

Research Article**Spurious Macrocytosis- Automated Cell Counters are Not Fool-Proof****M. C. Savithri, K. P. Kavitha**

Department of Pathology, Amala Institute of Medical Sciences, Amalanagar, Thrissur, Kerala, PIN-680555, India

***Corresponding author**

Dr. M. C. Savithri

Email: savithrimc@yahoo.co.in

Abstract: With increasing use of electronic hematology cell counters macrocytosis is often encountered. Various etiological factors contribute to the development of macrocytosis. This study is from Kerala State, India and is a retrospective analysis of cases of spurious macrocytosis which can occur with cell counters. The aim of the study was to find out retrospectively the prevalence and causes of spurious macrocytosis among cases sent for peripheral smear evaluation over a 30 month period. Macrocytosis was defined as MCV value more than 97 fl. Blood samples with MCV higher than 97 fl which were received in the Department of Pathology, Amala Institute of Medical Sciences, Thrissur, Kerala State, India for peripheral smear examination were selected for this study spanning a period of 30 months. There were 137 cases of macrocytosis detected by analyzers. From them those cases in which peripheral smear examination revealed no macrocytosis were selected. Among the 137 cases of macrocytosis 12 cases showed no macrocytosis in the blood smears. The causes we found were multiple myeloma (MM) which comprised 8 cases and 2 cases of hyperglycemia. Spurious macrocytosis is occasionally encountered with increased use of electronic hematology cell counters which can be due to many different reasons. It is important to be aware of this potential pitfall while evaluating hemograms.

Keywords: Macrocytosis, Automated cell counters, Spurious macrocytosis.

INTRODUCTION

Automated hematology cell counters are being increasingly used in routine laboratory practice. They provide results with good accuracy and precision. They are quick and easy to use and considerably reduces manpower. Macrocytosis is encountered frequently during medical practice.

Macrocytosis may be defined as Mean Corpuscular Volume (MCV) above 97 fl [1]. With increasing use of Electronic cell counters more cases are detected early and a new category –spurious macrocytosis has also come into being. Paraproteins, cold agglutinins and hyperglycemia are some conditions which can lead to false elevations in electronic MCV values.

Aims

To find out retrospectively the prevalence and causes of spurious macrocytosis among cases sent for peripheral smear evaluation over a 30 month period.

MATERIALS AND METHODS

This is a retrospective study. Macrocytosis was defined as MCV value more than 97 fl. Blood samples with MCV higher than 97 fl which were received in the Department of Pathology, Amala Institute of Medical Sciences, Thrissur, Kerala State, India for peripheral

smear examination were selected for this study spanning a period of 30 months, from April 2010 to end of September 2012. RBC indices were obtained using using 5 part automated hematology cell counter which was regularly calibrated and maintained.

There were 137 cases of macrocytosis detected by analyzers. From them those cases in which peripheral smear examination revealed no macrocytosis were selected. Case histories, physical examination findings and details of relevant investigations were retrieved from Medical Records Section.

RESULTS

Among the 137 cases of macrocytosis 12 cases showed no macrocytosis in the blood smears (Fig. 1).

The causes we found were multiple myeloma (MM) which comprised 8 cases and 2 cases of hyperglycemia (Fig. 2).

All cases of MM had anemia with hemoglobin values ranging between 2.6g/dl and 7.5g/dl. Both cases of hyperglycemia had normal hemoglobin.

The lowest MCV in cases of MM was 97.2fl and the highest value was 112fl. Cases of

hyperglycemia showed only borderline elevation – 97.7 and 97.5 fl.

Red cell distribution width (RDW) was normal in cases of hyperglycemia whereas all cases of MM showed raised RDW.

