	0	0	0	90	0
ICAM-2 (CD102)																			
0	0	0	0	0	0	0	0	0	11	11	0	20	18	23	0	10	9	11	0
ICAM-3 (CD50)																			
0	97	99	100	2	75	95	100	0	96	99	100	3	90	97	100	5	89	93	100
PECAM-1 (CD31)																			
0	54	99	99	32	51	96	98	0	56	98	99	31	46	93	95	33	44	96	97
VCAM-1 (CD106)																			
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Abbreviations: E, erythroblasts; L, lymphocytes; M, monocytes; N, neutrophils.

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Key words: hypercoagulability, hemoglobinopathies, adhesion molecules.

Correspondence: Giovanni Garozzo, M.D., Servizio di Immunoematologia e Medicina Trasfusionale, Centro di Diagnosi e Cura delle Talassemie e delle Emoglobinopatie, Azienda Ospedaliera "Civile-M.P. Arezzo", piazza Igea 1, 97100 Ragusa, Italy. Phone: international: +39.0932.600371. Fax: international +39.0932. 227065. E-mail: sitragusa@ntt.it

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