Prevalence of Haemolysis in Peripheral Blood Smear in Cases of Megaloblastic Anemia

Dear Editor,

Megaloblastic anaemia is characterised by inadequate synthesis of normal amount of DNA and formation of megaloblasts in bone marrow. The anaemia is due to the maturational derangements with an accumulation of megaloblasts in the bone marrow, yielding very few erythrocytes. Two concomitant processes further aggravate the anaemia (i) ineffective erythropoiesis, (ii) increased haemolytic destruction of red blood cells. Intramuscular haemolysis is also encountered. Even a poorly characterised plasma factor is believed to contribute to haemolysis [1]. Ineffective erythropoiesis in megaloblastic anaemia has been quantitated using incorporation of [¹⁵N]delta aminolaevulinic acid and [¹⁵N]glycine into early-labelled bilirubin [2]. Megaloblastic changes are not limited to the erythroid precursors, but are also seen in myeloid precursors and megakaryocytes.

We conducted a study to find out prevalence of haemolysis in peripheral blood in cases of megaloblastic anaemia diagnosed in bone marrow aspirate examination. A retrospective study was carried out on 104 bone marrow aspirates examined in a large zonal hospital in 2 years. Out of 104 bone marrow aspirates 26 showed megaloblastic changes and of these 12 showed evidence of haemolysis (46.1%). The features of haemolysis, presence of thrombocytopenia, leucopenia and unconjugated hyperbilirubinemia were studied. All cases showing haemolytic peripheral blood picture were further tested with direct/indirect coombs test, lactate dehydrogenase levels, G6PD deficiency assay, osmotic fragility test and sickling test, to rule out other causes of haemolysis.

In our study the mean age of patients (n=26) was 39.7 years, of which 30.7% cases were less than 20 years of age. 65.3% of patients were male and 61.5% strict vegetarians. Indian study done by Sarode et al [3] showed the peak of megaloblastic anaemias in second and third decades. In their study 56.6% cases were strict vegetarians that is statistically not different from our study. In the present study six cases having nucleated red blood cells had blood haemoglobin between 3.9-6.9 gm/dl. The packed cell volume ranged between 12 to 23 %. It is a known fact that when the nucleated RBC's are seen in peripheral blood smear of megaloblastic anaemia, the grade of anaemia is severe [4]. 34.6% of cases in our study showed polychromasia, 23% showed increased nucleated RBC's, 81% cases showed marked anisopoikilocytosis and 27% cases showed significant number of broken RBC as markers of haemolysis. None of the cases showed a lactate dehydrogenase value above 600 IU/L, negating the presence of active haemolysis in these cases. No other cause of haemolysis was detected in any of 12 cases by conducting various tests viz. coombs, osmotic fragility etc.

Thrombocytopenia was seen in 73%, leucopenia in 7.6% and unconjugated hyperbilirubinemia in 38.4% cases. There is an accumulation of unconjugated bilirubin in plasma due to death by apoptosis of nucleated red blood cells. Our study showed only 1 out of 10 cases of haemolysis (10%) showing positive reticulocyte response indicating again ineffective erythropoiesis.

The recent in vitro studies discuss the possibility of Vitamin B12 and folate deficiencies causing megaloblastic anaemia simultaneously inducing a significant alteration in homocysteine metabolism leading to hyperhomocysteinemia. Considering the possible effects of hyperhomocysteinemia in erythrocyte toxicity (due to oxidative damage and/or to interaction with sulfhydryl residues of structural and enzymatic proteins) it can be construed that this metabolite leads to haemolysis [5].

To conclude haemolytic peripheral blood picture can be encountered in cases of megaloblastic anaemia, which is explained by ineffective erythropoiesis. This is due to intramedullary destruction of megaloblasts, which undergo autohaemolysis and faster phagocytosis than normal erythroid precursors. Premature destruction of other lines lead to leucopenia and thrombocytopenia.

References

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