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Role Of Complete Blood Count In Analysis Of Macrocytosis In Adult Patient

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Abstract: ***The term macrocytosis describes the presence of macrocytes on a blood film, together with a raised mean corpuscular volume (MCV>100 fl). It is a common finding in the complete blood count(CBC) and may or may not be associated with anaemia. The aim of the study was to identify the underlying cause of macrocytosis and to analyze the haematological features of macrocytosis in routine complete blood count(CBC) and peripheral blood smear in different etiopathological factors.***

This study was carried out in 140 adult patients whose complete blood count and peripheral smear examination, serum vitamin B12 assay, folic acid assay, thyroid, liver and kidney function tests were done along with detailed medical history. In this study group, alcoholism (39.3%) was found to be the common causative factor of macrocytosis, followed by Vitamin B12 deficiency (27.6%) and medication(11.7%). In 26 patients, underlying cause of macrocytosis could not be ruled out. Anaemia was present in 70 cases (58.3%), being most common in Vitamin B12 deficiency. Hypersegmented neutrophils and macro-ovalocytes in peripheral blood film were found predominantly in megaloblastic disease. Macrocytosis needs to be evaluated even in the absence of anemia, as it may be the first clue to an underlying pathology. A detail evaluation of routine complete blood count (CBC) and peripheral blood smear greatly helps in identifying the underlying etiology for macrocytosis.

Keywords: Complete blood count (CBC), Macrocytosis, Mean Corpuscular Volume (MCV), Megaloblastic Anaemia, Peripheral Blood Smear.

I. INTRODUCTION

The term macrocytosis refers to a blood condition in which red blood cells (RBC) are larger than normal. Macrocytosis is reported in terms of mean corpuscular volume (MCV) more than 100 femtoliters (fl).[1,2] Normal MCV values range from 80 to 100 fl and vary by age and reference laboratory.[3] Macrocytosis can be identified by viewing peripheral blood smears and/or by automated red cell parameters. The peripheral blood smear is more sensitive than red cell parameters for identifying early macrocytic changes because the MCV represents the mean of the distribution curve and is insensitive to the presence of small numbers of macrocytosis.[4]The prevalence of macrocytosis in general population varies bewteen 1.7% and 3.6%. [5, 6]

Physiological macrocytosis is seen in pregnancy, newborns, infants and even sometimes as a normal variant in genetically predisposed individuals . Cold agglutinins, hyperglycemia, marked leukocytosis, reticulocytosis and delayed sample processing can result in false elevation of

MCV. [1, 6] Even in the absence of anemia, macrocytosis needs to be evaluated, as it may be the only clue to an underlying pathological condition.

The aim of the study was to identify the underlying cause of macrocytosis and to analyze the haematological features of macrocytosis in routine complete blood count(CBC) and peripheral blood smear in different etiopathological factors.

II. MATERIALS AND METHODS

This study was conducted in our Institut between January 2013 to February 2014. The study included 140 adult patients with MCV >100 fl. Newborn, children, pregnant women, and other cases of spurious macrocytosis were excluded from the study.

In all patients, a complete medical history including diet, medication and alcohol intake was recorded. A Complete blood count and peripheral blood smear examination was carried out in all cases. The patients were subjected to serum Vitamin B12 assay, serum folic acid assay, thyroid, liver and kidney function tests. Bone marrow aspiration was done only when clinically indicated.

Patients with Hb <11.6 g/dl (female) and Hb <13.2 g/dl (male) were classified as anemic macrocytosis. [7] Serum Vitamin B12 level <150 pmol/l (203 pg/ml) and serum folic acid level <10 nmol/l (4 ng/ml) were defined as deficiency state.[8] After identifying etiological factors , cases were categorised into megaloblastic and nonmegaloblastic groups. Complete blood count parameters and peripheral smear findings were evaluated in details and compared between these two groups

III. RESULTS

Out of 120 patients evaluated, underlying pathological factor could be identified in 94 cases (78.3%) as shown in
[Table 1]. In this study, alcoholism was the most common cause of macrocytosis found in 37 cases (39.3%), followed by Vitamin B12 deficiency identified in 26 cases (27.6%). Drug induced macrocytosis was seen in 11 patients (11.7%) and commonly encountered drugs were reverse transcriptase inhibitors (stavudine ,lamivudine ,zidovudine), chemotherapeutic agents(alkylating agents, pyrimidine, purine inhibitors) and anticonvulsants (valproic acid, phenytoin) . The other identified causes were liver disease, hypothyroidism, chronic renal failure on hemodialysis, myelodysplastic syndrome and aplastic anemia. In 26 patients, underlying cause of macrocytosis could not be ruled out.