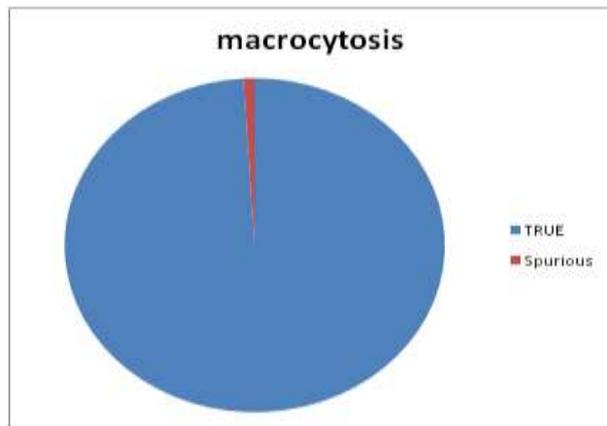


Fig. 1: Macrocytosis

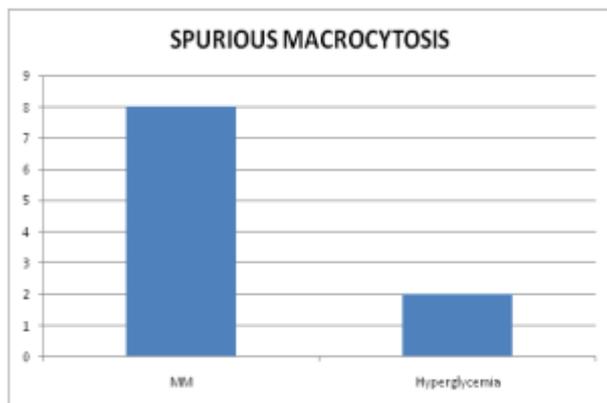


Fig. 2: Spurious macrocytosis

DISCUSSION

Modern day automated cell counters are highly sophisticated and give satisfactory performance in majority of parameters like total white cell count (TWC), hemoglobin, RBC count and MCV [2]. As the dependence on electronic hematology cell counters increases, more cases with raised MCV are being encountered. Various etiological factors contribute to the development of macrocytosis. The patient may or may not be anemic. Causes of macrocytosis include megaloblastic anemia which may be due to nutritional deficiency of vitamin B12 and folate or due to non nutritional causes like antifolate therapy. Other causes are non megaloblastic macrocytosis and spurious macrocytosis.

A significant subcategory is spurious or false macrocytosis and is a byproduct of the electronic era. This forms a small group but awareness is important in the evaluation of patients. Severe hyperglycemia, leukocytosis, cold agglutinins and presence of a paraprotein as in multiple myeloma can lead to artifacts

of electronic cell sizing [1, 3]. Moreover partial occlusion of instrument aperture, leaving the blood sample at room temperature for several hours and an excess of anticoagulants may also result in false elevations in MCV value [3, 4].

Presence of paraproteins as in monoclonal gammopathy and multiple myeloma can actually cause macrocytosis, but spurious increase in MCV can also occur. In a study from Mayo Clinic on newly diagnosed cases of MM 9% had macrocytosis with MCV more than 100fl of which majority were without identifiable causes [5]. Monoclonal gammopathies can also lead to unexplained macrocytosis [6]. In this study MM was the main cause for false elevation of MCV. Hyperproteinemia may cause RBC aggregation leading to a spuriously high MCV. Another mechanism for an increased MCV in neoplastic diseases such as multiple myeloma is folate deficiency caused by increased folate utilization by the neoplasm leading to a macrocytic anemia. Elevated protein concentration may expand the plasma volume and displace some of the RBCs, thereby reducing the hemoglobin concentration disproportionately to the total RBC mass and exaggerating the anemia [7].

The other cause for spurious macrocytosis was hyperglycemia in the present series. Hyperglycemic blood is more concentrated, the cells swell causing a false macrocytosis [8]. It is suggested that glucose in the cell produces a hyperosmolar state which results in the rapid diffusion of water into the cells in the counter. The phenomenon is dependent on the concentration of glucose to which the red cell is exposed. It is temperature dependent and it is rapidly reversible [9].

Other conditions also can lead to this artifact. Cold agglutinins make RBCs clump, making them appear larger to automatic cell counter. Intermittent macrocytosis which is abolished by warming the sample to 37 degree Celsius reflect cold agglutinin activity without overt hemolysis [10]. Non Hodgkin Lymphomas may be associated with cold agglutinins resulting in spurious macrocytosis [11]. Weiss and Bessman reports two patients with warm autoimmune HA whose MCV values were spuriously high. Red cell size distribution histogram showed doublets and triplets of normal sized red cells similar to cases with cold agglutinins. Since this artifact increases the MCV slightly less than it reduces the red cell count, the hematocrit is falsely low and MCHC is falsely high [11,12]. Since MCHC rarely exceeds 36% it is an important clue to spurious elevation of MCV [13].

Therapy with hydroxyurea can cause macrocytosis by interfering with nucleoprotein synthesis or can cause spurious macrocytosis [14]. Increased turbidity of a sample with marked leukocytosis also can cause the instrument to overestimate the cell size [7].

CONCLUSION

Causes of macrocytosis are varied. Spurious macrocytosis is occasionally encountered with increased use of automated hematology cell counters which can be due to many different reasons. It is important to be aware of this potential pitfall while evaluating hemograms.

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