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Vitamin B12 Deficiency Presenting as Hemolytic Anemia: A rare hematological finding

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ABSTRACT

Introduction: Co-existent hemolysis in patients with vitamin B12 deficiency is a rare presentation. Hemolysis in megaloblastic anemia was due to intramedullary destruction of RBCs (ineffective erythropoiesis). However some studies stated that Homocysteine is responsible for hemolysis in Vitamin B12 deficiency patients while its mechanisms are still not clear, so it is difficult to diagnosed clinically.

Material and methods: It is a two years retrospective study on 20 patients of Megaloblastic anemia with hemolysis were taken as cases and 20 cases of megaloblastic anemia without hemolysis were taken as control. Complete blood picture, peripheral smear finding(schistocyte count (expressed in percentage), nucleated RBCs), Bone marrow findings, along with biochemical investigations (vitamin B12, folic acid, serum LDH, bilirubin, Homocysteine) were done.

Result: Hemoglobin (Hb) values (gm/dl) in Megaloblastic anemia with hemolysis and without hemolysis were 5.34 ± 1.6 and 6.20 ± 2. Though mean total leucocyte count and total platelet count were within normal range in both these groups but some of the patients presented with leucopenia and thrombocytopenia. Reticulocyte count was increased i.e. 3.50 ± 1.2 in hemolysis group compared to control group where mean reticulocyte count was 1.02 ± 0.44. Schistocytes count is very much increased in hemolysis group. i.e 6.20 ± 3.14 and it was 1 ± 0.4 in control group. Homocysteine level was more increased in cobalamin deficiency with hemolysis i.e. 32.22 ± 12 as compared to control group where Homocysteine level was 25.15 ± 15. Indirect bilirubin was also increased in hemolytic cases. LDH level was slightly increase in cases where as it is normal in control groups.

Conclusion: In Vitamin B12 defeciency due to Cobalamine deficiency causes anemia,leucopenia,thrombocytopenia, pancytopenia as well as hemolytic blood picture.In Our study we found that there is a link between vitamin B12 and plasma homocysteine level. Both Bone marrow finding and Peripheral smear findings showed hemolysis and pancytopenia as well as hyperhomocysteinemia and were corrected by cobalamin treatments. So we can say that high homocysteine level may be an important factor which causes further hemolysis often seen in cobalamin deficiency.

Keywords: Megaloblastic Anemia,hemolysis, Hyperhomocystinemia

INTRODUCTION

Vitamin B12 deficiency producing severe complications, with reduces all the three cell lineages and causes pancytopenia, megaloblastic anemia and hemolysis [1]. Vitamin B12 deficiency is more commonly in elderly patients and young children but sometimes it is not recognized or not investigated because of lack of specific clinical findings. However serious clinical and hematological conditions need investigations of patients of vitamin B12 deficiency. Previously Vitamin B12 deficiency was diagnosed by presence of macro-ovalocytes, hyper segmented neutrophils in peripheral blood smear and progressive increase in mean corpuscular volume. But due to introduction of automated analyser for measuring serum levels of cobalamin and homocysteine made the diagnosis easier. Hematological outcomes of Vitamin B12 deficiency can be sever.10% of patients had suffered from life threatening conditions like symptomatic pancytopenia, hemolytic anemia and pseudo thrombotic microangiopathy[2, 3]. Hemolytic picture seen in patients with B12 deficiency is due to intramedullary destruction but various studies stated that increased hemolysis occurs due to increases level of homocystein in vitamin B12 deficiency.

II. Material & Methods

It is a retrospective study and was conducted in department of pathology

M.G.M. Medical College & M.Y. Hospital Indore from june 2017 to july 2019 over a period of 2 years. Total 40 cases have been studied and the study group was divided into two groups,i.e Megaloblastic anemia patients without hemolytic blood picture and megaloblastic anemia with hemolytic blood picture. Other conditions showing hemolysis were excluded from the study. Detailed clinical history from each patient was obtained and recorded. A presumptive diagnosis was made and subjected for different hematological investigations. All the hematological parameters (Hemoglobin, hematocrit, MCV, MCH, MCHC, RDW, WBC count, Platelet count) and biochemical parameters (vitamin B12, folic acid, serum LDH, bilirubin, Homocysteine) were studied from the records. The peripheral blood smear examination (, red cell morphology alteration, macrocytosis, anisopoikilocytosis, schistocytes, polychromasia, nucleated RBC, WBC morphology alteration and platelet morphology) were done by already prepared slides stained with field stain. Supravital stain was done and reticulocyte was counted. Bone marrow examination done by already prepared slides.

