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ORAL ABSTRACTS

322.DISORDERS OF COAGULATION OR FIBRINOLYSIS: CLINICAL AND EPIDEMIOLOGICAL

Comprehensive Characterization of Coagulation Parameters in Venous Malformations

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Introduction: Localized intravascular coagulopathy (LIC) is a well-recognized, though poorly characterized complication of venous malformations (VM) that can lead to bleeding, thrombosis, and phlebolith formation. While LIC has classically been characterized by elevations in D-dimer and reductions in fibrinogen, no comprehensive studies of coagulation parameters in VM have been performed to date. Since 2021, all patients with VM undergoing evaluation for LIC in the Yale Vascular Malformations Program (VaMP) and the Yale Classical Hematology clinic have been subjected to an extensive set of coagulation tests to fully analyze LIC. Our aim was to use these laboratory test results to comprehensively characterize LIC in this population.
Methods: We conducted a retrospective chart review of all VM patients presenting to the Yale VaMP and the Yale Classical Hematology clinic for assessment of LIC from 2021 to 2023. All included patients were evaluated for LIC using the following coagulation parameters: von Willebrand Factor (VWF) antigen, VWF activity, factor VIII (FVIII), alpha-2 antiplasmin (A2AP), plasminogen activator inhibitor-1 (PAI-1), thrombin-antithrombin complex (TAT), D-dimer (DD), fibrinogen, prothrombin time (PT), international normalized ratio (INR), and partial thromboplastin time (PTT). Measurements of VWF antigen, VWF activity, FVIII and A2AP were performed using an ACL TOP system (Instrumentation Laboratory; Bedford, MA, USA), while D-dimer and fibrinogen were measured using a BCS XP System (Siemens; Malvern, PA, USA) at our institution's clinical laboratory. PAI-1 and TAT were processed at national Clinical Laboratory Improvement Amendment-certified reference laboratories using ELISA-based assays. Baseline patient characteristics and coagulation test results were extracted via manual chart review. Data analysis was done using IBM SPSS statistics software and GraphPad Prism 9 software. Categorical variables were described using frequency and percentages, while quantitative variables were described using central tendency and dispersion measures. We performed univariate analysis using the Chi-square test. We also analyzed the coagulation tests using a correlation matrix. Statistical significance was set at $p<0.05$. This project was approved by our Institutional Review Board.
Results: A total of 23 patients with VM were included in the analysis (Table 1). The mean age was 38 ± 16 years; the majority (82.6%) were female. The most common anatomic location was the head and neck (52.2%), while the most frequent extent

of tissue involvement was muscle (54.5%), with most patients having a single lesion (59.1%) rather than multiple ones. No patients had venous thromboembolism. Normal DD and high TAT levels were observed in most patients (68.2% and 69.6%, respectively). VWF activity, VWF antigen, FVIII, PAI-1, and fibrinogen all were positively correlated (Figure 1). TAT was positively correlated with PAI-1 and inverselycorrelated withPT and INR. DD was positively correlated only with vWF activity. TAT and DD had a poor correlation; among patients with a normal TAT (n=7), 85.7% had a normal DD, while among patients with a normal DD (n=15), only 40% had a normal TAT. Three out of 4 (75%) patients with skin involvement had a high TAT with normal DD, while 2 out of 3 (66.7%) patients with visceral involvement had both high TAT and DD, although these patternswere not statistically significant (P=0.42 and 0.31, respectively). Among patients with muscle involvement (n=11), 45.5% had a high TAT and normal DD while 36.3% had both high TAT and DD.

Conclusions: In this first comprehensive hematologic study of VM, we demonstrate that VM-related LIC is characterized by derangements of multiple coagulation parameters. Due to this, measurements of DD and fibrinogen alone may be inadequate for assessing LIC, and the addition of TAT and multiple other coagulation tests may yield a more complete picture of hemostatic derangements in LIC. A lack of correlation between DD and TAT is unexpected and merits further study. Differences in the depth of the VM tissue involvement and TAT/DD correlation may indicate a progression of coagulopathy related to the extent of VM but require further investigation in a larger study.