Table 1: Various etiological factors identified in macrocytosis

Etiological factor	**No of cases (%)**
Alcoholism	37 (39.3%)
Vitamin B12 deficiency	26 ((27.6%)
Drug induced	11 (11.7%)
Folate deficiency	7 (7.4%)
Chronic liver disease	5 (5.3%)
Hypothyroidism	1 (1.0%)
Chronic renal failure(Hemodialysis)	4 (4.2%)
Myelodysplastic syndrome	1 (1.0%)
Aplastic anemia	2 (2.1%)
Unexplained	26 (21.6%)

Anaemia was present in 70 cases (58.3%) and remaining 50 cases (41.6%) had isolated macrocytosis without anemia [Fig 1]. Anemia was found in 75.7% (25 cases) of Vitamin B12/folate deficiency patients, while only 37.8% (14 cases) were anemic in alcoholism

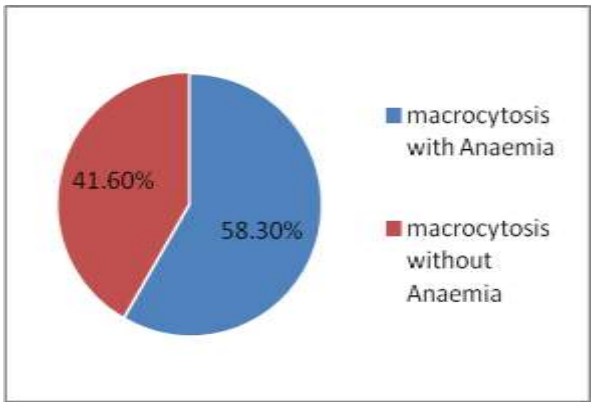

Figure 1 Prevalence of anemia in macrocytosis**.**

Bone marrow evaluation was done 25 cases of which 14 cases revealed megaloblastic marrow changes, 8 cases appeared normoblastic marrow, 2 cases revealed hypoplastic marrow and 1 case showed dysplastic changes. Based on haematological parameters and bone marrow evaluation, 26 cases of Vitamin B12/folate deficiency were categorized as megaloblastic macrocytosis and 34 cases of alcoholism, 7 cases of drug toxicity, and 4 cases from liver disease were categorized as (total 45 cases) non-megaloblastic(normoblastic) macrocytosis. Haematological parameters [Table2] and peripheral blood smear findings [Fig 2&3] were documented and compared between megaloblastic and non-megaloblastic(normoblastic) macrocytosis. The mean MCV was higher in megaloblastic group (119.2fl) in compare to alcoholism(106.8 fl). The mean RDW was significantly higher in the megaloblastic cases(22.1%) than normoblastic group(14.2%). Peripheral smear revealed hypersegmented neutrophils and macro-ovalocytes mostly in megaloblastic group. In non-megaloblastic cases, uniform round macrocytes noted with normal RDW.

Table 2: Red cell parameters in megaloblastic and non-megaloblastic macrocytosis

Parameters	**Megaloblastic category (26 cases)**	**Nonmegaloblastic category (45cases)**
Hb (g/dl)	7.9 (2.6–13.8)	12.3 (9.1–15.7)
MCV (fl)	119.2 (107.4–148.3)	102.8 (101.2–110.6)
MCH (pg)	36.0 (30.9–47.2)	34.1 (28.7–40.7)
MCHC	34.1(32.0–41.2)	32.9(32.5–39.8)
HCT(%)	20.6(6.8–41.4)	35.9(25.7–49.0)
RDW-CV %	22.1 (14.7–43.4)	14.2 (12.9–29.4)
Red cell count × 10^6/ ul	2.04 (1.10–4.51)	3.90 (3.40–5.56)
Total leukocyte count × 10^3/ ul	4.93 (1.2–10.4)	7.84 (3.1–14.5)
Platelet count × 10^3/ ul	174 (10–514)	234 (80–608)

Mean values are presented along with the range in brackets.

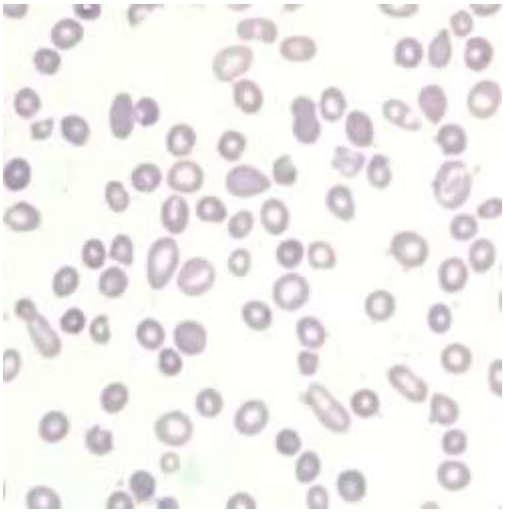

Figure 2 photomicroghaph of peripheral blood smear showing macro-ovalocytes and anisopoikilocytosis in a case of vitamin B12 deficiency.

