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Research Article

The Chronic Myeloid Leukemia In A Black African Drepanocytic Subject: About A Case In The Clinical Hematology Department Of The Donka Hospital And University Center/Conakry.

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Abstract: Sickle cell disease is a chronic congenital hemoglobinopathy with some major forms having high morbidity and mortality. The occurrence of chronic myeloid leukemia type malignant hematopathy in this area is rare but not excluded. This association has drawn our attention to its clinical impact and the challenges of organizing care.

To this end, we report a case of chronic myeloid leukaemia on homozygous SSFA2 major sickle cell disease, diagnosed in a 35-year-old patient. He was treated with Imatinib Mesylate for CML and transfusional exchanges for sickle cell disease. Despite a toxicity noted at the beginning of treatment, the overall evolution thereafter was good with normalization of the blood count and stabilization of the clinical condition.

Keywords: Chronic myeloid leukaemia; Sickle cell disease; CHU DONKA, CONAKRY

Introduction

Chronic myeloid leukaemia (CML) is a myeloproliferative syndrome characterized by a predominant proliferation on cells of the granular lineage, associated with a specific chromosomal abnormality which is the translocation t(9 ;22)[1]. The abnormal chromosome called Philadelphia chromosome (Ph1) results from the reciprocal translocation between the long arms of chromosomes 9 and 22 which produces a hybrid bcr-abl gene, responsible for a BCR-ABL protein that has high tyrosine kinase activity[1]. This protein activates several signaling pathways. The result is an increase in cell proliferation, survival and adhesion with transformation of myeloid cells and proliferation of granular cells[2]. CML accounts for 15% of adult leukaemias and about 600 new cases per year in France[3]. Sickle cell disease is a genetic disease with autosomal recessive transmission that affects the beta chain of hemoglobin, characterized by an abnormal hemoglobin called hemoglobin S that polymerizes and crystallizes with the result that the red blood cell becomes rigid and less deformable[4].

The essential characteristics of this condition lie in the multiplicity of its complications, some of which are fatal[5].

Although no causal link has been established between these two pathologies reported in the literature, their association is extremely rare (no cases found by us), which prompts us to report one case while describing the clinical-biological and therapeutic characteristics.

Case Report

Mr MCA is a 35 year old patient living in the provinces, a teacher by profession, followed by a homozygous major sickle cell disease of the SSFA2 type with a hemoglobin base level of 8.5g/dl under folic acid 5 mg and Tanakan® 40 mg. He consulted during the inter-critical period for progressive onset physical asthenia, headaches, dyspnea, visual blurred vision, ringing in the ear and osteoarticular pain without a febrile context.

The physical examination found a patient who had a normal consciousness, hemodynamic constants were stable. No hemorrhagic signs, no signs of infectious calls. No peripheral tumor syndrome (no hepatosplenomegaly or peripheral adenopathies).

Pulmonary auscultation found fine crackling rasps in both pulmonary fields while cardiac auscultation was normal.

On the paraclinical level:

-The hemogram showed strong hyperleukocytosis at 202,600/mm3, Hb : 6.1g/dl, platelets : 210.000/mm3 with significant and polymorphic myeloma (Myeloblast (1%); myelocyte (4%); myelocyte (23%); metamyelocyte (25%) polynuclear neutrophil (42%); polynuclear eosinophil (3%); polynuclear basophil (1%) and monocyte (1%)

-The myelogram performed showed hyperplasia of the

granular lineage (84% of the medullary cells with 2% myeloblasts)

FISH finds the BCR-ABL transcript on almost all the cells analyzed and cytogenetics finds Ph1 on 96% of the cells. No other adverse anomalies found.

The multiparametric biochemical balance sheet found:

Micro albuminuria at 197.0 mg/l Total bilirubin = 42.3µmol/l; Direct bilirubin = 29.5µmol/l; Indirect bilirubin = 22.8µmol/l; ASAT = 106UI/l/l; ALAT = 28UI/l; LDH = 2369UI/l, uric acid : 516 mg/l. The hemostasis test (TP, TCA, Fibrinogen) was normal.

Viral serologies for hepatitis B and C and HIV were negative.

The radiograph of the pelvis face found an early necrosis of the head of the left femur (FICAT stage III).

In total, it was a major homozygous SSFA2 sickle cell disease in hemolytic crisis and osteonecrosis of the femoral head associated with chronic chronic myeloid leukemia in chronic phase with leukostasis syndrome. The Sokal's prognosis score was 0.693 (low risk).

