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Megaloblastic anemia at the Mohamed VI University Hospital of Marrakech: About 132 cases

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Abstract

Megaloblastic anemia is a common form of anemia that may be related to a vitamin B12 or B9 deficiency. It results from an abnormality of DNA synthesis and is diagnosed on the myelogram by a cellular gigantism of the medullary erythroblasts called megaloblasts but also in all cells with rapid renewal (oral, intestinal, vaginal epithelium...). Megaloblastic anemias are predominantly found in subjects over 60 years of age, with a male predominance. The clinical signs are dominated by digestive and neurological disorders. The diagnosis of megaloblastic anemia, guided by the hemogram, is classically confirmed by vitamin assays and the myelogram, which reveals a medullary megaloblastosis. However, for some authors, the myelogram is no longer systematic when the epidemiological, anamnestic and clinical data make it possible to eliminate other causes of macrocytic anemia and to retain a vitamin deficiency. Confirmation of this deficiency is done by vitamin assays. Megaloblastic anemias are generally of deficiency origin, in which case their management is based on vitamin supplementation for curative or preventive purposes.

Keywords: Anemia; Macrocytosis; Megaloblasts; Vitamin B12; folate assays

1. Introduction

Megaloblastic anemias are macrocytic anemias resulting from a blockage of thymine synthesis, alterations involving all rapidly renewing tissues. They are related to a defect in DNA synthesis due in most cases to a deficiency in folate and/or cobalamins (Vitamin B12).

Megaloblastic anemias are characterized by a mean blood volume (MBV) greater than 100 fl and by cellular gigantism identified in medullary erythroblasts, thus called megaloblasts, but also in all rapidly renewing cells (oral, intestinal, vaginal epithelium, etc.)

In Morocco, macrocytic anemias represent 23% of all anemias [1]. In recent decades, the development of standardized and automated assay techniques has facilitated its diagnosis [2]. In our context, in the absence of routine vitamin assays, the diagnosis of these deficiencies is essentially hematological and a marrow puncture is inevitable to make the diagnosis, which will be confirmed or excluded by the test treatment and the evolution of the patient's condition under vitamin treatment.

The objective of our work is to determine the prevalence of megaloblastic anemia, to specify its epidemiological, clinico-biological and etiological particularities based mainly on hematological data.

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2. Patients and methods

We report the results of a retrospective study spread over a period of 2 years, from January 2020 until December 2021 about 132 cases, on profile of megaloblastic anemias, collected in the clinical hematology department of the CHU Mohamed VI of Marrakech. All patients with anemia (hemoglobin level < 13.5 g/dl in men and < 12g/dl in women), with or without thrombocytopenia or leukopenia with medullary megaloblastosis were included in this study. Other types of anemia were excluded from our study. The epidemiological, clinical, biological and etiological characteristics of the 132 cases of megaloblastic anemia were collected on case report forms.

3. Results and discussion

During the study period, 132 cases of megaloblastic anemia were identified. The mean age was 56 years with extremes ranging from 15 to 100 years. The sex ratio M/F was 0.61. The origin of the patients was urban in 33.5%, rural in 58%, and unspecified in 8.5%. 15 patients had hypertension as a pathological history, 12 had type 2 diabetes. The average time to consultation was 6 months with extremes ranging from 8 weeks to 2 years.

The anemic syndrome was the main circumstance of discovery of megaloblastic anemia (96%) associated with an alteration of the general state (33%). The different clinical signs reported by the patients at the time of diagnosis are summarized in Figure I.

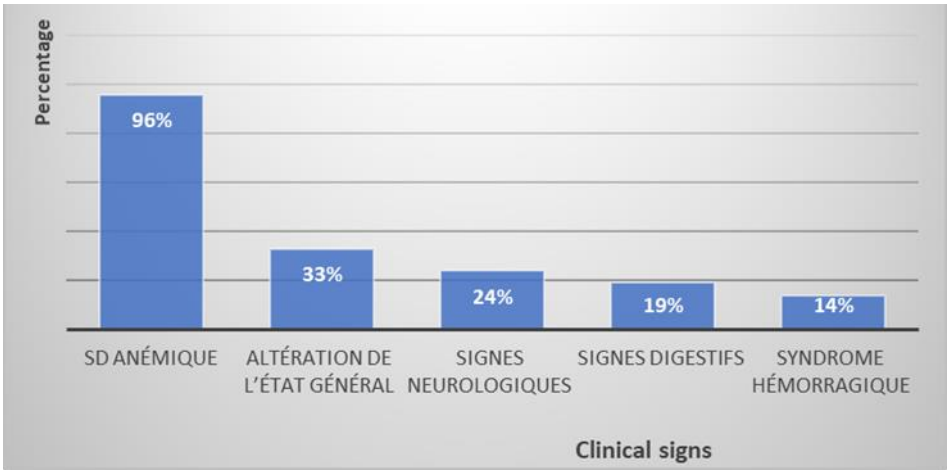

Figure 1 Clinical sign

Biologically, the haemogram showed anaemia in all patients, the mean haemoglobin level was 7g/dl (1.9-12g/dl), macrocytic in 91% with a mean GMV of 114fl (95- 152fl). Bicytopenia was associated in 34% of cases and pancytopenia in 50%. Table 1.

Table 1 Cases

	Workforce	**%**
Anemia	132	100%
SevereanemiaHb‹6	79	60%
High VGM	120	91%
Leukopenia	70	53%
Thrombocytopenia	105	79%
bicytopenia	45	34%
Pancytopenia	66	50%

Anemia was aregenerative in 98% of patients.

