Abstract: PB2189

Title: UNUSUAL SITE THROMBOSIS IN PATIENTS WITH MYELOPROLIFERATIVE NEOPLASMS: THE EXPERIENCE WITH 66 CONSECUTIVE CASES.

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Background:

Myeloproliferative neoplasms (MPN) constitute the most frequent underlying cause of venous thrombosis in unusual site (US-VTE), including cerebral vein thrombosis (CVT) and splanchnic vein thrombosis (SVT), notably Budd–Chiari syndrome (BCS) and non-malignant and non-cirrhotic portal vein thrombosis (PVT).

Aims:

The aim of this study is analyzed in a retrospective cohort of patients with MPN clinical characteristics, molecular features and outcome data in patients who have experienced an US-VTE.

Methods:

The current study constitutes the "Azienda Ospedaliera Universitaria delle Marche" and "Ospedale Santo Spirito - Pescara" experience with 66 consecutive cases of US-VTE in patients with MPN. Diagnosis of MPN was according to World Health Organization diagnostic criteria 2008-2016 and CVT and SVT was confirmed in all cases by imaging studies. The study was approved by local institutional review boards. Statistical analysis was performed using JMP 14.0 software and significance was defined as P value <.05.

Results:

Sixty-six cases were retrospectively recruited: essential thrombocythemia (ET) 31.8%, primary myelofibrosis (PMF) 31.8%, polycythemia vera (PV) 24.2%, and MPN-unclassified (MPN-U) 12.1%,driver mutational frequencies were JAK2 in 85.9%, CALR 9.4%, and MPL 3.1%; 29 % of the patients were male and median age at diagnosis was 50 years, as reported in Table 1. The diagnosis of MPN was concomitant to thrombosis in 36 patients and median time from initial diagnosis of MPN to diagnosis of SVT was 5.6 years in the remaining 30 cases. Differences between these two groups were observed in terms of median platelet levels (354 *109/L vs 461*109/L, pV= 0.023); presence of splenomegaly (58.3% vs 86.7%, pV= 0.004); and presence of vascular risk factors including diabetes, hypertension, active smoke (47.2% vs 17.7%, pV= 0.009). Most patients included in this analysis experienced SVT, followed by CVT in 22.7%. The SVT distribution of events included isolated PVT (30.3%), followed by PVT + mesenteric (13.6%), and BCS (9.1%). History of previous thrombosis before the index event was documented in only 13.6% and included antecedent VTE in 7.5%. Initial treatment included systemic anticoagulation (SA) only in 7.6 % of the patients and SA + cytoreductive drug in 92.6% of patients. All patients were reported to have received low-molecular-weight heparin therapy followed by warfarin therapy in the majority (68.1%) or by novel oral anticoagulants in 18% of cases.

At a median follow up of 7.4 years, 10 deaths and 2 leukemic transformations were recorded. Post-US-VTE survival was significantly shorter in patients with MF, compared to those with PV or ET (pV = 0.0075, HR 5.4, 95% CI 1.4-12.6). Other significant risk factors for overall survival, in multivariable analysis, included older age (HR 4.2, 95% CI 1.6–12.5), splenomegaly (HR 1.6 95%, C.I. 1.1-2.3) and lower Hb level (HR 1.5, 95% CI 1.2–2.4). Recurrent thrombosis was reported in 12.1% of patients, including 3 (4.5%) with recurrent SVT.

Conclusion:

In the current study, post-US-VTE survival in MPN was primarily influenced by the expected natural history of the underlying MPN rather than the SVT event, emphasizing the importance of proper risk-adapted management of MPN patients. Moreover, patients with SVT concomitant to diagnosis showed differences in clinical features but

not in survival. The limited number of patients does not allow to identify reliable predictors of SVT recurrence in our court and to date further studies are needed to improve our understanding of MPN-SVT and the outcomes of patients with this debilitating complication.

