

Short Report

Myeloperoxidase Index and Subtypes of Acute Myeloid Leukemia

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Abstract

Acute myeloid leukemia (AML) should be classified into subtypes according to the French-American-British (FAB) or, preferably, the newer World Health Organization (WHO) classification schemes. FAB is purely a morphological classification. It does not determine treatment (except M3) or prognosis for the patient which requires cytogenetics. Haematological analyzer had been used for classification of leukaemia in several studies. Neutrophil myeloperoxidase activity (MPXI) can be performed by Technicon H1 (Bayer) automated cell counter. The aim of this study was the statement of myeloperoxidase index and subgroups of AML. In the study of medical records of 72 patients with AML from 2006-7, we found that MPXI was negative in M4 and M5 while 75% of M3 cases had high MPXI values. MPXI level may help to differentiate subtypes of AML.

Introduction

Acute myeloid leukaemia (AML) should be classified into the appropriate variant, according to the French-American-British (FAB) or, preferably, the newer WHO classification schemes. FAB classification for leukemias has been widely accepted due to its objectiveness and good reproducibility.

FAB M0 - Acute myeloid leukaemia, minimally differentiated, FAB M1 - Acute myeloid leukaemia without maturation, FAB M2 - Acute myeloid leukaemia with maturation. FAB M3 - Acute promyelocytic leukaemia (APL), with both hypergranular and variant microgranular (FAB M3v) subtypes, FAB M4 - Acute myelomonocytic leukaemia (AMML), including the variant AMML with abnormal eosinophils (FAB: M4Eo, WHO: AMML Eo), FAB M5 - Acute monoblastic leukaemia, including poorly differentiated i.e., acute monoblastic leukaemia, FAB M5a and differentiated i.e., acute monocytic leukaemia, FAB M5b.

FAB M6 - Acute erythroleukaemia, FAB M7 - Acute megakaryoblastic leukaemia.¹

Several studies had been done by haematological analyzer for detection and classification of leukaemia.²⁻⁴ Tsakona CP et al had used flow cytochemistry via the H*1 system for FAB identification of acute leukaemias.⁵ In their study mean peroxidase activity value in AML was -

12.6±SD. They distinguished the FAB subtypes of AML from each other on the basis of characteristic patterns of cell distribution in the peroxidase cytogram when the total white cell count was over $10 \times 10^9/l$. Even with lower counts the differences were distinctive provided that circulating blasts were present. Several studies had been done previously by Bendix-Hansen K. et al about myeloperoxidase deficiency of polymorphonuclears in AML. They concluded that an increased number of MPO-deficient PMN in acute leukaemia speaks in favour not only of AML, but suggests the diagnosis of subtypes with some granulocytic component, most likely M1, M2, M3 or M4.⁶

Myeloperoxidase is a microbicidal protein, which is present in the primary granules of myeloid cells and takes part in the defense of the organism. It is synthesized in the promyelocytes where it is packed into azurophilic granules. Technicon H*1 (Bayer) has been used in several studies for the diagnosis of megaloblastic anaemia. Gulley and colleagues reported the observation of a high neutrophil myeloperoxidase activity (MPXI) in patients with megaloblastic anaemia and described its simplicity and role in masked megaloblastic anaemia.^{7,8}

This study was carried to know the effectiveness of myeloperoxidase index (MPXI) for classification of AML in an era of technical advancement. Our study denotes mean peroxidase value is negative in AML. Interestingly, the FAB subtypes of AML have different pattern of MPXI. All M4 and M5 cases have negative value which may be related to monocytoid cells while 75% of M3 cases have high MPXI value which may be related to high myeloperoxidase enzyme in promyelocytes.

Methods and Results

We studied medical records of 72 adult patients with AML from 2006-7 admitted in our haematology ward which is the major haematology unit for adults in the northwest of Iran. Patients were diagnosed by peripheral blood and bone marrow aspiration (stained with May-Graunwald-Giemsa and Sudan Black and PAS staining) and trephine biopsies stained with haematoxylin and eosin. Two haematologists made comments on peripheral smear and bone marrow slides while trephine biopsies were assessed by an expert haemato-pathologist. They were grouped as unknown type when subtyping was impossible according to morphology and/or immunophenotyping.

Table: Clinical characteristics and MPXI in patients with various types of AML (n=72).