On the therapeutic level:

- Concerning CML, he benefited in the emergency from parenteral hydration (1000 ml of physiological saline and 500 ml of bicarbonated saline with diuresis bar); initiation of Hydrea® 500 mg (2 capsules x2/day) and Zyloric® 300 mg/day in one dose. Mesylate imatinib (Glivec®) was subsequently introduced at 400 mg/day as a single dose with very good clinical tolerance of Glivec®. However, we noted the normalization of leukocytes and the installation of severe bicytopenia, in particular thrombocytopenia with haemorrhagic syndrome, which required the discontinuation of Glivec before resuming it for a week at 300 mg/day. Good tolerance and good clinical and hematological response thereafter
- For sickle cell disease, he was transfused with red blood cells after stabilization of leukostasis syndrome; the usual treatment continued with Folic Acid 5 mg and Tanakan® 40 mg. A monthly transfusion exchange system has been set up.

Very good overall clinical and hematological progress with seizure spacing and normalization of the blood count.

An orthopaedic consultation was organized to follow up on his early necrosis of the left femoral head.

Discussion:

The joint presence in the same patient of these serious pathologies has no direct causal relationship established despite the fact that hemoglobinopathy is congenital genetic. Although their association is rare but it is not excluded, especially since chronic myeloid leukaemia can occur in any subject exposed to a promoting factor regardless of co-morbidity. But what arouses interest as a hematologist is the clinical-biological impact and the coordination of therapeutic management and monitoring. Chronic myeloid leukemia affects both sexes ; however, male predominance has been reported in several studies[6,7,8,9] with respective sex ratios of 1.42; 1.5; 1.75 and 2.12. On the other hand, a female predominance was observed in the study of TOLO-DIEBKILE A et al[10] where the sex ratio was 0.9. Chronic myeloid leukaemia is a pathology of the young adult, which corresponds to the age of this patient, which was 35 years old. In the study by TOLO DIEBKILE A et al[10], the mean age of patients was 39 years with extremes of 24 years and 62 years.

The coexistence of these two pathologies will necessarily have a clinical impact on the patient that is likely to accentuate the alteration of his general state and maximize the symptoms common to both pathologies.

Biologically, hemolytic anemias, sometimes severe in relation to its major sickle cell disease without significant damage to the granular and megacaryocytic lineage, are those found because the cytogenetic anomaly concerns the structure of the hemoglobin contained in the red blood cells.

It should be noted that the progression of CML and the treatments administered may be confronted with worsening cytopenias and the disease of several blood lines. In our patient, the administration of Glivec at normal doses caused symptomatic cytopenias leading to dose adjustment.

The other beneficial effect we found was the transfusional exchanges that stabilized and spaced sickle cell crises and improved treatment performance for CML management.

In recent years, the treatment of chronic myeloid leukaemia has undergone several revolutions, the main one being the advent of targeted therapies, drugs acting on the signals responsible for the uncontrolled growth of cancer cells.

In chronic myeloid leukemia, these drugs target diseased cells carrying the Philadelphia chromosome and the bcr-abl gene, preventing the progression of chronic myeloid leukemia and maintaining it in its chronic phase[11]. In chronic myeloid leukemia, these drugs are used to prevent the progression of chronic myeloid leukemia and to maintain it in its chronic phase.

Currently, five molecules (targeted therapies such as tyrosine kinase inhibitors) are available to treat CML: imatinib (Glivec®), dasatinib (Sprycel®), nilotinib (Tasigna™), lebosutinib (Bosulif®) and ponatinib (Iclusig ™)[12].

Thanks to the use of one of these drugs, the number of white blood cells decreases and gradually returns to normal. At the same time, the amount of BCR-ABL in the blood decreases and the Philadelphia chromosome eventually disappears from the bone marrow[13].

Gleevec®, a first generation tyrosine kinase inhibitor, was the one used in our patient with a very good response associated with hematological toxicity.

In the study by KUEVIAKOE M I et al6, the causes of death were acutisation with mutation (29.41%), severe anemia (47.06%), acute renal failure (5.88%) and haemorrhagic syndrome (17.65).

In our patient, we continued to take folic acid supplementation and Tanakan® for its vasodilatory effect, which has a positive impact on minimizing vaso-occlusive seizures.

Conclusion

The combination of chronic myeloid leukemia and major sickle cell disease (both serious pathologies) in the same patient will certainly have a clinical impact on the patient in terms of morbidity. But it will surely make demands on the

doctor who organizes the follow-up by the rhythm of regular and close monitoring. The issue is not only limited to pathologies but also to the therapeutic aspects of the two chronic hematological diseases.

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