Table 1. Clinical and laboratory characteristics of 66 patients with myeloproliferative neoplasms (MPN) and unusual site thrombosis (US-VTE), stratified by type of MPN

Variables	All patients n=66	Myelofibrosis n= 21	Polycythemia Vera n= 16	Essential Thrombocythemia n= 21	pValue
Age at diagnosis in years, median (range)	50 (11-80)	62 (28-80)	54 (19-71)	43 (11-65)	**0.001**
Age at thrombosis in years, median (range)	52.5 (16-82)	64 (28-82)	41.5 (17-81)	45 (23-77)	**0.004**
Male sex, n (%)	29 (43.9)	7 (33.3)	8 (50)	9 (42.8)	0.584
Type of thrombosis, n (%)					0.455
CVT	15 (22.7)	3 (14.3)	4 (25)	5 (23.8)	
SVT	51 (77.3)	18 (85.7)	12 (75)	16 (76.2)	
PVT	20 (30.3)				
PVT+MVT	9 (13.6)				
BCS± other SVT	6 (9.1)				
Other SVT	16 (24.2)				
Driver mutation, n (%)	N tot = 64	N tot=21	N tot = 16	N tot=19	
JAK2	55 (85.9)	16 (76.2)	16 (100)	16 (84.2)	0.085
CALR	6 (9.4)	2 (9.5)	0	3 (15.8)	
MPL	2 (3.1)	2 (9.5)	0		
Triple negative	1 (1.5)	1 (4.8)	0		
Karyotype, n (%)	N tot= 54	N tot=19	N tot =14	N tot= 16	
normal	48 (88.9)	15 (83.3)	14 (100)	15 (93.8)	0.374
abnormal	6 (11.1)	4 (16.7)		1 (6.2)	
Hemoglobin g/dl, median (range)					
at diagnosis	14.5 (8.6-49.5)	11.4 (8.6-18.6)	16.9 (13.8-20.5)	13.1 (9.2-15.8)	**<0.001**
at thrombosis	13.3 (8.5-18.6)	11.6 (8.8-18.6)	16.3 (11-18)	13.1 (9.2-15.8)	**< 0.001**
Leukocytes x 10*9/L, median (range)					
at diagnosis	7.67 (3-17.77)	6.21 (3.3-17.77)	10.84 (3-16.8)	7.05 (4.58-11.46)	**0.0231**
at thrombosis	9.18 (1.4-30.96)	7.75 (3.3-30.96)	10.80 (1.4-19.5)	8.54 (4.9-19.7)	0.922
Platelets x 10*9/L, median (range)					
at diagnosis	362 (44-1384)	288 (44-661)	365 (164-828)	666 (388-1384)	**<0.001**
at thrombosis	361 (44-1632)	246 (44-661)	370 (164-800)	568 (263-1632)	**< 0.001**
Thrombosis concomitant to diagnosis, n (%)	36 (54.5)	13 (61.9)	9 (56.3)	9 (42.9)	0.606
Splenomegaly, n (%)	47 (71.2)	19 (90.1)	13 (81.2)	9 (42.9)	**0.025**
Hereditary thrombophilia, n (%)	N tot= 49	N tot= 14	N tot= 12	N tot= 16	0.263
	28 (57.1)	6 (42.9)	9 (75)	9 (56.3)	
Other vascular risk factors, n (%)	22 (33.3)	10 (47.6)	4 (25)	5 (23.8)	0.193
History of thrombosis, n (%)	9 (13.6)	4 (19.0)	2 (12.5)	2 (9.5)	0.801
arterial	4 (6.1)	1 (4.7)	1 (6.3)	1 (4.8)	
venous	5 (7.5)	3 (14.3)	1 (6.3)	1 (4.8)	
Management, n (%)					0.534
SA only	5 (7.6)	1 (4.7)	2 (12.5)	1 (4.7)	
SA+ cytoreduction	61 (92.6)	20 (95.3)	14 (87.5)	20 (95.3)	
Death, n (%)	10 (15.2)	6 (28.6)	1 (6.3)	3 (14.2)	0.175
Myelofibrosis evolution, n (%)	9 (13.6)	0	2 (12.5)	6 (28.6)	0.289
Leukemic transformation, n (%)	2 (3.0)	2 (9.5)	0	0	**0.019**
Recurrent thrombosis, n (%)	8 (12.1)	2 (9.5)	4 (25)	1 (4.7)	
arterial	2 (3.0)	0	1 (6.3)	1 (4.7)	0.195
venous	3 (4.5)	1 (4.7)	1 (6.3)	0	
SVT	3 (4.5)	1 (4.7)	2 (12.5)	0	

CVT: cerebral vein thrombosis; SVT: splanchnic vein thrombosis; PVT= portal vein thrombosis; MVT: mesenteric vein thrombosis; BCS: Budd Chiari syndrome; SA: systemic anticoagulation.

Keywords: Thrombosis, Myeloproliferative disorder