

A Prospective Etiological Assessment of Hypersegmented Neutrophils in Peripheral Blood Smear

Nivedita Singh¹, O.P.Dwivedi²

¹M.D. (Pathology) Tutor, Department of Pathology, Nalanda Medical

²Professor, Department of Pathology, NMCH, Patna, Bihar, India.

Received: 19-06-2022 / Revised: 29-07-2022 / Accepted: 14-08-2022

Corresponding author: Dr. Nivedita Singh,

Conflict of interest: Nil

Abstract

Background: Hypersegmented Neutrophils Are Usually Associated With Deficiency Of Or Failure To Utilize Cobalamin Or Folate And Impaired DNA Synthesis Is The Accepted Mechanism For The Morphological Changes Seen In Megaloblastosis.

Material & Methods: This Is A Prospective Study Conducted In Department Of Pathology, NMCH, Patna, Bihar, India, From April 2018 To March 2019

Results: Cases Were Further Analyzed For Associated Peripheral Smear Picture. Although Major Cases Were Contributed By Macrocytic Anemia, 46 Cases Were Having Microcytic Hypochromic Anemia. Out Of The 120 Cases, Only 4 Had Thrombocytopenia. 91 Cases Had Platelet Count In The Normal Range.

Conclusion: The Present Study Indicates That Other Than The Already Established Causes Of Neutrophil Hyper Segmentation, Microcytic Hypochromic Anemia, Myelodysplastic Syndromes And Inflammatory Conditions Also Can Cause Hypersegmented Neutrophils In Peripheral Smears.

Keywords: Hypersegmented, Neutrophils, Anemia

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Pancytopenia is an important clinico hematological entity encountered in our day-to-day clinical practice. There are varying trends in its clinical pattern, treatment modalities, and outcome. [1] It is a disorder in which all three major formed elements of blood (red blood cells, white blood cells and platelets) are decreased in number. [2]

It is not a disease entity but a triad of findings that may result from a number of disease processes – primarily or secondarily involving the bone marrow. [3] The severity of pancytopenia and the

underlying pathology determine the management and prognosis of the patients. [4]

Hyper segmentation of neutrophils is defined as presence of 5% or more neutrophils with five or more lobes or single neutrophil with 6 lobes. [5] It is usually associated with deficiency of or failure to utilize cobalamin or folate and impaired DNA synthesis is the accepted mechanism for the morphological changes seen in megaloblastosis. [6-7]

Material & Methods:

This is a prospective study conducted in Department of Pathology, NMCH, Patna, Bihar, India, from April 2018 to March 2019

EDTA blood samples received in our hematology laboratory were analyzed for hyper segmentation of neutrophils using geimsa stained peripheral smears. Neutrophils hyper segmentation is defined as the presence of five or more five-lobed neutrophils per 100, or any neutrophils with six or more lobes. 120 such cases which satisfied the inclusion criteria were taken as sample size.

Complete blood count of individual cases was obtained using Sysmex SE9000 analyser and peripheral smear picture was compared with blood counts. These 120 cases were classified according to the peripheral smear picture. Patients with microcytic hypochromic anemia were separately assessed for serum Vit B12 and folic acid values using ion capture assay and microparticle enzyme intrinsic factor assay. Presence of thrombocytosis in pure microcytic hypochromic anemia cases were checked separately and it was compared with presence of thrombocytosis in cases with NH without microcytic

hypochromic anemia. Patients with known medical conditions like pregnancy, uremia, renal failure and exposure to drugs like chemotherapy, steroid and GCSF were excluded.

Results:

Cases were further analyzed for associated peripheral smear picture. Although major cases were contributed by macrocytic anemia, 46 cases were having microcytic hypochromic anemia. Detailed picture is given in Table 1.

Table 2 clearly shows that out of total 120 cases 16 cases showed normocytic normochromic blood picture. So we can come to the conclusion that out of the 120 cases with hypersegmented neutrophils in peripheral smear 38.3% cases were having pure microcytic hypochromic anemia without any Vit. B12 or folic acid deficiency.

Platelet count of all cases was assessed. Results are shown in Table 3. 1.5-4.5 lakh/microliter is considered as normal platelet count. Out of the 120 cases, only 4 had thrombocytopenia. 91 cases had platelet count in the normal range.

Table 1: peripheral smear picture of cases with hyper segmented neutrophils

Macrocytic anemia	50
Microcytic hypochromic anemia	46
Normocytic normochromic blood picture	16
Myelodysplastic syndrome	8
Total	120

Table 2: Serum Vit B12 and folic acid values of cases with neutrophil hyper segmentation in microcytic hypochromic blood picture

Vit B12(in pg /ml)	Observed frequency	Folic acid (in ng/ml)	Observed frequency
<200pg/ml	8	<2ng/ml	4
200-500pg/ml	22	2-8ng/ml	10
500-700pg/ml	11	8-15ng/ml	19
700-900pg/ml	3	15-20ng/ml	13
>900pg/ml	2	>20ng/ml	0
Total	46		46

Table 3: Correlation of neutrophil hyper segmentation and platelet count

Platelet count	Macrocytic anemia	Microcytic hypochromic Picture (Normal B12 and folic acid)	Microcytic hypochromic Picture (subnormal B12 and folic acid)	Myelodysplasia	Normocytic Normochromic Blood picture
<1.5 lakh/microliter	1	0	0	3	0
1.5-4.5 lakh/microliter	46	10	16	5	14
>4.5 lakh/microliter	3	20	2	0	2
Total	50	28	18	4	16

Discussion:

Macrocytosis refers to a condition in which red blood cells are larger than normal. It is evaluated by measuring mean corpuscular volume. Normal MCV ranges from 80-100 femtolitres and varies with age and reference laboratory. [8]

MCV = hematocrit%/RBC count in 106/microliter.

