Single Circulating Blast in the Peripheral Blood Film in Normal Individuals and Patients of Non-neoplastic Haematological Disorders and Non-hematological Neoplasms/Disorders- A Study at a Tertiary Care Centre

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ABSTRACT

Introduction: The blasts in the peripheral blood is usually associated with a haematological disorder. Study aimed to see if a single blast seen in a peripheral blood film of healthy individuals and patients of non-neoplastic haematological disorders and non-hematological neoplasms/disorders did have any clinical significance.

Material and Methods: The period of study was from 2014 to 2018 conducted at a tertiary care hospital. The study was done exclusively on Peripheral Blood Films. The films were stained with Leishman stain. An occasional blast was detected in some healthy subjects and patients of non-neoplastic haematological disorders and non-hematological neoplasms/disorders.

Result: The routine smears were analyzed with caution after the first case of a patient of Iron Deficiency Anemia revealed a clear-cut Blast. In the period of 4 years from 2014 to 2018, a total of 23 cases of apparently normal individuals or patients with non neoplastic haematological disorders and non-hematological neoplasms/disorders showed at least 1% on one separate occasion.

Conclusion: A careful morphological examination in the peripheral smears of few normal individuals and individuals with non neoplastic haematological disorders and non-hematological neoplasms/disorders showed at least 1% Blast on one separate occasion. The cells were clear cut blasts with a large size, fine nuclear chromatin, one to two nucleoli with round to slightly irregular nuclear contours and a mild amount of pale agranular cytoplasm. On thorough investigations of these individuals there was no evidence of a neoplastic haematological disorder. Therefore a single blast in a peripheral blood seen in a healthy individuals or patients with benign haematological disorder and non-neoplastic neoplasms/disorders may not always indicate a neoplastic process.

Keywords: Peripheral Blood Film; Blast; Non-Neoplastic

INTRODUCTION

The presence of blasts in the peripheral blood is traditionally always been associated with a haematological disorder. Depending on the number of blasts one can categorize the disorders into various categories like if there are ≥20% blasts a diagnosis of Acute Leukemia is confirmed.[1,2] If there are <20% blasts on the PBF one would think of Subleukemic Leukemia, Myelodysplastic Syndrome, an accelerate phase of an MPN or MPN/MDS etc.[3,4] Presence of <5% blasts can be seen in MPNs especially CML and also sometimes when a patient has Leukemoid reaction secondary to sepsis or patient on G-CSF, you may find 1 or 2 blasts in the PBF.[5,6] But presence of Blast in a normal healthy individual or patients with a non-neoplastic haematological disorder and non-haematological neoplasms/disorders may not always indicate a neoplastic process.

In our study of 4 years we observed that the PBF of some normal individuals and patients with a non-neoplastic haematological disorder and non-haematological neoplasms/disorders with an apparently normal counts showed 1% circulating blast on a single occasion. The aim of our study was to see if there was any clinical significance of these blasts seen.

MATERIAL AND METHODS

This was a study conducted in the Department of Hematopathology, Sher-I-Kashmir Institute Institute of Medical Sciences, Soura- a tertiary care centre for a period of 4 years from March 2014 to July 2018. In this study the PBFs of normal individuals and patients of non-neoplastic hematological disorder and non-haematological neoplasms/disorders were thoroughly examined and looked for any circulating blasts. In our study of 4 years we found that 23 cases showed 1% circulating blast on PBF on a single occasion. The study was established because in one of our patient who was a 60 year old male suffering from Iron Deficiency Anemia had a clear cut Blast on his PBF. The clinicians were informed and an immediate Bone Marrow Aspiration and Biopsy was advised. On bone marrow examination there were just features of Nutritional Anemia

