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Blood 142 (2023) 3198–3200

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

Marrow Hypercellularity Does Not Exclude the Diagnosis of Essential Thrombocythemia (ET)

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Background: The 2022 WHO criteria do not list bone marrow cellularity as a criterion for ET diagnosis (dx) [1], but a review discussing the International Consensus Classification criteria states that the marrow should be normocellular for age, with rare cases of mild hypercellularity [2]. The ELN also cited normocellularity as a key factor in differentiating ET from polycythemia vera (PV) or prefibrotic myelofibrosis (MF), further suggesting that normocellularity is the expected standard in ET [3]. However, we encountered a number of cases in our hematology practice with increased cellularity in bona fide ET patients (pts). Therefore, we decided to more systematically review the marrow cellularity and its prognostic impact.
Methods: Medical records were queried for pts with ET per the ICD, versions 9-10. The dx of ET per WHO 2022 was confirmed by manual review. Cases lacking marrow biopsy were excluded. Structured query language was used for automated extraction of clinical, lab, and molecular findings. We utilized our previously described natural language processing pipeline to extract cellularity information from marrow reports [4]. All hematopathology reports of hypercellular marrows were manually reviewed by 3 observers for confirmation and a randomly selected subset of the core and clot sections were reviewed for histomorphology and cellularity by 2 expert hematopathologists and 1 histomorphologist, blinded to pt age and clinical information prior to their review. Quantitative cellularity was determined independently and then congruently for consensus. Qualitative cellularity was defined using (100-age) ± 20% as the normal range with increases above this range considered hypercellular for age. Disease progression was defined as either progression to post-ET MF (PETMF) or direct transformation to acute myeloid leukemia. Transformation to PV was defined as pts with a JAK2 mutation for whom PV was thoroughly excluded at the time of ET dx but who developed absolute erythrocytosis and met the PV WHO diagnostic criteria later in their disease course. We performed univariable and multivariable analysis of progression, PV transformation, thrombosis and mortality risk using Cox proportional-hazards models. Overall (OS), progression-free (PFS), PV-free (PVFS) and thrombosis-free (TFS) survival were estimated using Kaplan-Meier methods.
Results: 382 pts met WHO defined ET with marrow dx, of which 145 had pre-treatment diagnostic marrows available for review at Weill Cornell. In the other 237, the diagnostic biopsies had either been performed after treatment was initiated or only the report was available. Thirty-three (23%) were described as hypercellular and 112 (67%) were not. Review of 20 randomly selected marrows from the hypercellular group confirmed age-adjusted hypercellularity ranging from 30 to 80%. The hypercellular pts were significantly older at dx compared to those without hypercellularity (59 vs 50 yrs, p <0.001, Table 1). We identified no other significant differences in blood counts at dx, sex, driver mutation or thrombosis history between the groups. Univariate and multivariate analyses demonstrated no significant difference between the groups in PFS (HR 1.29, p=0.871), TFS (HR 1.39, p=0.671) or OS (HR 0.50, p=0.487) using age, thrombosis history and sex as covariates. A Cox model could not be generated for PVFS due to the low number of events. The 15-year PFS for pts with hypercellularity vs those without was 97% and 94% respectively (p=0.56, Figure 1), 15-year PVFS was 100% and 67% respectively (p=0.12), 15-year TFS was 79% and 87% respectively (p=0.53) and 15-year OS was 84% and 81% respectively (p=0.74).
Conclusion: Our data to date suggests that hypercellularity is of importance diagnostically but not prognostically. Nearly a quarter of our pts with WHO ET had marrow that was hypercellular for age at dx. Pts with increased marrow cellularity tended to be older but were clinically indistinguishable from the remainder in terms of driver mutation, blood counts and thrombosis history. Univariate and multivariate analyses demonstrate that hypercellularity does not confer increased risk of progression, thrombosis or mortality. Thus, hypercellularity alone should not be used as a factor for excluding ET dx.
References:
1. Khoury et al. *Leukemia*, 2022.