The blood smear revealed in all our patients:

- At the level of the redbloodline: Macrocytosis; Anisocytosis; Jolly bodies.
- In the white bloodcell line: Polysegmentation of polynuclearcells.
- Platelets: Macroplateletsin 05 cases

A myelogram was performed in all patients, showing frank megaloblastosis in 118 cases and moderate megaloblastosis in 14 cases.

A vitamin assay (Vit B12 and Vit B9 assay) was performed in 129 patients, showing a vitamin B12 deficiency in 56% and a vitamin B9 deficiency in 44% of cases.

A FOGD was performed in 34 patients showing atrophic gastritis in 10 cases, biermer's disease in 5 cases, chronic HP+ gastritis in 9 cases and an unspecified etiology in 10 cases.

A favorable response to vitamin treatment was obtained in 90% of our patients.

Anemia was poorly tolerated and required transfusion in 18 patients.

4. Discussion

Megaloblastic anemia is a frequent etiology of anemia, bi- or pancytopenia and is a common cause of macrocytic aregenative anemia. It is due to a deficiency in vitamin B12 and/or folic acid which may or may not be Biermerian. There are also rare non-carerative megaloblastic anemias, notably congenital or toxic.

Its prevalence is close to 20% in the general population [3]. In the elderly, the prevalence appears to be higher: between 30 and 40% [3].

In this study, the average age was 56 years compared to 56.7 years for Ben Salem [4], in a study of 93 patients admitted for macrocytic anemia. It was 57.7 years for Ben Ahmed, in a study in the Tunisian Cap Bon region involving 40 cases [5]. The sex ratio M/F in our series was 0.61 while it was 0.47 for Ben Salem against 0.82 for Ben Ahmed. In a recent study of patients admitted for megaloblastic anemia [6], Kechida found an average age of 63 years and a sex ratio of 1.08. For Médaoud [7], the sex ratio was 0.91, the average age was 53 years.

The clinical signs are polymorphous and of variable severity, ranging from a well-tolerated anemic syndrome to more severe pancytopenia. In our study, clinical signs are dominated by anemia (96%), followed by neurological signs (24%) and digestive signs (19%).

The blood smear examination shows various abnormalities. Morphological abnormalities of the red blood cells commonly include anisocytosis, macroovalocytosis, poikilocytosis, polychromasia, pear-shaped red blood cells and often Jolly bodies in many red blood cells indicating a disorder of cell division [8]. Schizocytosis is often present, especially in severe vitamin B12 deficiency [9].

Analysis of the bone marrow smear suggests a diagnosis of megaloblastic anemia: at low magnification, the marrow appears rich and blue. At high magnification, the marrow has increased erythroblastosis and the erythroblasts are megaloblastic [10, 11]. All stages of erythroblast maturation are represented but the asynchrony of nucleocytoplasmic maturation is marked with young nuclei and an already acidophilic cytoplasm. Consequently, the diagnosis of megaloblastic anemia, oriented by the hemogram, is classically confirmed by vitamin assays and the myelogram, which shows a medullary megaloblastosis giving the marrow a bluish appearance related to hypercellularity and hyperbasophilia [12]. However, for some authors, the myelogram is no longer systematic when the epidemiological, anamnestic and clinical data make it possible to eliminate other causes of macrocytic anemia and to retain a vitamin deficiency. Confirmation of this deficiency is done either by vitamin assays or by therapeutic tests. [13, 14, 15-16],

Folate and/or vitamin B12 (cobalamin) deficiency are among the most frequent causes of macrocytic anemia. In our patients, a vitamin B12 deficiency was dominant at 56% against 44% for vitamin B9. For Ben Ahmed, vitamin B12 deficiency was the cause of 12.5% of cases of anemia.

The presence of macrocytosis, and especially of anemia, indicates collapsed vitamin reserves. Therefore, the absence of anemia or even macrocytosis does not exclude a deficiency in one of these two vitamins; the diagnosis can be made early on the basis of decreased vitamin levels before the appearance of hematological signs, the deficiency having been suspected in a context of autoimmune pathologies (Biermer's disease attested by the presence of anti-parietal cell antibodies), neurological or psychiatric illnesses, depression, cancer, certain malformations, in particular neural tube defects, and thromboembolic accidents. Macrocytic megaloblastic anemia may also result from a congenital condition, such as oroticoaciduria or thiamine-dependent megaloblastic anemia. Macrocytic anemia is frequently observed outside of any deficiency pathology, notably in several hematological disorders: myelodysplastic syndromes, leukemias, bone marrow aplasias.... Macrocytic anemia may be caused by the administration of certain drugs that block DNA biosynthesis [8].

The treatment of our patients is based on the parenteral administration of vitamin B12, in the form of hydroxocobalamin at a dosage of 5000 ug/d for the first week followed, in case of reticulocytic crisis, by a dosage of 5000 ug/week for one month, then 5000ug/month [17]. Folic acid, available as tablets or injectable solutions, is used for the treatment of deficiencies at a dose of 5 mg to 15 mg/d, except in the case of drug accidents with antifolate drugs or when using methotrexate in high doses, or in acute folate deficiencies. In this case, it is replaced by injectable folinic acid in doses ranging from 10 to 50 mg [8]. In our patients, the reticulocytic crisis and the normalization of the blood count took place within the usual time frame.

5. Conclusion

Megaloblastic anemias are frequent in Morocco and still constitute a public health problem. They can be responsible for a significant morbidity. The diagnostic approach must be based primarily on anamnesis data, on the precise analysis of the haemogram and blood smear, its positive diagnosis is easy based on bone marrow cytology, however the etiological diagnosis is more difficult. The etiologies are dominated by Biermer's disease. A well-conducted treatment allows rapid improvement of clinical and biological signs.

Compliance with ethical standards.

Disclosure of conflict of interest

The authors declare no conflicts of interest.

Contributions of the authors

All authors contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors'.

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