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POSTER ABSTRACTS

634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

Thrombotic and Bleeding Events in Japanese Adolescent and Young Adult PV and ET: Results from Japanese Multicenter Retrospective Study

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[Background] There were no large-scale retrospective studies about adolescent and young adult (AYA) polycythemia vera (PV) or essential thrombocythemia (ET) in Japan. The characteristics in AYA PV or ET in Asia are not well-reported, except for one retrospective study using the Health Insurance Review and Assessment Service database in Korea. To reveal the clinical features, especially with regard to thrombotic and bleeding events in Japanese AYA PV and ET, we decided to perform secondary data analysis of Japanese multicenter large registry data, JSH-MPN-R18.

[Methods] Data of PV and ET aged 20 to 39 at the initial visit were extracted from registration data in JSH-MPN-R18 as AYA cohort, and were compared to non-AYA cohort over 40 years old. Differences among categorical and continuous variables were evaluated by chi-square test or Fisher's exact test, and by Mann-Whitney U test, respectively.
[Results] 31 PV (median age; 33 years[range 26-39], male/female; 19/12) and 141 ET (median age; 32 years[range 20-39], male/female; 52/89) were identified as AYA cohort, which represented 5.2% and 12.2% of overall PV or ET cohort, respectively. Non-AYA cohort consisted of 565 PV and 1011 ET. Regarding laboratory parameters, neutrophil ratio and counts were lower in AYA PV than in non-AYA PV, whereas, leukocyte counts, neutrophil ratio and counts, LDH and D-dimer level were lower in AYA ET than in non-AYA ET. The frequency of *JAK2* V617F-mutated patients was lower in AYA than in non-AYA PV and ET (PV; 61.2% vs.77.2%, p=0.05, ET; 46.0% vs. 57.8%, p<0.01). Regarding the treatment, antiplatelet or anticoagulant therapy was introduced into 61.3% of AYA PV and 51.8% of AYA ET patients. Cytoreductive therapy (CRT) was provided to eight (25.8%) AYA PV and 61 (43.3%) AYA ET. In 62.5% of AYA PV and 75.4% of AYA ET, who received CRT, CRT was adopted for the reasons except for the past or recent thrombotic events (TE)/bleeding events. AYA PV patients experienced only one pulmonary embolism before diagnosis and one lacunar cerebral infarction (CI) at diagnosis. There were no TE after diagnosis in AYA PV. In terms of bleeding events, AYA PV had one event (details unknown) before diagnosis and two events (gastrointestinal bleeding and details unknown) after diagnosis. The frequency of AYA PV patients with TE had a tendency to be lower than that of non-AYA PV (6.5% vs 19.1%, p=0.09), although there were no statistical differences between the numbers of bleeding events between AYA and non-AYA PV during all of the course. AYA ET had nine TE (3 CI, 2 deep vein thrombosis (DVT), 1 transient ischemic attack (TIA), 1 peripheral arterial disease (PAD), 2 details unknown) before diagnosis, six TE (3 DVT, 2 CI, 1 TIA) at diagnosis, and six TE (1 myocardial infarction, 1 CI, 1 PAD, 1 TIA, 2 details unknown) after diagnosis. Fewer TE occurred in AYA ET than in non-AYA ET before (6.4% vs 19.8%, p<0.01) and at diagnosis (4.3% vs 9.5%, p=0.04). However the frequency of TE was not different (4.3% vs. 6.7%, p=0.36) after diagnosis. AYA ET had experienced only one bleeding event (oral mucosal bleeding) before diagnosis. Bleeding events were never found at or after diagnosis. Fewer bleeding events were detected in AYA ET than non-AYA ET during all of the course (0.7% vs 8.6%, p<0.01). The percentage of venous TE in total TE was higher in AYA-MPN than in non-AYA MPN (26.1% vs 5.4%).
[Conclusion] Our analysis is the first retrospective cohort which revealed clinical features related to TE and bleeding events in Asian AYA MPN from large multicenter registry data. Lower neutrophil ratio and absolute counts at diagnosis might be attributable to lower mutated *JAK2* allele burden in AYA PV, and lower frequency of *JAK2*-mutated ET in AYA ET. Regarding bleeding events, fewer bleeding events were found in AYA ET than in non-AYA ET. However in PV, there were no statistical differences in bleeding events between AYA and non-AYA. About TE, AYA PV and ET had fewer TE than non-AYA PV and ET. The percentage of venous TE in total TE was higher in AYA MPN than in non-AYA MPN also in Japan, but it was much lower than those reported in previous European or US cohorts, in which venous TE were more common than arterial TE. Especially after diagnosis, venous TE were never detected in either AYA PV or ET in Japan. Considering that the frequency of venous TE in the Korean receipt data was as low as that in our cohort, fewer venous TE might be one of the specific characteristics in Asian AYA MPN different from European or US AYA MPN.

