Aberrant expression of CD56 on granulocytes and monocytes in myeloproliferative neoplasm and myelodysplastic syndrome

Ping Gong MD, Fernanda Metrebian MD, Alina Dulau-Florea MD, Zi-Xuan Wang PhD, Renu Bajaj PhD, Stephen C. Peiper MD, Jerald Z. Gong MD

Department of Pathology, Thomas Jefferson University Hospital, Philadelphia, PA

ABSTRACT

INTRODUCTION:

CD56 is a cell adhesion molecule normally expressed in neural tissue and cytotoxic lymphocytes. Aberrant expression of CD56 can be seen in various hematologic malignancies and has been well characterized in acute myeloid leukemia and plasma cell myeloma. However, limited and inconsistent data are available regarding CD56 expression in chronic myeloid neoplasms.

DESIGN:

We reviewed CD56 expression in granulocytes and monocytes from 81 cases of myeloproliferative neoplasm (MPN) and 42 cases of myelodysplastic syndrome (MDS). Forty cases of negative staging bone marrow for lymphoma were used as negative controls. CD56 expression on granulocytes and monocytes were analyzed using four-color flow cytometry in all the cases. In addition, CD56 expression on granulocytes was analyzed in patients with series bone marrow samples following treatment and compared with molecular genetic results.

RESULTS:

In negative control cases, CD56 expression in granulocytes and monocytes was below 2%. Using 10% as positive threshold, CD56 was positive on granulocytes in 17% and positive on monocytes in 37% of all cases. Aberrant CD56 expression can be seen in all subtypes of MPN (ET 6%, PV 13%, MPN-U 18%, CML 19% to PMF 28%) and in high grade MDS (RCMD 18%, RAEB 27%). CD56 expression was present more frequently in primary myelofibrosis and high grade MDS than other types of MDS and MPD. In general, cases with CD56 expression on granulocytes also had CD56 expression on monocytes, but monocytes usually had higher percentage of CD56. Series specimens were available in 5 cases with positive CD56 expression (2 CML, 1 PMF, 1 PV, 1 NPM-U). CD56 expression correlated with recurrent disease by bone marrow morphology. Where BCR/ABL transcript and bone marrow engraftment studies were available, CD56 reduction correlated with reduced BCR/ABL transcript and/or recipient cell percentage.

CONCLUSIONS:

Aberrant CD56 expression on granulocytes is seen in all subtypes MPN and high grade MDS. CD56 expression in MPN correlated with bone marrow morphology, BCR/ABL transcript, and bone marrow engraftment study following treatment. Identification of abnormal CD56+ granulocytes and monocytes is helpful in both the initial diagnosis and long-term follow up of patients with MPN and MDS.

REFERENCES

1. Lanza F, Bi S, Castoldi G, and Goldman JM. Abnormal Expression of N-CAM (CD56) Adhesion Molecule on Myeloid and Progenitor Cells from Chronic Myeloid Leukemia. Leukemia 1993;7:1570-1575.
2. Feng B, Verstovsek S, Jorgensen JL, Lin P. Aberrant Myeloid Maturation Identified by Flow Cytometry in Primary Myelofibrosis. Am J Clin Pathol 2010;133:314-320.

INTRODUCTION

- Diagnosis of Myeloproliferative neoplam (MPN) and myelodysplastic syndromes (MDS) require a combination of analyses of morphology, immunophenotype, genotype, and clinical presentation.
- Phenotypic aberrancy in granulocytes, monocytes and erythroid precursors detected by flow cytometry assists the diagnosis of these diseases.
- CD56 is an adhesion molecule most often expressed in neural tissue and in granular Imphocytes.
- Aberrant expression of CD56 has been well characterized in acute and chronic monocytic leukemia, acute myeloid leukemia and plasma cell myeloma.
- However, limited and inconsistent data are available regarding CD56 expression on granulocytes in chronic myeloid neoplasms.
- We analyzed CD56 expression on granulocytes and monocytes in all subtypes of MPN and MDS. We also investigate the abnormal CD56 clone in response to therapy