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2. Gianelli et al. *Virchows Archiv*, 2023.
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4. Sholle et al. *IEEE Int Conf Healthc Inform*, 2018.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-187769

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Table 1.
Demographics and clinical characteristic for ET patients

	Overall (N=145)	HYPER (N=33)	NON-HYPER (N=112)	p-value
Age at diagnosis (yrs)[1]	51 (13-86)	59 (34-80)	50 (13-86)	<0.001
Sex[2]				0.8
Female	99 (68)	23 (70)	76 (68)	
Male	46 (32)	10 (30)	36 (32)	
Race/Ethnicity[2], *n=139*				>0.9
White	100 (72)	23 (72)	77 (72)	
Black, Asian, or Hispanic	35 (25)	8 (25)	27 (25)	
Other	4 (3)	1 (3)	3 (3)	
Driver mutation[2], *n=134*				>0.9
JAK2	91 (68)	21 (68)	70 (68)	
CALR	32 (24)	8 (26)	24 (23)	
MPL	5 (4)	1 (3)	4 (4)	
Triple Negative	6 (5)	1 (3)	5 (5)	
Thrombosis history at diagnosis[2]	3 (2)	0 (0)	3 (3)	>0.9
Lab values at diagnosis[3]				
HCT (%)	41.2 (3.8)	40.3 (3.2)	41.5 (3.9)	0.2
HGB (g/dL)	13.87 (1.27)	13.62 (1.13)	13.96 (1.32)	0.4
RBC (x10^6/uL)	4.68 (0.59)	4.60 (0.51)	4.71 (0.61)	0.5
MCV (fL)	88.5 (5.8)	88.2 (7.1)	88.6 (5.3)	>0.9
WBC (x10^3/uL)	8.27 (2.29)	7.97 (2.64)	8.39 (2.16)	0.2
PLT (x10^6/uL)	726 (273)	774 (249)	708 (281)	0.2
LDH (U/L)	199 (50)	219 (66)	192 (42)	0.3
Follow up duration (yrs)[1]	5 (0-27)	8 (0-18)	5 (0-27)	0.005

[1] *Median (range),* [2] *n (%),* [3] *Mean (standard deviation)*

Figure 1. Progression free survival of ET patients by biopsy cellularity

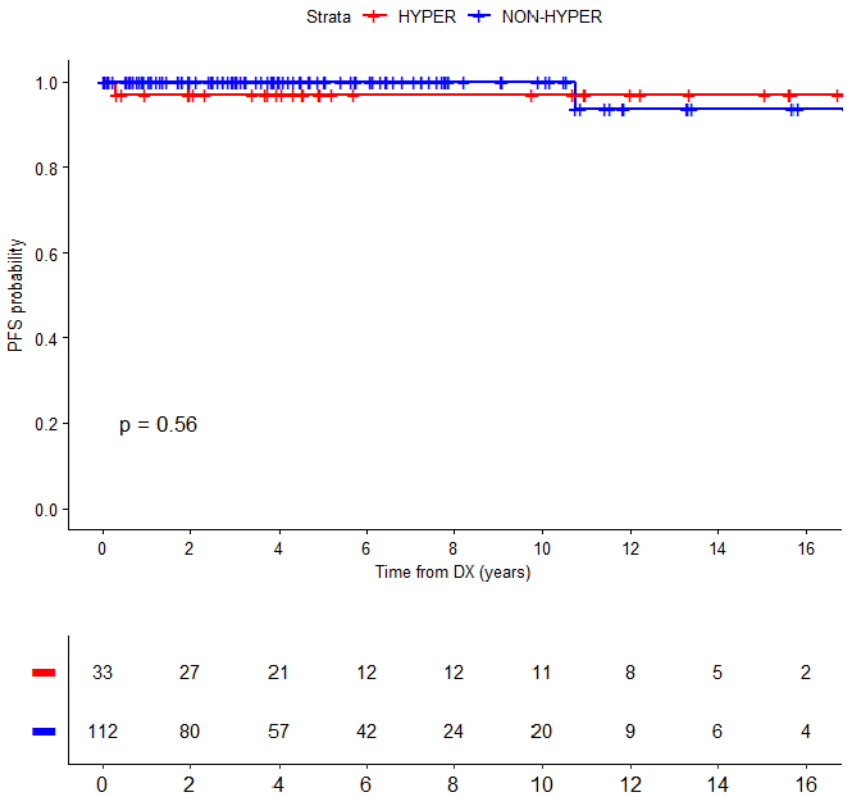

Figure 1

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