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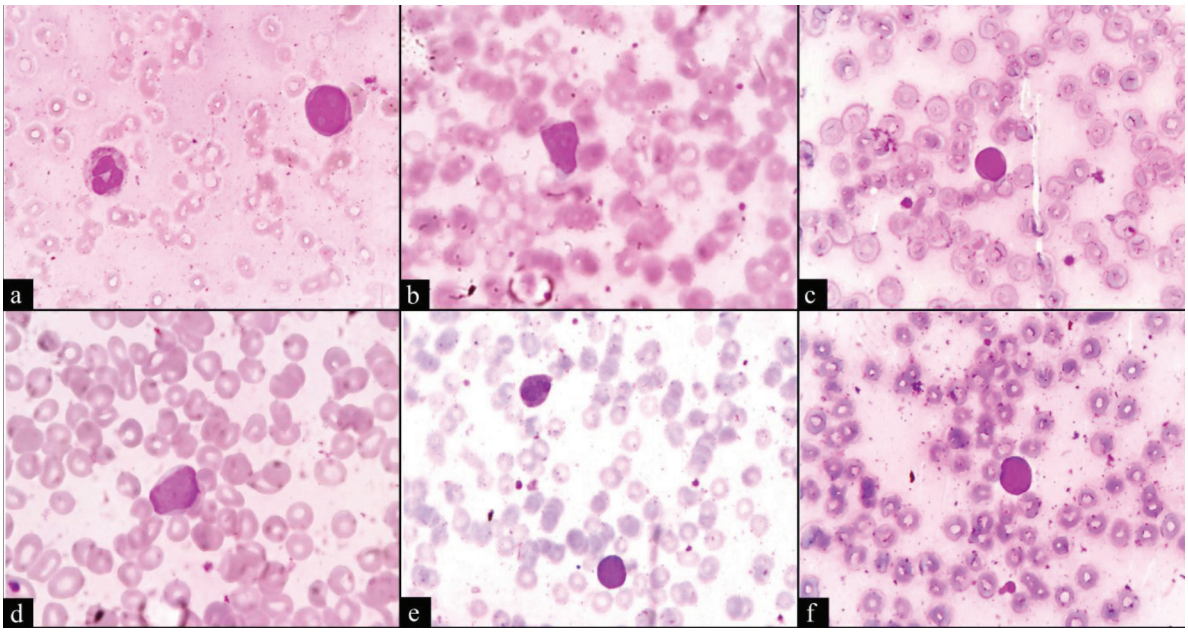

Figure-1: PBF from a patient with Iron Deficiency Anemia showing a blast with large size, high Nuclear Cytoplasmic ratio, fine chromatin, 2 prominent nucleoli with a scant amount of cytoplasm. b) PBF from a normal individual showing a blast with 2 prominent nucleoli. c) A case of SLE showing a blast on PBF. d) A case of ITP showing a blast on the PBF with a large size and very fine chromatin. e) A single blast seen in a patient of Cholelithiasis having a high Nuclear Cytoplasmic ratio with a dispersed chromatin. f) A case of Rectal carcinoma showing a clear cut blast on the PBF. These patients were all on follow-up and a blast was never noted on the PBF again.