III. Results and Observations

20 cases of vitamin B12 deficiency with hemolytic blood picture were included in our study and 20 consecutive cases of Vitamin B12 deficiency without hemolytic blood picture were taken as control. Features of hemolysis was considered in terms of either increase LDH, increase indirect bilirubin or presence of schistocytes, nucleated RBCs, normocytic & polychromatic cells in peripheral blood smear. Various hematological and biochemical parameters of the cases were seen and compared with the control groups. Hemoglobin (Hb) values in Megaloblastic anemia with hemolysis were 5.34 ± 1.6 and those in control group were 6.20 ± 2. Though mean total leucocyte count and total platelet count were within normal range in both these groups but some of the patients presented with leucopenia and thrombocytopenia. Reticulocyte count was increased i.e. 3.50 ± 1.2 in hemolysis group compared to control group where mean reticulocyte count was 1.02 ± 0.44. Schistocytes count is very much increased in hemolysis group. i.e 6.20 ± 3.14 and it was 1 ± 0.4 in control group.(Table-1).

Table 1: Various hematological parameters among control and cases

Hematological Parameters	Megaloblstic anemia with hemolysis (cases)(N = 20) (Mean ± SD)	Megaloblastic anemia without hemolysis control (N = 20) (Mean ± SD)
Hemoglobin	5.34±1.6	6.20±2
Total Leukocyte count	5032.2± 2114.61	4062±1342.25
Total platelate count	98670 ± 53763	112310± 50711.25
Reticulocyte count	3.50±1.2	1.02±0.44
Schistocytes	6.20±3.14	1±0.4

Vitamin B12 level was decreased in both the groups (80.2± 30.2 in cases and 90.3 ± 71.2 in control group). Homocysteine level was more increased in cobalamin deficiency with hemolysis i.e. 32.22 ± 12 as compared to control group where Homocysteine level was 25.15 ± 15. Indirect bilirubin was also increased in hemolytic cases. LDH level was slightly increase in cases where as it is normal in control groups.(Table-2)

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Table 2: Various biochemical parameters among control and cases

Biochemical Parameters	Megaloblstic anemia with hemolysis (cases)(N = 20) (Mean ± SD)	Megaloblastic anemia without hemolysis control (N = 20) (Mean ± SD)
LDH	340.33 ± 120.23	230.11±109.12
Total Bilirubin	1.12 ± 0.53	1.13±0.35
Vitamin B12	83.40 ± 40.43	91.43±78.21
Homocysteine	32.22±12	25.15±15
Folic acid	4.44± 4.10	5.02±5.71

Bone Marrow Findings –

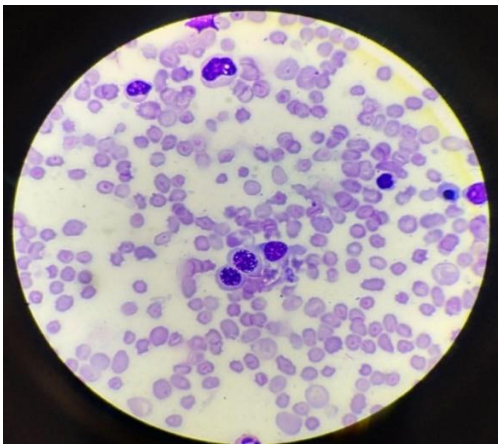

Figure 1 – Megaloerythroblasts

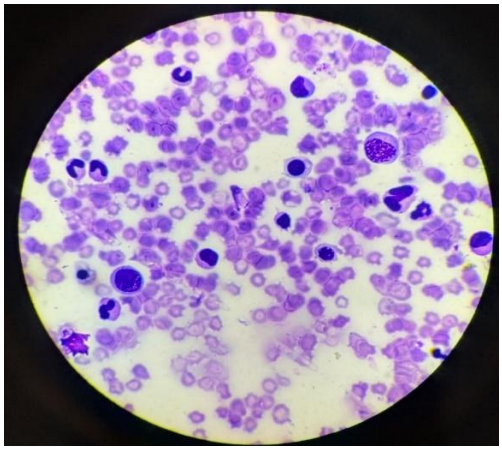

Figure 2 – Giant metamyelocyte

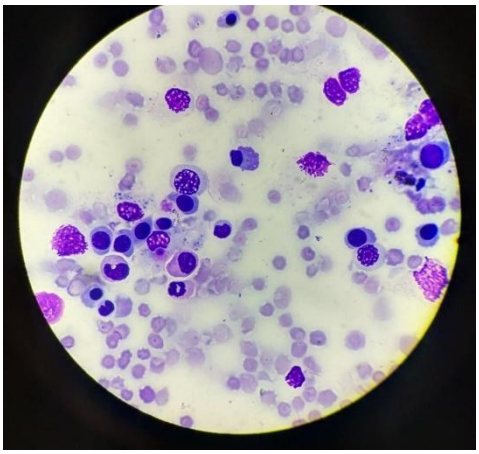

Figure 3 – Megaloerythroblasts with open sieve like nuclear chromatin and Hypersegmented neutrophil, increased histiocytes with Iron pigment