METHOD

- We retrospectively reviewed flow cytometry data from Thomas Jefferson University Hospital in the past 5 years
  - 81 myeloproliferative neoplasms (MPN) (including 27 CMLs, 17 ETs, 8 PVs, 18 PMFs, and 11 MPN-Us)
  - 42 MDS (including 11 RAEB1/2, 26 RCMDs, 3 RCUD/RARS, and 2 MDS-Us).
  - Negative controls: 40 bone marrow cases from negative staging bone marrow for lymphoma.
- CD56 expression on granulocytes and monocytes are analyzed using 4 color flow cytometry.
  - All negative controls: <2% of granulocytes positive for CD56
  - Positive: ≥10% of granulocytes positive for CD56
- Serial followup specimens were available in 5 cases with positive CD56 expression (2 CML, 1 PMF, 1 PV, 1 MPN-U). CD56 expression is correlated with morphology, BCR-ABL quantification and recipient cell percentage post bone marrow transplant

Table 1: Aberrant CD56 expression in granulocytes and monocytes in MPN and MDS

	No. Cases	CD56 Pos cases (%)		CD56 Neg cases (%)		Max	Min	Mean
	Grans/Mono	Granulocytes	Monocytes	Granulocytes	Monocytes	Gran/Mono	Gran/Mono	Gran/Mono
Normal	40/35	0	0	40 (100%)	35 (100%)	1.8/8.3	0/0.4	0.8/4.3
CML	27/27	5 (19%)	7 (26%)	20 (81%)	21 (74%)	73.2/76.3	0.1/1.2	6.3/14.9
ET	17/17	1 (6%)	6 (35%)	16 (94%)	9 (65%)	13.8/60.0	0.3/3.1	2.3/15.4
PV	8./8	1 (13%)	3 (36%)	7 (87%)	6 (64%)	11.1/37.3	0.6/1.8	3/11.2
PMF	18/18	5 (28%)	8 (44%)	13 (78%)	10 (56%)	61.3/79.6	0.2/2.2	10.6/18.9
MPN-U	11./11	2 (18%)	6 (55%)	9 (82%)	6 (45%)	36.1/63.9	0.4/4.0	6.6/23.8
Total MPN	81/81	14 (17%)	30 (37%)	67 (83%)	52 (64%)	36.1	0.4	6.6
RCUD/RARS	3	0 (0%)	1 (33.3%)	3 (100%)	2 (66.7%)	1.69/21.51	2.55	1.13/10.25
RAEB1/2	11	3 (27.3%)	6 (54.5%)	8 (72.7%)	5 (45.5%)	29.21/68.17	0.13/0	7.65/13.82
RCMD and RCMD-R	26/26	4 (18.4%)	8 (30.8%)	22 (84.6%)	18 (69.2%)	45.69/75.26	0.31/0	6.23/13.56
MDS-U fibrosis	2	0 (0%)	1 (50%)	2 (100%)	1 (50%)	1.85/17.11	0.64/5.56	1.25/11.34
MDS	42/42	7 (16.7%)	16 (38%)	36 (86%)	26 (62%)	45.68/75.26	0.13/0	6/13.3

RESULTS

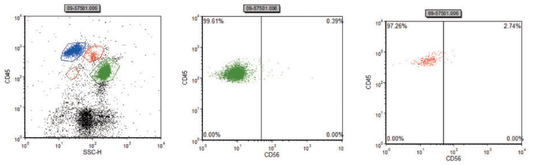

Figure 1: Negative CD56 expression on granulocytes and monocytes in normal controls

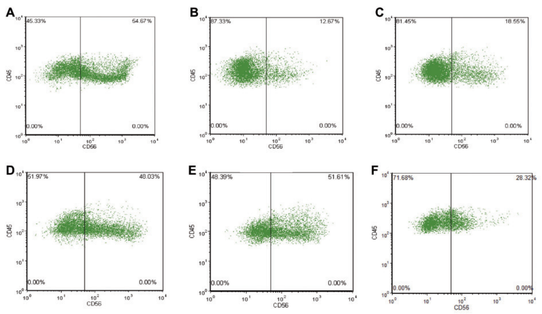

Figure 2: Positive CD56 expression on granulocytes in MPN and MDS. (A) CML. (B) ET. (C) PV. (D) PMF. (E)MPN-U. (F) MDS.

