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Original Research Article

Prospective Assessment of the Association between Neutrophil Hypersegmentation in Microcytic Hypochromic Anemia and Thrombocytosis

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Abstract

Aim: The aim of the present study to evaluate peripheral smears with hypersegmented neutrophils and classified the etiological factors.

Methods: The present study was conducted in Department of Pathology, Patna Medical College, Patna, Bihar, India. EDTA blood samples received in the hematology laboratory were analysed for hypersegmentation of neutrophils using geimsa stained peripheral smears. Neutrophils hypersegmentation is defined as the presence of five or more five-lobed neutrophils per 100, or any neutrophils with six or more lobes. 100 such cases which satisfied the inclusion criteria were taken as sample size.

Results: Majority of cases was males and majority of cases were in the age group 40-60. The major cases were contributed by macrocytic anemia, 40% cases were having microcytic hypochromic anemia. The result showed that out of the 41 cases with normocytic normochromic blood picture, only 10 had subnormal levels of either Vit B12 or folic acid values. Rest of the 30 cases had normal Vit B12 and folic acid levels. So we can come to the conclusion that out of the 100 cases with hypersegmented neutrophils in peripheral smear 31% cases were having pure microcytic hypochromic anemia without any vit B12 or folic acid deficiency.

Conclusion: The present study indicated 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.

Keywords: Microcytic hypochromic anemia, Neutrophil hypersegmentation, Thrombocytosis.

Introduction

Pancytopenia is an important clinic 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]

Usually patients with pancytopenia present symptoms attributable to anemia and thrombocytopenia. [9] The most common clinical manifestations are fever, fatigue, dizziness, weight loss, anorexia, night sweats, pallor, bleeding, splenomegaly, hepatomegaly and lymphadenopathy. [10] There is a wide disparity between clinical pictures gleaned from different studies. Detailed complete blood count with peripheral film and reticulotcyte count is the basic investigation to be done. Bone marrow examination using biopsy is extremely useful in the evaluation of pancytopenia, as it enables complete picturization of the marrow architecture and the distribution of any abnormalities in the form of infiltrates and focal lesions. [8]

Hypersegmentation of neutrophils is defined as presence of 5% or more neutrophils with five or more lobes or single neutrophil with 6 lobes. [11] 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. [7,12]

Hypersegmented neutrophils are also seen as a part of myelodysplastic syndromes which is usually designated as bone marrow (BM) failure are a heterogeneous group of myeloid clonal disorders caused by a failure of blood cells maturation. The co-morbidities result from a variable degree of cytopenia and clonal instability with a tendency to progression mainly into acute myeloid leukemia (AML). [13]

Here in the present study we evaluated peripheral smears with hypersegmented neutrophils and classified the etiological factors. Patients with microcytic hypochromic anemia were further evaluated for underlying vit B12 and folic acid deficiency. This study also checks whether there is any association between neutrophil hypersegmentation in microcytic hypochromic anemia and thrombocytosis.

Materials and Methods

The present study was conducted in Department of Pathology, Patna Medical College, Patna, Bihar, India for six months

Inclusion criteria

Cases 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.

Exclusion criteria

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

Methodology

100 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.

EDTA blood samples received in the hematology laboratory were analyzed for hypersegmentation of neutrophils using geimsa stained peripheral smears. Neutrophils hypersegmentation is defined as the presence of five or more five-lobed neutrophils per 100, or any neutrophils with six or more lobes.

Results

Table 1: Age and gender distribution of all cases showing hyper segmented neutrophils in peripheral smears

Gender	Below 20	20-40	40-60	Above 60	Total
Male	10	10	20	15	55
Female	5	10	20	10	45
Total	15	20	40	25	100

Majority of cases were males and majority of cases were in the age group 40-60.

Table 2: Peripheral smear picture of cases with hyper segmented neutrophils

Macrocytic anemia	45
Microcytic hypochromic anemia	40
Normocytic normochromic blood picture	10
Myelodysplastic syndrome	5
Total	100

Cases were further analysed for associated peripheral smear picture. Although major cases were contributed by macrocytic anemia, 40% cases were having microcytic hypochromic anemia.

Table 3: Serum Vit B12 and folic acid values of cases with neutrophil hypersegmentation in microcytic hypochromic blood picture

Vit B12(in pg /ml)	Observed frequency	Folic acid (in ng/ml)	Observed frequency
<200pg/ml	7	<2ng/ml	3
200-500pg/ml	22	2-8ng/ml	8
500-700pg/ml	8	8-15ng/ml	18
700-900pg/ml	2	15-20ng/ml	11
>900pg/ml	1	>20ng/ml	0
Total	40		40

Table 3 clearly shows that out of the 41 cases with normocytic normochromic blood picture, only 10 had subnormal levels of either Vit B12 or folic acid values. Rest of the 30 cases had normal Vit B12 and folic acid levels. So we can come to the conclusion that out of the 100 cases with hypersegmented neutrophils in peripheral smear 31% cases were having pure microcytic hypochromic anemia without any vit B12 or folic acid deficiency.

Table 4: Correlation of neutrophil hypersegmentation and platelet count

Platelet count	Macro cytic anemia	Microcytic hypochromic Picture (Normal B12 and folic acid)	Microcytic hypochromic Picture (subnormal B12 and	Myelodysplasia	Normocytic Normochromic Blood picture

			folic acid)		
<1.5 lakh/microlitre	1	0	0	2	0
1.5-4.5 lakh/microlitre	40	12	9	3	9
>4.5lakh/micro litre	4	18	1	0	1
Total	45	30	10	5	10

1.5-4.5 lakh/microliter is considered as normal platelet count. Out of the 100 cases, only 3 had thrombocytopenia.73 cases had platelet count in the normal range. 25 cases had thrombocytosis. Out of the 30 cases with microcytic hypochromic anemia and neutrophil hypersegmentation, 18 cases had thrombocytosis. In all other cases majority were in normal range group.