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Peripheral Smear finding –

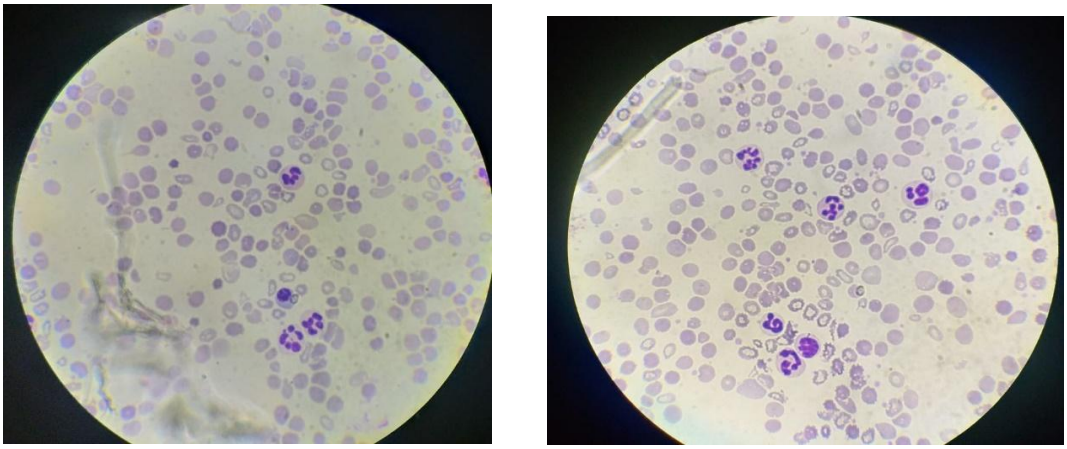

Figure 4 – show hypersegmented neutrophils with macrocytic picture and Nucleated RBCs

IV.Discussion

This study done in patients with well documented Vitamin B12 deficiency. All the patients in our study fulfilled the criteria of B12 deficiency (i.e. serum vitamin B12 levels <200pg/ml). This study shows that almost all patients with B12 deficiency have some degree of hematological manifestation in the form of anemia,leucopenia thrombocytopenia. In our study reticulocyte Hematological Findings in Cobalamin Deficiency count was increased i.e. 3.50 ± 1.2 in hemolysis group compared to control group where mean reticulocyte count was 1.02 ± 0.44. Indirect bilirubin and LDH level were also increased in hemolytic cases, where as it is normal in control groups. It indicates that intramedullary hemolysis is occuring in hemolytic groups. Schistocytes count is very much increased in hemolysis group. i.e 6.20 ± 3.14 and it was 1 ± 0.4 in control group. Homocysteine level was also more increased in cobalamin deficiency with hemolysis i.e. 32.22 ± 12 as compared to control group where Homocysteine level was 25.15 ± 15.So it clearly indicates that increase homocysteine level might causing intravascular hemolysis and in turn producing more scistocytes in the peripheral blood.Secondly normalisation of schistocytes count occurs after giving cobalamine treatment. Though the mechanism is not clearly understood but hemolysis in patients with cobalamin deficiency is a well-recognized phenomenon. It is assumed that hemolysis in Vitamin B12 diet is due to intramedullary hemolysis In our study both features of intramedullary destruction and extravascular hemolysis were evident and both hemolysis and pancytopenia as well as hyperhomocysteinemia were corrected by cobalamin treatments. So we hypothesize that high homocysteine level may be an important contributor leading to further hemolysis which is often seen in cobalamin deficiency. **3.1** Homocysteine has been proposed as a hemolytic toxin. (4,5) However, the exact mechanism of hemolytic effects of homocysteine is not clear. (6,7) It is assumed that high homocysteine level leads to endothelial damage with ensuring microangiopathy causing hemolysis. Evidences suggest that hyperhomocysteinemia is associated with thrombosis (6,7,) and endothelial damage or dysfunction. (7,8) The prooxidant effects of homocysteine were presumed as the likely of endothelial damage. Elevated homocysteine levels have been described in literature as a possible etiology for both intravascular and intramedullary hemolysis with the role of homocysteine in increasing the risk of hemolysis in vitamin B12 deficiency being demonstrated in vitro (9)

V. Conclusion

Hemolysis in cobalamin deficiency is though a rare presentation but requires high clinical suspicion for early diagnosis and treatment. So in any case of hemolytic blood picture focus should be given for presence of macroovalocytes and hypersegmented neutrophils to rule out more common Megaloblastic anemia.

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