CLINICAL SIGNIFICANCE OF PNH CLONES IN 3085 PATIENTS WITH CYTOPENIA: A LARGE SINGLE-CENTER EXPERIENCE.

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Contributions

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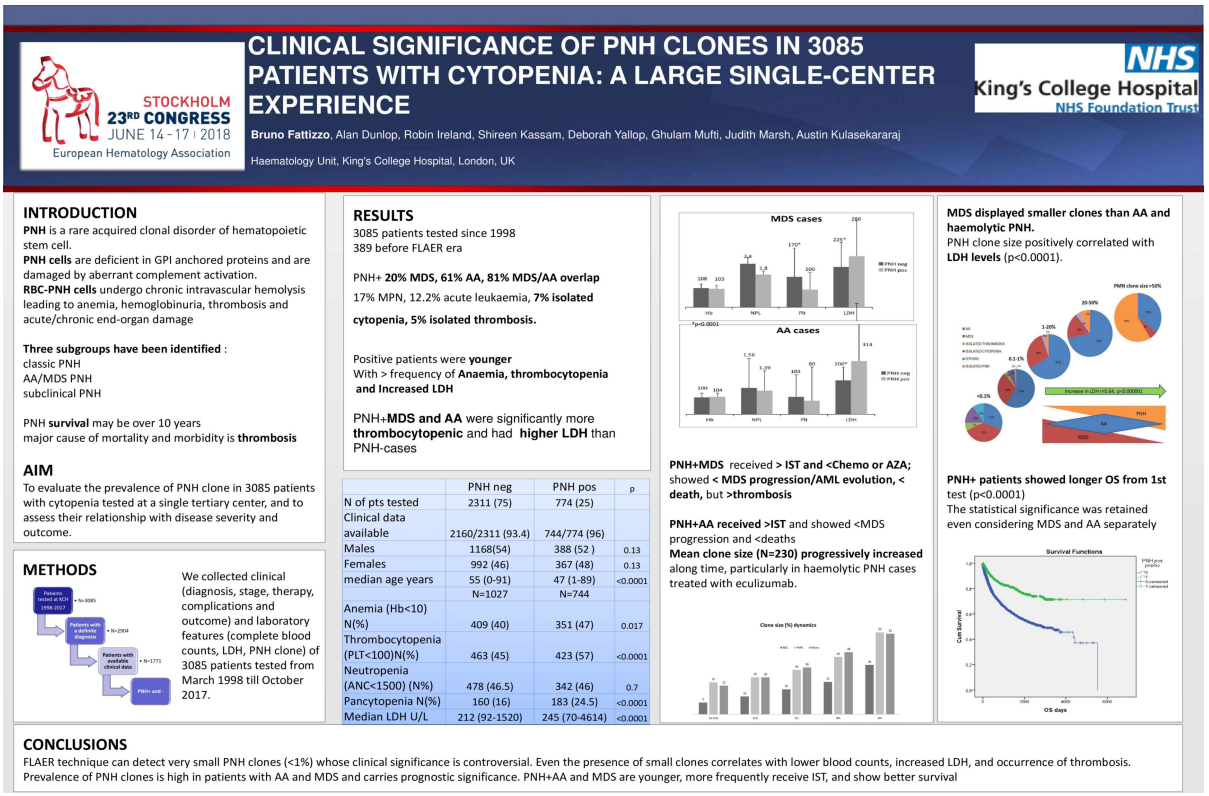

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Abstract

Abstract: PF304

Type: Poster Presentation

Presentation during EHA23: On Friday, June 15, 2018 from 17:30 - 19:00

Location: Poster area

Background

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare clonal disorder due to GPI anchored proteins deficiency on blood cells surface, resulting in complement activation and chronic intravascular hemolysis. Along with classic one, PNH in the setting of bone marrow disorder [aplastic anemia (AA)/myelodysplastic syndrome (MDS)], and subclinical PNH, with a small PNH population and no evidence of hemolysis, have been described. The prevalence and clinical significance of PNH clones, especially small ones, detected by high sensitive FLAER are still under debate.

Aims

To evaluate the prevalence of PNH clone in 3085 patients with cytopenia tested at a single tertiary center, and to assess their relationship with disease severity and outcome.

Methods

We collected clinical (diagnosis, stage, therapy, complications and outcome) and laboratory features (complete blood counts, LDH, PNH clone) of 3085 patients tested from March 1998 till October 2017.