S.No.	Diagnosis	Hb	MCV	RBC	Plts	TLC	DLC
1.	Iron Deficiency Anemia (M)	9.3	72.3	3.88	300	6.7	$N_{61}\ L_{27}\ M_{06}\ E_{01}$
2.	Healthy Individual (M)	14.3	86.0	5.10	255	5.3	$N_{51}\ L_{35}\ M_{06}\ E_{06}Ba_{01}$
3.	Healthy Individual (F)	12.7	83.5	4.32	276	5.9	$N_{58}\ L_{30}\ M_{06}\ E_{05}$
4.	Hashimotos Thyroiditis (F)	11.3	77.4	4.13	387	6.2	$N_{56}\ L_{34}\ M_{05}\ E_{04}$
5.	ITP (F)	9.8	76.4	3.86	54	5.5	$N_{44}\ L_{41}\ M_{09}\ E_{04}Ba_{01}$
6.	Pre Anesthetic Check-up (M)	15.3	90.5	5.31	210	8.6	$N_{67}\ L_{23}\ M_{06}\ E_{03}$
7.	DDA (F)	8.7	87.9	4.43	103	5.3	$N_{43}\ L_{45}\ M_{06}\ E_{05}$
8.	ITP (F)	9.6	74.3	4.32	83	8.3	$N_{72}\ L_{22}\ M_{03}\ E_{02}$
9.	Healthy Individual (M)	14.4	86.0	4.93	187	6.3	$N_{53}\ L_{34}\ M_{08}\ E_{03}Ba_{01}$
10.	Healthy Individual (F)	12.7	80.3	4.14	202	7.6	$N_{58}\ L_{35}\ M_{04}\ E_{02}$
11.	Rectal Carcinoma (M)	9.1	98.5	3.20	404	3.5	$N_{39}\ L_{48}\ M_{09}\ E_{02}Ba_{01}$
12.	Iron Deficiency Anemia (F)	8.7	74.2	4.11	306	7.7	$N_{73}\ L_{22}\ M_{03}\ E_{01}$
13.	ITP (M)	11.3	79.5	3.59	33	6.1	$N_{54}\ L_{38}\ M_{05}\ E_{02}$
14.	Healthy Individual (M)	13.5	85.7	5.03	164	7.2	$N_{58}\ L_{31}\ M_{06}\ E_{03}Ba_{01}$
15.	Endometrial Carcinoma (F)	11.8	82.9	4.13	206	6.7	$N_{54}\ L_{34}\ M_{06}\ E_{05}$
16.	Chlolelithiasis (F)	10.6	77.3	3.94	145	8.9	$N_{48}\ L_{40}\ M_{07}\ E_{04}$
17.	Healthy Individual (M)	15.4	88.6	4.96	221	5.4	$N_{56}\ L_{35}\ M_{04}\ E_{04}$
18.	Ca Prostate (M)	11.3	81.9	4.11	107	4.8	$N_{43}\ L_{42}\ M_{10}\ E_{03}$
19.	Multinodular Goitre (F)	9.3	72.3	3.88	276	7.4	$N_{62}\ L_{29}\ M_{06}\ E_{01}Ba_{01}$
20.	ITP (M)	11.6	82.3	4.42	86	8.8	$N_{46}\ L_{39}\ M_{09}\ E_{05}$
21.	Iron Deficiency Anemia (F)	10.1	75.5	4.21	315	5.9	$N_{71}\ L_{25}\ M_{02}\ E_{01}$
22.	SLE (F)	8.3	77.2	3.41	77	3.3	$N_{34}\ L_{50}\ M_{10}\ E_{05}$
23.	Healthy Individual (M)	14.1	85.4	5.23	204	5.8	$N_{60}\ L_{31}\ M_{05}\ E_{03}$

Table-1: Detail of cases with 1% Blast on PBF. Hb- Hemoglobin in gram%; MCV- Mean Corpuscular Volume in Famtolitres; RBCs- Red Blood Cell count in millions per cubic millimetres; Plts- Platelets in lakhs x 10^9 per Litre; TLC- Total Leucocyte Count in thousands x 10^9 per Litre; DLC- Differential Leucocyte Count; M- Male; F-Female; ITP- Immune Mediated Thrombocytopenia Purpura; DDA- Dual Deficiency Anemia; Ca- Carcinoma; SLE- Systemic Lupus Erythematosus.

with BM blasts accounting for ~02% of all nucleated cells counted. The 1% blast that we had reported had all the features of a blast and was labelled as a blast by experts and could not be categorized as atypical lymphocyte or an abnormal monocyte. The patient was kept on follow-up and no blast was reported again on his PBF. Thereafter we meticulously looked at the PBFs of normal individuals and patients of non-neoplastic haematological disorder and non-haematological neoplasms/disorders and looked for 1% circulating blast.

RESULTS

We found that in 23 patients a 1% circulating blast was seen on a single occasion. The details of the cases in our study are given in Table 1.

Among the 23 cases that were taken up for the study 7 cases were of normal healthy individuals who had come to the hospital for a routine health check-up with no significant medical history. 4 cases in the study were that of deficiency anemias with 3 cases of Iron Deficiency Anemia and 1 case of Dual Deficiency Anemia. 3 cases were that of solid organ malignancies, 4 cases of ITP, 1 case each of SLE, Multinodular Goitre, Cholelithiasis and Hashimotos thyroiditis. 1 case in the study was a 53 year old male for Pre-anesthetic check-up who was to be operated for Inguinal Hernia. Interestingly in all the patients in the study there was no suspicion for any hematological neoplasm. However bone marrow examination was performed in 4 cases in the study. The first of these cases was the 60 year old male patient who had iron deficiency anemia. On his PBF 1% blast was noted based on which bone marrow examination was advised. However BMA showed just erythroid hyperplasia with reduced iron stores and just ~2% blasts. The next case we performed BMA was the 32 year old female diagnosed with ITP as she had bicytopenia and 1% Blast on PBF. Though there was no clinical suspicion of any hematological malignancy, it was advised to do a BMA to rule it out. BMA surprisingly revealed just erythroid hyperplasia with reduced iron stores and just ~1% blast. It had created a panic and the clinician had to be explained of this finding. The next case in whom BMA was done on the basis of circulating 1% blast was the 65 year old male of Ca rectum. His BM examination also did not show any increase in blasts. The last such case in whom BMA was performed was a 31 year old female of SLE, wherein no increase in blasts were seen. In the rest of the patients bone marrow examination was not performed but kept on follow-up instead. On an average the PBFs were repeated for a minimum of 3 occasions and there were no blasts seen in any of the cases in the study in the subsequent PBFs. Though BMA was done in only 4 patients but the other patients were kept on follow-up and no peripheral blood blasts were ever noted again. The exclusion criteria of the study included diagnosed cases of Acute Leukemias, Myelodysplastic Syndromes, Myeloproliferative syndromes, Myeloproliferative syndrome/Myeloproliferative syndrome, patients with sepsis, patients on G-CSF and the patients suspected to have a haematological neoplasm.