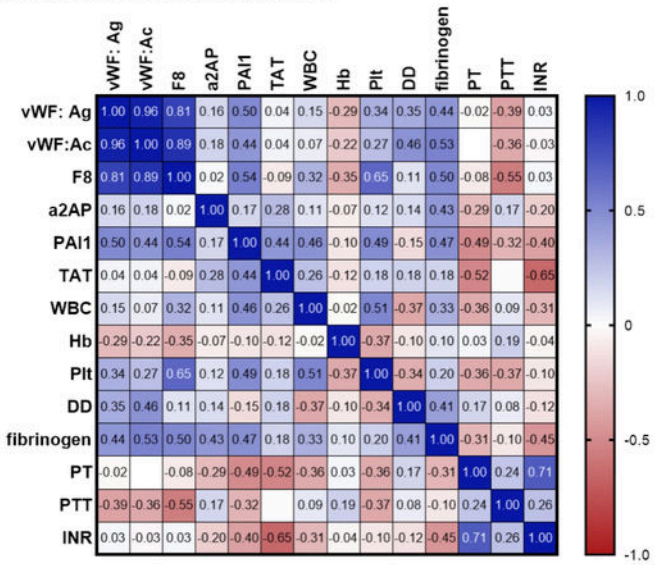
Disclosures No relevant conflicts of interest to declare.

Table 1: Summary of patient characteristics and coagulation parameters. (Normal laboratory range values are detailed in footnote)

	n (%)	Missing	Mean	SD	Normal range: n (%)	Above normal range: n (%)	Below normal range: n (%)
VM syndrome		0					
None	19 (82.6)						
Blue Rubber Bleb Nevus Syndrome	2 (8.7)						
Klippel-Trenaunay Syndrome	2 (8.7)						
Location		0					
Head and neck	12 (52.2)						
Trunk	4 (17.4)						
Limbs	6 (26.1)						
Organs	1 (4.3)						
Tissue involvement		1					
Skin and SC tissue	4 (18.2)						
Muscle	12 (54.5)						
Bone	3 (13.6)						
Viscera	3 (13.6)						
Surface area of lesions*		7					
Surface area ≥ 10 cm^2	8 (50.0)						
Surface area < 10 cm^2	8 (50.0)						
Number of lesions		1					
Single	13 (59.1)						
Multiple	9 (40.9)						
VWF antigen (%)	23 (100)	0	125.6	47.2	18 (78.3)	5 (21.7)	0 (0.0)
VWF activity (%)	21 (91.3)	2	100.8	33.6	20 (95.2)	1 (4.8)	0 (0.0)
FVIII activity (%)	23 (100)	0	122.8	49.8	13 (56.5)	8 (34.8)	2 (8.7)
Alpha-2 Antiplasmin (%)	22 (95.7)	1	115.4	11.3	17 (77.2)	5 (22.8)	0 (0.0)
Plasminogen activator inhibitor (PAI-1) (%)	23 (100)	0	27.9	25.7	17 (73.9)	5 (21.7)	1 (4.4)
Thrombin-Antithrombin (TAT) complex (mcg/L)	23 (100)	0	5.9	4.2	7 (30.4)	16 (69.6)	
Platelet count	23 (100)	0	275.9	72.3	22 (95.7)	0 (0.0)	1 (4.3)
D-dimer	22 (95.7)	1	2.4	7.4	15 (68.2)	7 (31.8)	
Fibrinogen	22 (95.7)	1	294.2	81.0	21 (95.5)	0 (0.0)	1 (4.5)
Prothrombin time (PT)	20 (87)	3	10.4	0.7	16 (80.0)	1 (5.0)	3 (15.0)
International normalized ratio (INR)	20 (87)	3	0.97	0.68	18 (90.0)	0 (0.0)	2 (10.0)
Partial thromboplastin time (PTT)	23 (100)	0	26.8	2.8	22 (95.7)	1 (4.3)	0 (0.0)

Abbreviations: SD: Standard deviation; VM: Venous malformations; vWF: Von Willebrand Factor; FVIII: Factor VIII; SC: Subcutaneous tissue.
*Sum in cm^2 of the surface area of all the lesions the patient has.
Note: The laboratory results of the coagulation parameters were interpreted using Yale New Haven Hospital's normal range for each test. These are as follows: vWF antigen: 62-175%; vWF activity: 58-163%; FVIII activity: 66-143%; Alpha-2 antiplasmin: 72-122%; Plasminogen activator inhibitor 1 (PAI-1) antigen: 4-43 ng/mL; Thrombin-Antithrombin (TAT) complex: < 4 mcg/L; Platelet count: 150.000-450.000 /µL; D-dimer: ≤ 0.5 mg/L; Fibrinogen: 187-446 mg/dL; Prothrombin time (PT): 9.5-12.1 seconds; International normalized ratio (INR): 0.89-1.15; Partial thromboplastin time (PTT): 22.5-30.0 seconds.

Figure 1: Correlation matrix of coagulation parameters



Comparison of the relationship between all coagulation parameters. All cells with a correlation coefficient R > 0.43 have a p-value < 0.05 and therefore show a significant correlation.

Figure 1

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