Macrocytosis is a common finding with a prevalence estimating from 1.7% to 3.6 %. [9-11] The significance of macrocytosis has been underestimated by medical professionals because about 60% of the patients present without associated anemia [12]

According to Thompson et al, in 91% of 515 patients, hypersegmented neutrophil was a more sensitive indicator as compared to MCV. [13] Terpstra et al. reported >50% of plasma cells in the bone marrow in 12 of 54 patients with multiple myeloma in their study. [14]

There are several studies showing that hypersegmented neutrophils can be seen as a part of trauma and chronic infections. It is also said to be recruited to bloodstream during inflammation. [15] In our study several cases showed neutrophil toxic granules along with hypersegmentation. Both toxic granules and vacuoles are

known to be the response to infection, inflammation and stress. [16]

2 cases in our study were diagnosed as myelodysplastic syndromes. There are several earlier studies demonstrating that neutrophil hypersegmentation can be seen as a part of myelodysplasia .[17-19]

Conclusion:

The present study indicates that other than the already established causes of neutrophil hypersegmentation, microcytic hypochromic anemia, myelodysplastic syndromes and inflammatory conditions also can cause hypersegmented neutrophils in peripheral smears.

References:

1. Kar M, Ghosh A. Pancytopenia Journal, Indian Academy of Clinical Medicine 2002;3:29-341.
2. Ishtiaq O, Baqai HZ, Anwer F, Hussain N. Patterns of pancytopenia patients in a general medical ward and a proposed diagnostic approach. J Ayub Med Coll Abbottabad. 2004 Jan-Mar;16(1):8-13.
3. Guinan EC, Shimamura A. Acquired and inherited aplastic anemia syndromes in: Greer JP, Foerster J, Lukens JN, Rodgers GM, Paraskevas F, Glader B, editors. Wintrobe's Clinical Hematology. 11th ed,

- Philadelphia: Lippincott Williams and Wilkins; 2004:1397-419.
4. Tilak V, Jain R. Pancytopenia-A Clinco-hematologic analysis of 77 cases. *Indian J Pathol Microbiol* 1992; 42:399-404.
 5. Herbert V. Nutrition science as a continually unfolding story: the folate and vitamin B12 paradigm. *Am J Clin Nut.* 1987;46(3):387-402.
 6. Agarwal KN. Indicators for assessment of anemia and iron deficiency in community. *Pediatr Oncall J.* 2010; 7 (2):29-34.
 7. Westerman DDA, Evans D, Metz J. Neutrophil hypersegmentation in iron deficiency anemia: A case control study. *Br J Haematol.* 1999;107 (3):51 2-5.
 8. Chanarin I, Metz J. Diagnosis of cobalamine deficiency: the old and new. *Br J Haematology* 1997; 97(4):695-700.
 9. Davidson RJ, Hamilton PJ. High mean red cell volume: its incidence and significance in routine haematology. *J Clin pathology* 1978;31(5):493-8.
 10. Breedveld FC, Bieger R, Van Wermeskerken RK. The clinical significance of macrocytosis. *Acta Med Scand* 1981;209(4):319-22.
 11. Colon-Otero G, Menke D, Hook CC. A practical approach to differential diagnosis and evaluation of the adult patient with macrocytic anemia. *Med Clin North Am* 1992;76(3):581-97.
 12. Nathan DG, Orkin SH, Hook AT, et al. Nathan and Oski's hematology of infancy and childhood. 6th edn. Philadelphia: Saunders 2003:1841.
 13. Thompson WG, Cassino C, Babitz L, et al. Hypersegmented neutrophils and vitamin B12 deficiency. Hypersegmentation in B12 deficiency. *Acta Haematol* 1989;81(4):186-91.
 14. Terpstra WE, Lokhorst HM, Blomjour F, Meuwissen OJ, Dekker AW. Comparison of plasma cell infiltration in Bone Marrow Biopsies and Aspirates in patient with Multiple Myeloma. *Br J Hematol* 1992; 82:46-9.
 15. Tak T, Wijten P, Heeres M, Pickkers P, Scholten A, Heck A. Human CD62L dim neutrophils identified as a separate subset by proteome profiling and in vivo pulse -chase labelling. *Blood.* 2017;129:3476 – 86.
 16. Manonneaux S. Non malignant leukocyte disorders. In: Rodaks hematology clinical applications and principals. St. Louis, Missouri: Saunders; 2015: 475-97.
 17. Yoshida Y. Physical Education. Myelodysplastic syndrome. *Oncologist.* 1996; 1(4):284-7.
 18. Abramson SD, Abramson N. Common' uncommon anemias. *Am Fam Physician.* 1999; 59(4):851-8.
 19. De Leo, S. (2021). Effectiveness of the mRNA BNT162b2 vaccine against SARS-CoV-2 severe infections in the Israeli over 60 population: a temporal analysis done by using the national surveillance data: Effectiveness of the mRNA BNT162b2 vaccine. *Journal of Medical Research and Health Sciences,* 2021; 4(10): 1511-1517.