CLİNİCAL SİGNİFİCANCE OF CALR MUTATİON İN PATİENTS WİTH ESSENTİAL THROMBOCYTHEMİA

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Aim: In essential thrombocythemia (ET), CALR mutation is associated with younger age, higher platelet count and lower rate of thrombosis. We examined the demographic, laboratory and clinical features of the CALR mutation in the Turkish population and its impact on prognosis.

Materials and Methods: A cohort of 394 ET patients diagnosed from 1995 and 2022 were included in this retrospective, multicenter study.

Results: Clinical and laboratory features of 394 ET patients are summarized in Table-1. In CALR+ patients, the frequency of female gender, mean leukocyte count, Hb and Hct at time of diagnosis are lower and the mean serum LDH level, platelet count and frequency of platelet count ≥ 1.109/µL are higher. The frequency of overall arterial and venous thrombosis and only arterial thrombosis before diagnosis ET are significantly lower for CALR+ patients than JAK2V617F+ patients. In subanalysis of patients aged ≤60 years at diagnosis, frequency of overall arterial and venous thrombosis and only venous thrombosis are lower in CALR+ and triple-negative patients than in JAK2V617F+ patients. In multivariate analysis for thrombosis, CALR mutation was not protective against thrombosis and arterial thrombosis while female gender was protective. CALR+ patients were more frequently exposed to multipl-line therapies and interferon-based therapy. Frequency of malignancy was higher in CALR+ and JAK2V617F+ patients than in triple-negative patients. There was no significant difference for myelofibrotic transformation and bleeding complications between JAK2V617F+, CALR+ and triple negative groups. In survival analysis, overall survival (OS) and thrombosis-free survival (TFS) were similar between mutation groups. The presence of CALR+ mutation was associated with lower leukemia-free survival (LFS).

Conclusion: In our study, CALR+ patients were associated with lower frequency of female gender, and lower leukocyte counts, Hb and Hct levels and higher platelet count and LDH levels. In multivariate analysis, CALR mutation lost its protective effect against thrombosis. In a large cohort of Turkish patients with long follow-up period, our study demonstrated the demographic characteristics of ET patients and impact of CALR gene mutation on age, gender, blood count parameters, spleen size, complications including thrombosis/bleeding/malignancy and myelofibrotic transformation in the Turkish population

	ET Patients (394) (mean ± SD) (n %)	JAK2V617F+ (278) (mean ± SD) (n %)	CALR+ (72) (mean ± SD) (n %)	Triple Negative (41) (mean ± SD) (n %)	p*
Gender					
Female	249 (63,2)	183 (65.8 [i])	33 (45.8) [b]	32 (78) [a]	0.001 [1]
Male	145 (36,8)	95 (34.2 [i])	39 (54.2) [b]	9 (22) [a]	
Age at MPN diagnosis, (mean ± SD)	59,3 ± 16,4	52.5 ±16.6	49.9 ±16.5	47.6 ±16.1	0.142 [2]
≤60	262 (66,5)	178 (64)	50 (69.4)	32 (78)	0.174 [1]
>60	132 (33,5)	100 (36)	22 (30.6)	9 (22)	
WBC at MPN diagnosis, (mean ± SD) (.10 ^{3} / µL)	10,5 ± 4,1	10.9± 4.5 [a]	9.6± 3.1 [b]	9.9±2.9 [a, b]	0.029 [2]
<11 000/ µL	250 (63,5)	173 (62.2)	49 (68.1)	25 (61)	0.628 [1]
≥ 11 000 / µL	144 (36,5)	105 (37.8)	23 (31.9)	16 (39)	
HB at MPN diagnosis, (mean ± SD)	13,4 ± 1,7	13.7 ±1.6 [a]	12.7 ±1.8 [b]	13.1 ± 1.6 [b]	<0.001 [2]
HCT at MPN diagnosis, (mean ± SD)	40,8 ± 5,1	41.7 ±4.9 [a]	38.1 ±5.1 [b]	39.7 ± 4.8 [b]	<0.001 [2]
Plt at MPN diagnosis, (mean ± SD) (.10 ^{3} / µL)	904,7 ± 357,6	858.1 ± 306.4 [a]	1078.5 ±468.3 [b]	922.9±381.8 [ab]	<0.001 [2]
<1 000 000 / µL	278 (70,6)	207 (74.5 [i])	38 (52.8) [b]	30 (73.2) [ab]	0.001 [1]
≥ 1 000 000 / µL	116 (29,4)	71 (25.5) [a]	34 (47.2) [b]	11 (26.8) [ab]	
LDH at MPN diagnosis, (mean ± SD) (U/L)	307,5 ±169,6	314.6 ±185.7 [a]	321.5 ±128.9 [a]	232.1 ± 61.2 [b]	0.010 [2]
Spleen size at MPN diagnosis, (mean ± SD) (mm)	130,1 ± 26,9	132.6±29.8 [a]	125.7 ±18.2 [ab]	121.8 ±14.5 [b]	0.016 [2]
CV risk factors		193 (69.4 [i])	41 (56.9) [ab]	20 (48.8) [b]	0.010 [1]
Revised IPSET risk score					
Very low	75 (19)	-	46 (63.9)	28 (68.3)	0.090
Low	140 (35,5)	136 (48.9)	2 (2.8)	1 (2.4)	
Intermediate	23 (5,8)	-	16 (22.2)	6 (14.6)	
High	156 (39,6)	142 (51.1)	8 (11.1)	6 (14.6)	
Thrombosis	128 (32,5)	105 (37.8 [i])	15 (20.8) [b]	8 (19.5) [ab]	0.004 [1]
Arterial thrombosis before diagnosis	68 (14,7)	59 (21.2) [a]	4 (5,6) [b]	5 (12,2) [ab]	0.005 [1]
Venous thrombosis before diagnosis	35 (6,3)	31 (11.2)	3 (4.2)	1 (2.4)	0.055 [1]
Arterial thrombosis after MPN diagnosis	31 (7,1)	21 (7.6)	8 (11.1)	2 (4.9)	0.455 [1]
Venous thrombosis after MPN diagnosis	15 (3)	14 (5.1)	1 (1.4)	-	0.229 [2]