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. [14]

In this study of 100 cases with peripheral smears, showed that there was many causes for neutrophil hypersegmentation other than already established macrocytic anemia. Microcytic hypochromic anemia, melodysplastic syndrome and normocytic normochromic blood picture show neutrophil hypersegmentation in peripheral smear. Deficiency of or failure to utilize cobalamin or folate and impaired DNA synthesis is the accepted mechanism for the morphological changes seen in megaloblastosis. [7,12]

The underlying mechanism of neutrophil hypersegmentation in microcytic hypochromic anemia is not fully understood. There are several studies explaining this as undetected Vit B12 and folic acid deficiency. 4,5 But that is unlikely as 31% cases of NH were pure microcytic hypochromic anemia without Vit B12 and folic acid deficiency. As per previus studies which excluded underlying Vit B12 and folic acid deficiency there are significant association between iron deficiency (presenting as microcytic hypochromic anemia) and neutrophil hypersegmentaion.7 Some other studies shows that iron deficiency can affect the folate dependant degradation of Figlu catalysed by enzyme Figlu transferase. [15,16]

In our study 22 cases showed neutrophil toxic granules along with hypersegmentation.18 cases showed vacuoles also. Both toxic granules and vacuoles are known to be the response to infection, inflammation and stress. [17] The presence of toxic granules and vacuoles along with hypersegmentation in our study also point towards the appearance of hypersegmentation as a part of inflammation.

3 cases in our study were diagnosed as myelodysplastic syndromes. There are several earlier studies demonsrating that neutrophil hypersegmentation can be seen as a part of myelodysplasia. [18,19] One case of myelodysplastic syndrome in this study showed hypolobated neutrophil along with hyper segmented neutrophils. [20]

In the present study out of the 25 cases having thrombocytosis (>4.5lakhs/ml), 18 cases are having microcytic hypochromic anemia with normal vit B12 and folic acid values. But further detailed studies are to be done to know whether there is any

association between neutrophil hypersegmentation and thrombocytosis.

Conclusion

The present study indicated 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. Early diagnosis and treatment can prevent complications; reduce mortality and morbidity especially in reversible conditions such as megaloblastic anemia. Hence further studies are recommended to be undertaken for developing diagnostic algorithms for assessing patients presenting with pancytopenia and for further treatment modalities.

References

1. Kar M, Ghosh A. Pancytopenia Journal, Indian Academy of Clinical Medicine 2002;3:29-341.
2. Ishtiaq O, Baqai HZ, Anwer F, Hussai 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. Acquired and inherited aplastic anemia syndromes. Wintrobe's Clinical Hematology. 2004:1396-419.
4. Tilak V, Jain R. Pancytopenia- A clinic-hematologic analysis of 77 cases. Indian journal of pathology & microbiology. 1999 Oct 1;42(4):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. Makheja KD, Maheshwari BK, Arain S, Kumar S, Kumari S. The common causes leading to pancytopenia in patients presenting to tertiary care hospital. Pakistan journal of medical sciences. 2013 Sep;29(5):1108.
9. Ishtiaq O, Baqai HZ, Anwer F, et al. Patterns of pancytopenia patients in a general medical ward and a proposed diagnostic approach. J Ayub Med Coll Abbottabad, 2004; 16(1): 8-13.
10. Imbert M, Scoazec JY, Mary JY, Jouzult H, Rochant H, Sultan C. Adult patients presenting with pancytopenia: a reappraisal of underlying pathology and diagnostic procedures in 213 cases. Hematol Pathol., 1989; 3(4): 159–67.
11. Herbert V. Nutrition science as a continually unfolding story: the folate and vitamin B12 paradigm. Am J Clin Nut. 1987;46(3):387–402.
12. Agarwal KN. Indicators for assessment of anaemia and iron deficiency in community. Pediatr Oncall J. 2010; 7(2):29–34.
13. Steensma DP. Myelodysplastic syndromes: diagnosis and treatment. Mayo Clin Proc. 2015;90(7):969–83.
14. Chanarin I, Metz J. Diagnosis of cobalamine deficiency: the old and new. Br J Haematology 1997; 97(4): 695-700.
15. Chanarin I, Bennett MC, Berry V. Urinary excretion of histidine derivative in megaloblastic anemia and other conditions in comparison with the folic acid clearance test. J Clin Pathol. 1962;15(3):269–73.
16. Vitale JJ, Restrepo A, Riker JB, Hellerstin EE. Secondary folate deficiency induced in rat by dietary iron deficiency. J Nutr. 1966;88(3):31 5–22.
17. Manonneaux S. Nonmalignant leukocyte disorders. In: Rodaks hematology clinical applications and

principals. St. Louis, Missouri: Saunders; 2015: 475–97.
18. Yoshida Y. Physical Education. Myelodysplastic syndrome. Oncologist. 1996;1(4):284–7.
19. Abramson SD, Abramson N. Common' uncommon anemias. Am Fam Physician. 1999;59(4):851–8.
20. Gallouo M., Tsikambu A. C. D., Alafifi M., Alafifi R., Boucbhareb E. M., Benghanem M., Moataz A., Dakir M., Debbagh A., & Aboutaieb R. Anuria: Causes and Management in Casablanca. Journal of Medical Research and Health Sciences. 2022; 5(5): 1986–1993.