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RESEARCH ARTICLE

MACROCYTIC ANEMIA: STUDY OF MYELOGRAM IN MILITARY HOSPITAL AVICENNA IN MARRAKECH

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ABSTRACT

Background: Anemia is one of the most common health problems in the primary care setting. Macrocytosis in adults is defined as a red blood cell mean corpuscular volum >95 fL. Macrocytic anemias are generally classified into megaloblastic or non-megaloblastic anemia. **Methods and Material:** Retrospective descriptive study included 290 samples of myelogram received in the Hematology Labortory belonging to patients admitted to the Military hospital of Avicenna in Marrakech, over a period of 42 months (from January 2016 to June 2019), aimed to assess the etiological profile of macrocytic anemia in patients whose bone marrow smears were received in our laboratory. **Results:** Out of 290 myelogram samples, 103 cases of macrocytic anemia were received. The male gender was predominant with a sex-ratio (M/F) at 3,3. The average age was 56.7 years old with extremes ranging from 30 to 90 years. The discovery of macrocytic anemia was fortuitous in 35% of cases. 45% of our population presented anemic syndrom, 12% hemorrhagic syndrome, 8% infectious syndrome. The hemoglobin varyied between 4,7 g/dL and 11,9 g/dL with an average of 7.2 g/dL. The mean corpuscular volume was 107 fL. The bone marrow smear confirmed megaloblastic anemia in 54,3% of cases of macrocytic anemia. **Conclusion:** The diversity and complexity of factors leading to macrocytic anemia preclude a single or uniform method of investigation. The investigative pattern must be tailored to the individual patient, giving importance to the clinical presentation.

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INTRODUCTION

Anemia is one of the most commonly diagnosed conditions by primary care physicians. In 2010, global anemia prevalence was 32.9%, that is more than 2.2 billion people were affected (1). The World Health Organization (WHO) defines anemia as a hemoglobin (Hb) count of less than 13 g/L in men, less than 12 g/L in nonpregnant women, and less than 11 g/L in pregnant women and the elderly. The cause of anemiavaries by age, sex, and geography (1). For differential diagnosis, it is useful to classify the type of anemia based on the red cell indices of Wintrobe (1), which is calculated from red blood cell count, hemoglobin concentration, and hematocrit. The mean corpuscular volume (MCV) is the value of average volume of the red cells calculated by the coulter counter from hematocrit (%) × 10/RBC count (106/µl). Upon determining the MCV various pathologic processes might be thought and few others could be excluded. Normal range of MCV is between 78 femtoliter (fL) and 94 fL.

Macrocytosisis defined as MCV >95 fL and it occurs in approximately 1,7-3,6% of patients seeking for medical care and it is a common finding in any clinical setting (2-4). Macrocytosis often precedes anemia but is notinvestigated, especially if anemia is slight (5,6). The causes of macrocytic anemias aregenerally classified as megaloblastic or non-megaloblastic. Disorders that affect the synthesis of DNA in the precursors of erythrocytes leads to megaloblastic anemia and other disorders through various processes causes non-megaloblastic anemia. The aim of this study was to assess the etiological profile of macrocytic anemiain adult patients whose bone marrow (BM) smears were received in our laboratory.

MATERIALS AND METHODS

This retrospective descriptivestudy included 290 samples of myelogram received in the Hematology Labortory belonging to patients admitted to the Military hospital of Avicenna in Marrakech, over a period of 42 months (from January 2016 to June 2019).

We included myelograms associated to macrocyticanemia identified when peripheral blood (PB) examinationshowed anemia (Hb count less than 13 g/L in men, than 12 g/L in non pregnant women, and than 11 g/L in pregnant women and the elderly), with a MCV>95 fL. Any sample not respecting the pre-analytical phase was excluded. The PB count was performed using the Sysmex XT-4000I analyzer from blood samples collected by venipuncture on EDTA (ethylenediaminetetraacetic acid) tubes. The myelogram was performed by an operator that is aware of the clinical indications. Informed consent was obtained from all patients.PB and BM smears were stained with MGG (May-Grünwald-Giemsa). The BM smear preparation were first viewed under low power magnification (*10) to determine the number and cellularity of particles, the number of megakaryocytes, and to scan for clumps of abnormal cells. Areas of well-spread marrow cells were selected for assessment at higher magnification (i.e.*20, *40, *100) for morphological assessment of cells, including cytological detail.

