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Confrontation between Myelogram and Cytogenetics in 35 CML Malagasy Patients

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Abstract

Introduction: Chronic Myeloid Leukemia is a myeloproliferative disorder affecting hematopoietic stem cells. The specific cytogenetic abnormality is translocation (9; 22) which leads to the BCR-ABL fusion gene. Methods: We did a bone marrow aspiration in our laboratory of haematology of university hospital Joseph Ravoahangy Andrianavalona Antananarivo. We studied myelogram and compared its result to the cytogenetic result. Results: Men were the most affected by this pathology and diagnostic average age was 51.2 years. Splenomegaly leukocytosis and myelemia were often present. Myelogram showed granulocytic hyperplasia and the t (9; 22) were present in all the patients. Conclusion: Diagnosis is based on data from the NFS, the myelogram, the search for the Philadelphia chromosome and BCR-ABL fusion gene. These specialized techniques are still inaccessible for Malagasy patients.

Keywords

Chronic Myeloid Leukemia, Madagascar, t (9; 22), BCR-ABL

1. Introduction

Chronic Myeloid Leukemia (CML) is a myeloproliferative syndrome associated to the clonal proliferation of hematopoietic stem cell, leading to primarily myeloid expansion [1]. It is associated with a specific chromosomal marker: the Philadelphia chromosome (Phl) characterized by the genetic abnormality which is a reciprocal translocation between the long arm of chromosome (9q) and the long arm of chromosome (22q), denoted by: t (9; 22) (q34.1; q11.2) and its molecular equivalent: BCR-ABL rearrangement, found in bone marrow cells of 95% of patients [2]. In the chronic phase of the

disease, tyrosine kinase constitutively active produced by the BCR-ABL fusion gene generated by ph1 chromosome, stimulates a hyperproliferative myeloid cells that preserve their ability to differentiate [3].

We report in this study the cases of 35 patients with leucocytosis, myelemia and splenomegaly evoking the diagnosis of CML. We did a confrontation between myelogram results and those of cytogenetics.

2. Patients and Methods

We performed in our paraclinic unit of training and research in hematology at the University Hospital Joseph Ravoahangy Andrianavalona Antananarivo Madagascar during 4 years between June 2012 to June 2016, a bone marrow aspiration of 35 patients aged between 45 and 68 years who had presented leukocytosis with myelemia associated with splenomegaly evoking CML.

The bone marrow aspiration was preceded in advance by a specialized haematological consultation posing its indication, informing the patient about the progress of the act, searching for the existence of any cons-indications such as a bleeding disorder, anticoagulant therapy, or a major thrombocytopenia, and obtained their informed consent for the study.

We used xylocaine 2% without epinephrine to anesthetize the puncture site previously disinfected (sternal manubrium or posterior iliac). Mallarme trocar was used for bone marrow aspiration. Approximately 0.5cc of bone marrow was aspirated with a sterile syringe for making 10 smears, and then using another syringe, 2cc was sucked and collected in an EDTA tube for cytogenetics. A blood count was systematically done with the myelogram. Bone marrow smears were stained with May-Grünwald Giemsa and seen by optical microscopy in our unit while bone marrow for cytogenetics study was sent to an outside laboratory to the patient management. The technique used by the laboratory to search for Philadelphia chromosome is conventional karyotype with Fluorescent *In Situ* Hybridization (FISH). Subsequently we compared the outcome of myelogram and cytogenetics.

3. Results

Patients had between 45 and 68 years old with a median of 51.2 years. There was a slight male predominance with a male/female ratio equal to 1.3.

Blood count showed that all patients had a frank leukocytosis with a mean value of white blood cell around 150 G/L associated with neutrophilia and a near-constant basophilia. Anemia, often moderate with an average hemoglobin equal to 10.7 g/dl was found in 15 patients (42.8%).

Blood smears study showed a balanced myelemia (on average 40% of the leukocyte formula) made essentially by myelocytes and metamyelocytes but sometimes with promyelocytes (<5%), undifferentiated blasts and myeloblasts (<2%) (**Figure 1**).

Medullary smears were in all cases richly cellular with sometimes increased number of megakaryocytes. Granular hyperplasia at the expense of other cellular lines was

found on all smears (Figure 2). Patients were all in the chronic phase of the disease. The genetic abnormality, t (9; 22) was found in all patients.

4. Discussion

The incidence of CML in Madagascar is still poorly understood. Cytogenetic and molecular study, keys of the diagnosis are inaccessible for the majority of Malagasy patients. Indeed, these expensive analyses are to the patient management because social security does not exist in Madagascar.