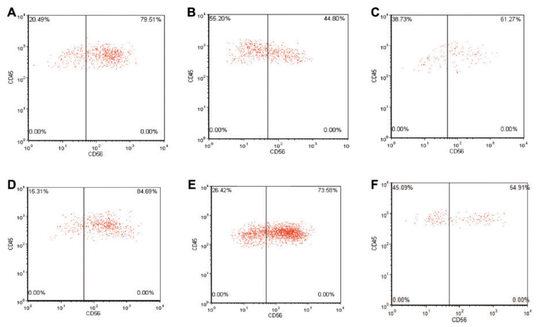

Figure 3: Positive CD56 expression on monocytes in MPN and MDS. (A) CML. (B) ET. (C) PV. (D) PMF. (E)MPN-U. (F) MDS.

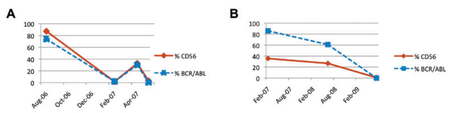

Figure 4: CD56 Reduction Parallels with Reduced BCR/ABL Transcript in CML after therapy. (A) Status post bone marrow transplant. (B) Status post chemotherapy.

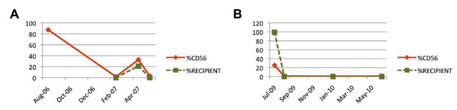

Figure 5: CD56 Reduction Parallels with Recipient Cell Percentage in MPN patients who have received bone marrow transplant. (A) CML patient. (B) MPN-U patient.

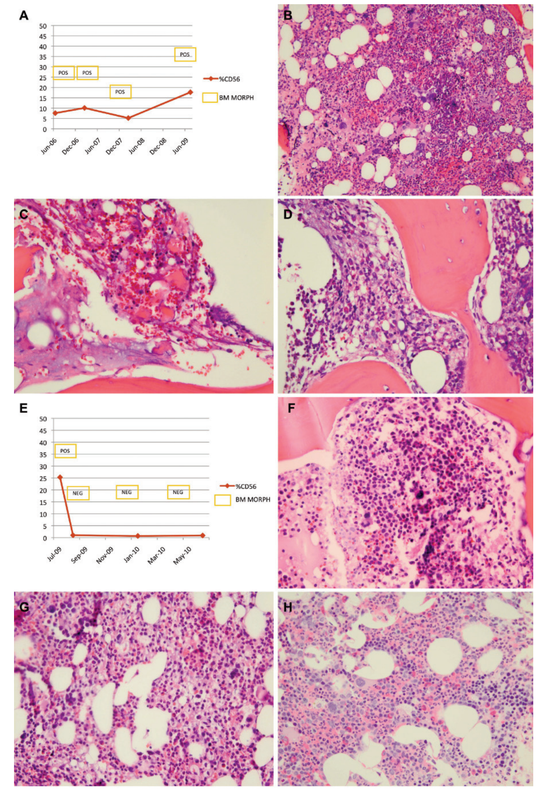

Figure 6: CD56 Expression Parallels with Recurrent Disease by Bone Marrow Morphology. (A) CD56 expression changes in a patient with ET and PMF transformation (B) ET with fibrosis. (C) Primary myelofibrosis, hypocellular (D) Primary myelofibrosis, hypercellular. (E) CD56 expression changes in a MPN-U patient F. MPN-U. G and H. Status post bone marrow transplant.

CONCLUSIONS

- Aberrant CD56 expression on granulocytes is seen in all subtypes MPN and high grade MDS.
- CD56 expression is expressed more frequently in primary myelofibrosis than other types of MPD.
- In general, cases with CD56 expression on granulocytes also have CD56 expression on monocytes, but monocytes usually have higher percentage of CD56. However, total numbers of monocytes may be small in MPN cases and analyses of CD56 expression may be difficult.
- CD56 expression in MPN correlates with bone marrow morphology following treatment.
- CD56 expression in CML parallels BCR/ABL transcript.
- CD56 expression in patients who received bone marrow transplant parallels recipient cell percentage.
- Identification of abnormal CD56+ granulocytes and monocytes is helpful in both the initial diagnosis and long-term follow up of patients with MPN and MDS.