RESULTS

A total of 290 myelogram samples were received in the Hematology Labortory of the Military hospital of Avicenna in Marrakech, including 103 cases of macrocytic anemia. The male gender was predominant with a sex-ratio (M/F) at 3,3. Majority of the population belong to the age group above 40 years, both in males and females. The average age was 56.7 years oldwith extremes ranging from 30 to 90 years. The majority of myelograms were performed in patients hospitalized mainly in internal medicine department (65%), 25% of requests were received for out-of-hospital patients. The discovery of macrocytic anemia was fortuitous in 35% of cases. 45% of our population presented anemic syndrom, 12% hemorrhagic syndrome, 8% infectious syndrome (Figure 1).

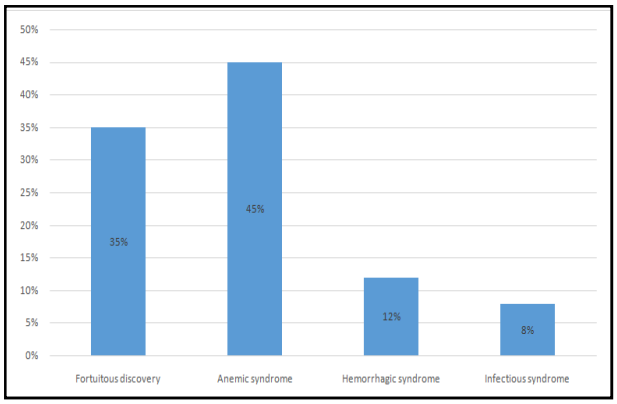

Figure 1. Circumstances of discovery of macrocyticanemia in our population (n=103)

The hematological study showedhemoglobin varying between 4,7 g/dL and 11,9 g/dL with an average of 7.2 g/dL. The meanMCV was 107 fL. 45% of patients had MCV in the 95–105 fl range. The reticulocyte count was less than 120 000 cells/mm3 in 78% showing an aregenrative anemia. Leukopenia, lymphopenia and thrombocytopenia were associated in 37, 44 and 49.4% of cases, respectively (Figure 2). The PB smear examination showed neutrophilic hypersegmantation with macro-ovalocytosis in 52 patients (50,48% of cases) suggesting megaloblastic erythropoiesis.

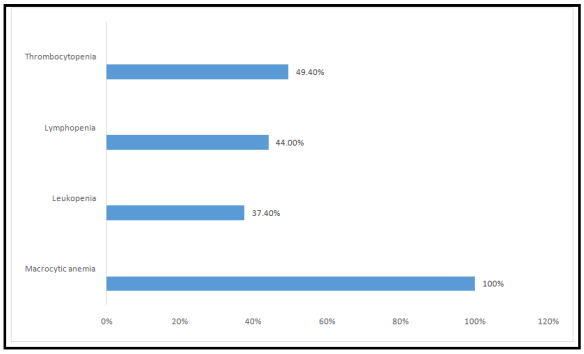

Figure 2. Distribution of PB count abnormalities in our population (n=103)

The BM smear confirmed megaloblastic anemia in 56 patients (54, 3% of cases of macrocytic anemia), showing a very rich marrow appearing ‘’blue’’ in low magnification related to basophilic immature erythroblats called megaloblastscharacterized by a large size and asynchronous nucleo-cytoplasmic maturation. A myelodysplastic syndrome (MDS) was found in 13.6% (14 cases) of which only one secondary case, a reactive marrow in 24,2% (25 cases), a balanced marrow in 3% (3 cases) and leukemia in 2% of all cases (2 cases) (Figure 3)

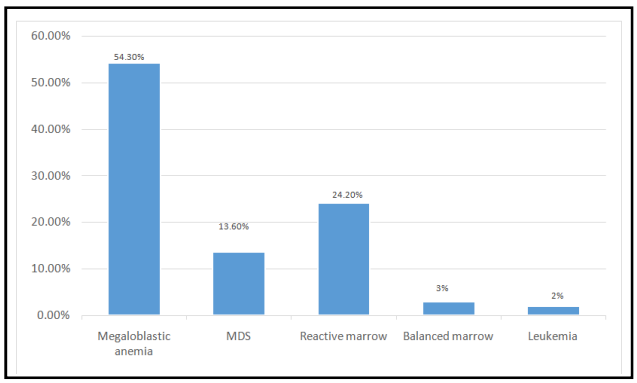

Figure 3. Myelogramresults in ourstudy population (n=103)