Chronic myeloid leukemia was more common in men with a sex ratio equal to 1.3 corroborated by the literature. The age of our patients was similar with the average age of diagnosis [4].

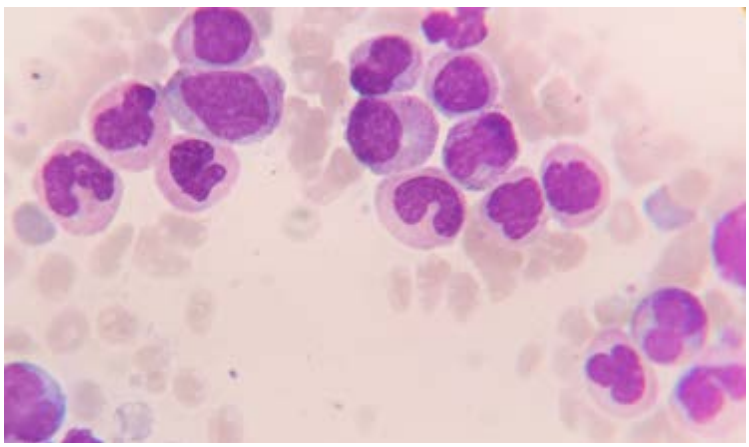

Figure 1. Blood smear stained by MGG, observed by optical microscopy objective ×100 (haematology laboratory of University Hospital Joseph Ravoahangy Andrianavalona Antananarivo Madagascar).

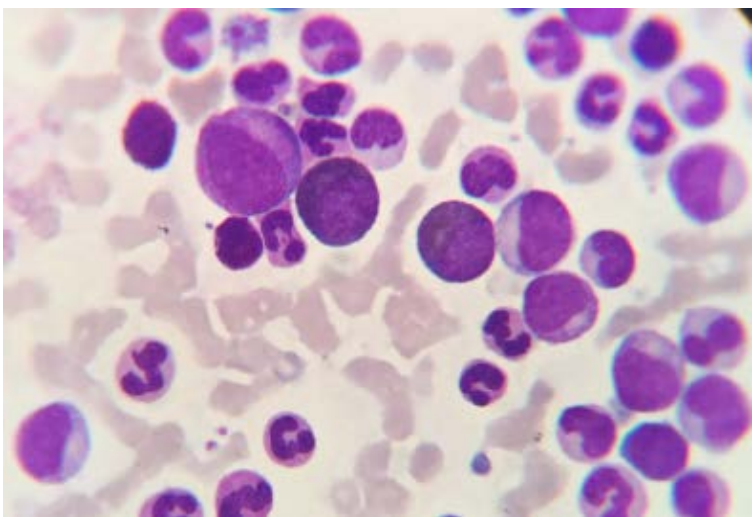

Figure 2. Bone marrow smear stained by MGG, observed by optical microscopy objective ×100 (haematology laboratory of University Hospital Joseph Ravoahangy Andrianavalona Antananarivo Madagascar).

The blood count is very important allowing to evoke the diagnosis. Une hyperleucocytose franche était chez tous les patients.

Studies report that the number of white blood cells is greater than 100 G/L in 50% of cases and can reach 500 G/l [5]. This leukocytosis was associated with a balanced myelemia. It is present in 30% - 60% of cases according to some authors [3] [6].

Anemia was present in 42.8% (15) cases with a mean hemoglobin equal to 10.7 g/dl. In the literature, anemia is moderate and uncommon, but some authors have described the presence of anemia in 50% of cases [3].

Bone marrow smears were richly cellular and sometimes rich in megakaryocytes. Although considered unnecessary for the diagnosis of chronic myeloid leukemia by some authors, bone marrow aspiration is the main diagnostic tool in our laboratories and used to confirm the phase of the disease and to perform the initial karyotype [3].

The presence of the Philadelphia chromosome ph1 and its transcript, the fusion gene BCR-ABL1 was demonstrated in all patients. Several studies have demonstrated the key role of this chromosome in various biological models including chronic myeloid leukemia [7].

In fact, the discovery of Philadelphia chromosome has been important in understanding the pathogenesis, biology and treatment of CML. In Madagascar, the treatment is based on the first-generation inhibitor of tyrosine kinase associated or not with a cytoreductive molecule.

5. Conclusions

Chronic myeloid leukemia is a myeloproliferative disorder affecting hematopoietic stem cells and predominant on the grainy line. The Philadelphia chromosome and its transcript BCR-ABL confirm the diagnosis.

We document, by this work, the diagnosis of CML in Madagascar. Furthermore, we try to share our experiences and problems we encounter in our daily practice of medicine.

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