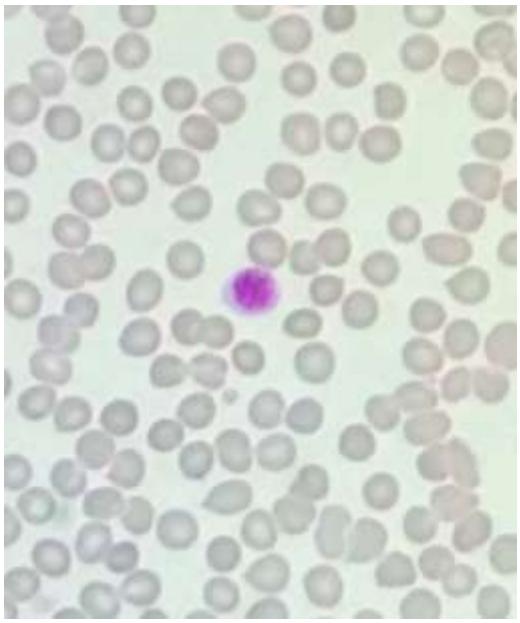

Figure 3 photomicroghaph of peripheral blood smear showing uniform round macrocytes in a alcoholic patient.

IV DISCUSSION

Macrocytosis is frequently encountered when a complete blood count is performed. It's significance tends to be underestimated by physicians, since about 60% of patients present without associated anemia.[9]

The underlying pathogenesis of macrocytosis are diverse and complex. In Vitamin B12/folate deficiencies, there is a defect involving nuclear maturation, which affects cell division. Hemoglobin synthesis proceeds normally, while nuclear division lags behind, thereby resulting in larger than normal red cells. Macrocytosis in alcoholism is related to the direct toxic effect of alcohol on the red cell membrane.[1] In myelodysplastic syndrome, macrocytosis results from the dysplastic changes in the erythroid precursors.[10] Reverse transcriptase inhibitors interfere with DNA production, thereby resulting in megaloblastic changes and macrocytosis.[1,6]

Many authors have reported medication and alcohol abuse as the most frequent cause of macrocytosis.[11,12,13] Breedveld et al.[14] ,P Veda[15] and Seppa et al.[2] have reported Vitamin deficiency and alcoholism as the most frequent etiological factors, which is similar to the findings of our present study. We observed macrocytosis with anemia in (58.3%) cases and without anemia in (41.6%) cases. Alcoholism was commonly associated with nonanemic macrocytosis. Another significant observation in our study is that 7 cases of Vitamin B12 deficiency had isolated macrocytosis which emphasizes the fact that macrocytes can be an early diagnostic harbinger.

The mean red cell distribution width (RDW) was significantly higher in megaloblastic conditions when compared to normoblastic conditions in present study which were similar to the observations made by Gupta et al [16] and Seppa et al.[2] The average value of MCV can masked by co-existing microcytic anemia,[17] therefore the peripheral blood smear examination is an essential to evaluate macrocytosis. In alcoholism, MCV ranges between 100-110 fl whereas in Vitamin B12/ folate deficiency it is much higher [5]. We noted almost similar findings in our study. Macro-ovalocytes and hypersegmented neutrophils are predominantly seen in megaloblastic conditions and is usually associated with increased RDW [6,18]. In non- megaloblastic

conditions uniform macrocytes are seen with normal RDW [1,17,19]. In this present study, Macro-ovalocytes and hypersegmented neutrophils were seen in megaloblastic group and uniform round macrocytes were observed in non megaloblastic group.

An elevated MCV is a useful parameter to assess macrocytosis which directs the further investigations and ultimately leads to a definite diagnosis [13]. Unexplained macrocytosis in elderly patients could be an early indicator of malignancy or MDS [13,20]. Therefore, a close attention has to be given while evaluating MCV.

V. CONCLUSION

The most common causes of macrocytosis are alcoholism, Vitamin B12 deficiency and medications. High MCV needs to be thoroughly investigated even in the absence of anemia, as it may be the early indicator of underlying disease state. In a resource constraint set-up, a complete blood count(CBC) and peripheral blood smear examination is a simple, inexpensive and valuable tool in evaluating macrocytosis along with the detail medical history and guide the further management.

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