DISCUSSION

The prevalence of macrocytosis has been estimated from 1.7% to 3.9% (7). Wintrobe established the value of morphologic classification of anemia. He characterized anemias as macrocytic, normocytic, simple microcytic and hypochromic microcytic (8). Several surveys of macrocytosis have been published. Relatively small numbers of patients were described in these reports and the definition of macrocytosis varied considerably. Some investigators have used a threshold MCV value of red blood cell of 100 fL ; others used values ranging from 105 to 115 fl. In our study, we defined macrocytic anemia when MCV >95 fL. Average age and sex ratio were variable depending on the different studies. Male gender was commonly affected with a sex-ratio (M/F) at 3,3, which was comparable to Unnikrishnan et al and Yoganathan et al studies (9,10), in contrast of any study on iron deficiency anemia where there is usually a female preponderance. Both macrocytosis and macrocytic anemia are associated with advanced age (11,12). Majority of the patients of our population belong to the age group above 40 years, both in males and females. The average age was 56.7 years old with extremes ranging from 30 to 90 years.

The discovery of macrocytic anemia was fortuitous in 35% of cases. 45% of our population presented anemic syndrom, 12% hemorrhagic syndrome, 8% infectious syndrome. In a study conducted in 100 patients by Tejas Shah and Tarun Rathod 96% presented with symptoms of fatigue, 30% and 42% of the study population had psychiatric and neurological symptoms, 2% had diarrhoea (13). In another study by Salma Haq et al in a population of 80 patients 84% had fatigability, 34% had bleeding manifestation and no patient had neurological symptoms (14). The hematological study showed hemoglobin varying between 4,7 g/dL and 11,9 g/dL with an average of 7.2 g/dL, which was similar to other studies. The mean MCV was 107 fL. 45% of patients had MCV in the 95–105 fl range. No correlation was found between the severity of anemia and the degree of elevation of the MCV (9,10). In our study hypersegmented neutrophils were observed in 52 patients (50,48% of cases) In other two studies there were lower percentage of hyper segmented neutrophils than our study, 25.5% in the study by Punia Bhatia and 43% in the study by Vineetha unnikrishnan et al (10,15). Macrocytic anemia has variable etiological factors classified into one of the following categories, megaloblastic or non-megaloblastic. Megaloblastic anemiais caused by deficiency or impairment of utilization of vitamin B12 or folate. Non-megaloblastic anemia may be the result of liver dysfunction, alcoholism, MDS, or hypothyroidism. Common causes of macrocytosis are different by region and setting. For example, in New York, 37% of cases diagnosed in hospitalized patients were medication related. Antiretroviral therapy forhuman immunodeficiency virus (HIV) infections accounted for 13% (16). In Finland, the common causes of macrocytic anemias were alcoholism (65%), and vitamin B12 or folate deficiency (28%) in out-patientsover 75 years of age. (17, 18). In Wintrobe's study the most common cause of macrocytic anemia was megaloblastic anemia produced by pernicious anemia. The other causes, in order of decreasing frequency, were disorders of the liver like cirrhosis, bone marrow disturbances like leukemia, myelodysplasia and aplasia, the anemia of acute blood loss and the anemia of pregnancy. Patients with pernicious anemia had extreme macrocytosis and severe anemia. (8,12). The findings in our series were parallel to these results with megaloblastic anemia being the most common cause of macrocytic anemia (54,3%), followed by primary bone marrow disorders.

Conclusion

Primary care physicians may encounter more cases of macrocytic anemias in the near future than they have over the past several decades, as the older population increases, because macrocytic anemias commonly appear in elderly patients. Although macrocytic anemias have many different etiologies, megaloblastic anemia still remains the most important cause of macrocytic anemia in our setting. The diversity and complexity of factors leading to macrocytic anemia preclude a single or uniform method of investigation. The investigative pattern must be tailored to the individual patient, giving importance to the clinical presentation.

Keypoints

The pathological conditions associated with macrocyticanemia are much more diverse than is often appreciatedand macrocytosis is not to be equated with megaloblastosis, since there are varied conditions associated with non-megaloblasticmacrocytosis.

However, the presence of macroovalocytes and hypersegmented neutrophils in peripheralsmear almost always goes with a diagnosis of megaloblasticanemia.

Glossary of Abbreviations

- **BM :** Bone marrow
- **DNA:** deoxyribonucleic acid
- **EDTA:** ethylenediaminetetraacetic acid
- **fL:** femtoliter
- **Hb**: hemoglobin**.**
- **HIV:** immunodeficiency virus
- **MCV:** mean corpuscular volume
- **MDS:** myelodysplastic syndrome
- **MGG**: May-Grünwald-Giemsa
- **PB:** peripheral blood
- **RBC:** Red blood cell
- **WHO:** World Health Organization

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