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Table 1. Clinical characteristics in Japanese PV (n=596) and ET (n=1152) (AYA vs non-AYA)

	PV (n=596)			ET (n=1152)		
	AYA PV (n=31)	non-AYA PV (n=565)		AYA ET (n=141)	non-AYA ET (n=1011)	
Variables	Median (range) or Number (proportion)	Median (range) or Number (proportion)	p-value	Median (range) or Number (proportion)	Median (range) or Number (proportion)	p-value
Age	33 y.o. (26-39)	66 y.o (40-93)		32 y.o. (20-39)	67 y.o. (40-94)	
Male, Female	19 (61.3%), 12 (38.7%)	327(57.9%), 238 (42.1%)	ns	52(36.9%), 89 (63.1%)	461 (45.6%), 550 (54.4%)	p=0.06
WBC (x 10^9/L)	9.5 (3.0-249.2)	11.9 (2.5-163.9)	p=0.07	8.665 (1.83-29.6)	9.4 (0.7-154)	p<0.01
Neutrophil (%)	71 (7.4-90)	78 (41-96.5)	p<0.01	68 (6.01-94)	70 (10.9-94)	p<0.01
Neutrophil (x 10^9/L)	6.5 (0.72-220.5)	9.238 (1.4-133.6)	p=0.03	5.68 (0.367-23.1)	6.56 (0.42-126.3)	p<0.01
RBC (x 10^{12}/L)	6.30 (4.43-9.24)	6.55 (2.24-10.24)	ns	4.72 (2.93-6.18)	4.74(1.81-9.24)	ns
Hb (g/dL)	17.7 (12.3-22.5)	18.3 (7.2-23.8)	ns	13.9 (8.6-18)	13.8 (5.7-21)	ns
Hct (%)	54.9 (38.9-65.6)	56 (23.4-75.4)	ns	42.3 (25.7-54.6)	42.4 (19.2-69.7)	ns
Plt (x 10^9/L)	433 (121-1091)	442.5 (94-2500)	ns	855 (253-3777)	830 (451-3810)	ns
LDH (IU/L)	242 (141-538)	258 (26-832)	ns	201 (115-589)	244 (23.5-2221)	p<0.01
EPO (mIU/mL)	7.3 (0.7-184)	5.0 (0-81.5)	ns	5.5 (0-44.8)	6.6 (0-358)	ns
D-dimer level (μg/mL)	0.475 (0-195)	0.5 (0-4)	ns	0.3 (0-1.2)	0.5 (0-17.0)	p<0.01
JAK2 V617F positive	61.2%	77.2%	p=0.05	46.0%	57.8%	p=0.01
JAK2 exon 12 positive	6.5%	1.4%	p=0.09	0%	0%	ns
CALR mutation positive	3.2%	0.35%	ns	16.3%	12.8%	ns
MPL mutation positive	0%	0%	ns	1.4%	2.2%	ns
Palpable splenomegaly	23.8%	15.2%	ns	6.3%	2.3%	p=0.02
Smoking at dignosis	9.1%	23.7%	ns	15.9%	22.3%	ns
Hypertension	7.4%	52.4%	p<0.01	1.4%	42.5%	p<0.01
Diabetes	3.7%	14.4%	ns	0%	14.2%	p<0.01
High LDL cholesterol	7.7%	16.0%	ns	2.2%	20%	p<0.01
Hypertriglyceridemia	0%	9.3%	ns	0.75%	8.5%	p<0.01
Congestive heart failure	0%	3.7%	ns	0%	4.0%	p=0.01
Normal karyotype	9.1%	12.1%	ns	3.9%	9.7%	p=0.03
Bleeding events before diagnosis	1 (3.2%)	12 (2.1%)	ns	1 (0.7%)	15 (1.5%)	ns
Bleeding events at diagnosis	0 (0%)	10 (1.8%)	ns	0 (0%)	22 (2.2%)	p=0.098
Bleeding events after diagnosis	2 (6.5%)	18 (3.2%)	ns	0 (0%)	59 (5.8%)	p<0.01
Thrombotic events before diagnosis	1 (3.2%)	69 (12.2%)	ns	9 (6.4%)	200 (19.8%)	p<0.01
Thrombotic events at diagnosis	1 (3.2%)	31 (5.5%)	ns	6 (4.3%)	96 (9.5%)	p=0.04
Thrombotic events after diagnosis	0 (0%)	27 (4.8%)	ns	6 (4.3%)	68 (6.7%)	ns
Duration of follow-up (days)	1233 (0-5565)	1465 (0-5436)	ns	1259 (0-5458)	1383 (0-5635)	ns

ns: not significant

Figure 1

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