AML Type	N (%)	Age= min, max, (median ± SD)	Gender (...F,...M)	MPXI(mean ±SD)
M0	3(4.2)	22 , 47 , (42±13.229)	1 , 2	1.4 (±7.5147)
M1	3(4.2)	23 , 56, (33 ±16.921)	1 , 2	-16.6 (±14.4108)
M2	28(38.9)	15 , 72 , (31.50±17.088)	13 ,15	-6.504 (±18.1108)
M3	7(9.7)	25 , 75, (53±21.447)	3 ,4	16.7(±21.8883)
M4	12(16.7)	18 , 71, (52.50±17.252)	9 ,3	-15.942(±12.326)
M5	2(2.8)	40 , 64 , (52±16.971)	0 ,2	-18.7(±6.2225)
M6	1(1.4)	27 , 27, (27±0)	1 ,0	1.8(±0)
M7	1(1.4)	79 , 79 , (79± 0)	0 , 1	-1.6(±0)
Unknown	15(20.8)	17 , 59 , (37.50 ± 17.070)	6 ,9	-2.967(±16.2996)
Total	72(1)	15 , 79, (40 ± 17.738)	34 ,38	-5.331(±18.1924)

Immunophenotyping of peripheral blood and bone marrow aspiration was done in some patients. All adult new AML cases who had not received chemotherapy or transfusion were included in the study. Patients who had received chemotherapy or transfusion or had relapsed or were pregnant were excluded from the study. Informed consent was taken from all patients and the study was approved by the ethical review committee of the institution.

MPXI were measured using the first blood sample of untreated patients obtained prior to any transfusion or medical therapy performed by Technicon H1 (Bayer) automated cell counter. MPXI is a direct and routine reading parameter in the machine result with the normal range between -10 and +10. Peroxidase activity and cell size were measured by light absorbance and scatter as each leukocyte flows through a mercury arc light beam. The value was computed as follows: $MPXI = \frac{\text{Mean X of Sample Neutrophil} - \text{Mean X of Archetype Neutrophil}}{\text{Mean of Archetype Neutrophil}} \times 100$. Mean of Sample Neutrophil is the average absorption channel (X) observed for neutrophils in the sample. Mean of Archetype Neutrophil is the average absorption channel (X) specified for the neutrophil cluster in the normal staining archetype. The values below -25 represented people with myeloperoxidase deficiency and autosomal recessive anomaly.⁷ Fifty adult persons enrolled as controls, were normal and healthy people, and were referred for routine CBC test. Data was analyzed by SPSS software and T test.

Mean MPXI was -5.3(Std 18.1924) in patients and 1.9 (Std 4.9256) in controls (p: 0.007, Df =120). Table shows clinical characteristics, AML subgroups and mean MPXI with Std. deviations.

Conclusion

It is concluded that mean MPXI is almost always negative in AML M1, M4 and M5 but it may be positive in AML M3. MPXI level may help to differentiate subtypes of AML.

References

1. Charles A Schiffer, Clinical features, diagnosis, and prognosis of acute myeloid leukemia-I. UpToDate 2005.
2. Fernandez-Castro M, Vilorio A., Utility of the Technicon H-1 flags in the detection of peripheral blood blast cells of paediatric acute leukaemia patients. *Acta Haematol* 1995; 93:9-12.
3. Hoyer JD, Fisher CP, Soppa VM, Lantis KL, Hanson CA, Detection and classification of acute leukemia by the Coulter STKS Hematology Analyzer. *Am J Clin Pathol* 1996; 106:352-8.
4. Kakkar N, Kaur R. Utility of white blood cell suspect flags and histogram pattern in the detection of acute leukemia by Advia-60 automated hematology analyzer. *Indian J Pathol Microbiol* 2004; 47:322-6.
5. Tsakona CP, Kinsey SE, Goldstone AH, Use of flow cytochemistry via the H*1 in FAB identification of acute leukemias. *Acta Haematol* 1992; 88:72-7.
6. Bendix- Hansen K, Nielsen HK. Myeloperoxidase deficient polymorphonuclear leucocytes. (IV): Relation to FAB-classification in acute myeloid leukaemia. *Scand J Haematol* 1985; 35: 174-7
7. Eivazi Ziaei J, Dastgiri S. Role of myeloperoxidase index in differentiation of megaloblastic and aplastic anemia. *Indian J Med Sci* 2004; 58, 8: 345-8.
8. Eivazi-Ziaei J, Dastgiri S, Sanaat Z. Estimation of the Diagnostic Value of Myeloperoxidase Index and Lactate Dehydrogenase in Megaloblastic Anaemia. *JCDR* 2007; 1: 380-4.