DISCUSSION

The presence of blasts in the peripheral blood is traditionally always associated with a haematological disorder. Despite the availability of automated cell analyzers which can perform a variety of functions from a Complete Blood Counts to Leucocyte Differential count and has virtually replaced the traditional manual assessment for initial screening and detection of a haematological abnormality; the peripheral blood film remains the most important method for detection of an abnormality which an analyzer cannot determine.[7,8,9] The flagging is provided by most of the analyzer which includes one for blasts as well. But analyzers cannot always determine if the cells in question are really blasts. Reactive lymphocytes, Atypical Lymphocytes, monocytosis, degenerated cells also give a flag for blasts quite often and sometimes the analyzers fail to give flags which could mask the abnormality if present. It is therefore necessary in suspicious cases to do a PBF routinely, the practice employed commonly at our centre. The Manual differential counting of cells though time consuming and labor intensive is considered as the gold standard for the accurate identification of cells in the peripheral blood.[10,11] Blasts can normally be seen in the bone marrow between 0 to 5%. But under normal circumstances no blasts should be ideally seen on a PBF. Even a presence of a single peripheral blood blast should be taken seriously and patient investigated thoroughly. Presence of a single peripheral blood blast can be seen in many conditions which include subleukemic leukemia, patients of acute leukemia who can present with severe leucopenia, MDS, MPN, MDS/MPN, patients of acute leukemia on treatment, relapsed cases of acute leukemias, patients with sepsis presenting with a leukemoid reaction, patients on G-CSF etc.[3,4,5,6] It is important to pick blasts especially when they are present in very low numbers. In normal individuals and patients of non-neoplastic haematological disorder and non-haematological neoplasms/disorders, the presence of blasts is not usually reported. The blasts that were picked up on DLC in our study were clear cut blast which were 12 to 16 µm in size, having a high Nuclear Cytoplasmic ratio, fine nuclear chromatin, 1 to 2 nucleoli, round to irregular nuclear contours and a mild amount of pale, agranular cytoplasm. One would argue that these could be the close mimickers of blasts which include atypical lymphocytes (Type II Downey cells) and sometimes abnormal monocytes would look like blasts.[12,13] But based on experience and consensus of expert hematopathologists these cells were labelled as blasts (Figure 1). We could not do any further analysis of these blasts noted. The best possible explanation for these blasts seen on PBF could be that these could be Hematopoietic Progenitor Cells (HPCs). Under normal conditions, HPCs in PB range from 0.01 to 0.05%.[14] J Oertel et al in their study "Detection of small numbers of immature cells in the blood of healthy subjects" concluded that the blasts that they found in the peripheral blood of normal individuals represent haemopoietic progenitor cells.[15] Also they detected in their study that a small population of cells with a blast-like morphology had an ovoid nucleus with fine stranded chromatin structure and more cytoplasm which were positive for HLA-DR and CD45 and concluded that the blast-like cells are poorly differentiated monocytes.[15]

CONCLUSION

It remains unexplained as to why 1% circulating blasts were seen once in the PBF of normal individuals and patients of non-neoplastic haematological disorder and non-haematological neoplasms/disorders. However we infer from our study that if you see 1% circulating Blast on

one occasion in a normal individuals and patients of non-neoplastic haematological disorder and non-haematological neoplasms/disorders, it is advised to closely follow up the patient. It may not always necessarily mean that the patient is having a haematological neoplasm. However a thorough investigation is always recommended, after all a blast on a PBF cannot be taken lightly.

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