Results

Main baseline clinical and laboratory characteristics of patients, divided according to presence or absence of PNH clones, are shown in table 1. PNH clone (PNH+) was found in 774 cases (25%), mostly AA (44%), MDS (24%), and florid hemolytic PNH (13%). Clone size, evaluated on granulocyte in 468 cases, was <1% in 224, 1-50% in 120, and >50% in 124, and correlated with LDH levels (p<0.0001). Considering diagnosis, PNH+ MDS displayed smaller clones compared to AA and haemolytic PNH ones (60% of cases with PNH clone size >50%). Serial PNH clone evaluation (n=230), showed mean clone size increase along time, particularly in haemolytic PNH cases treated with eculizumab. Among PNH- cases, the most frequent reason for testing were MDS (32%), idiopathic cytopenia (23.7%), and isolated thrombosis (13%). PNH+ cases were younger (p<0.0001), more frequently anaemic (p=0.01), thrombocytopenic (p=0.0003), or pancytopenic (p<0.0001), with higher LDH (p<0.0001). PNH+ patients also showed longer OS from first test [mean 14.24+0.35 years (95%CI 13.56-14.93) versus 8.16+0.26 years (7.64-8.68), p<0.0001]. PNH+ MDS patients (N=176, 20.3%) were significantly younger, more hypoplastic (p<0.001), and less frequently showed excess of blast (p=0.01); they also showed deeper cytopenias (p=0.04 for Hb, and p<0.0001 for PLT), and had higher LDH levels (p<0.0001). Moreover, they had more frequently received cyclosporine and ATG (p=0.0001), less frequently chemotherapy or azacytidine (p<0.0001 and p=0.002), and 7 cases had been treated with eculizumab. PNH+ MDS showed lower rate of higher risk progression (p=0.003), AML evolution (p=0.01), and death (p<0.0001), but had higher incidence of thrombotic events (p=0.05). Survival analysis also showed a longer OS for PNH+ MDS [mean 11.9+0.7 years (10.5-13.3) vs 7.3+0.3 (6.6-7.9), p<0.0001] compared to PNH- ones. PNH+ AA (61%) showed deeper thrombocytopenia (p<0.0001), higher reticulocyte counts (p=0.0004) and LDH values (p<0.0001). PNH+ AA were more frequently treated (p<0.0001), and showed lower MDS progression and deaths (p=0.01 and p<0.0001), and longer OS [mean 15.8+0.43 years (14.9-16.7) vs 6.5+0.35 (5.8-7.21), p<0.0001].

Table 1 Patients screened for PNH clones at our Institution

N 3085	PNH neg	PNH pos
Study period	Mar 1998 to Oct 2017	
Number of patients, N (%)	2311 (75)	774 (25)
Male/Female ratio	1.17	1.05
median age years (range)	55 (0-91)	47 (1-89)*
	N=2160	N=744
MDS N(%)	693 (32)	176 (23.6)*
AA N(%)	204 (9.4)	327 (43.9)*
MDS/AA N(%)	5 (0.2)	22 (2.9)*
Acute leukemia N(%)	209 (9.6)	29 (3.9)*
Haemolytic PNH N(%)	0 (0)	97 (13)
MPN N(%)	76 (3.5)	16 (2.15)
MDS/MPN N(%)	92 (4.2)	9 (1.2)*
Isolated cytopenia N(%)	512 (23.7)	39 (5.2)*
Isolated thrombosis N(%)	284 (13)	17 (2.3)*
Other reason N(%)	85 (3.9)	12 (1.6)*
Thrombosis occurrence N(%)	370 (17.12)	96 (12.9)
Death N(%)	725 (33.6)	141 (18.9)*
Lost to follow-up N(%)	146 (6.75)	75 (10)
Haematological parameters	N=1027	N=744
Hb<100 g/L, N(%)	409 (40)	351 (47)**
PLT<100x10^3/mmc, N(%)	463 (45)	423 (57)*
ANC<1.5x10^3/mmc, N(%)	478 (46.5)	342 (46)
Pancytopenia N(%)	160 (16)	183 (24.5)*
Median LDH U/L (range)	212 (92-1520)	245 (70-4614)*

*p≤0.0001, **p=0.01

Conclusion

Prevalence of PNH clones of any size is high in patients with bone marrow failure and carries prognostic significance. In this largest reported retrospective series, even the presence of small clones correlates with lower blood counts, increased LDH, and occurrence of thrombosis. Finally, PNH positivity seems to be more frequent in patients of younger age and to predict a better survival

Session topic: 12. Bone marrow failure syndromes incl. PNH - Clinical

Keyword(s): Aplastic anemia, Myelodysplasia, Paroxysmal nocturnal hemoglobinuria (PNH)

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