Case study

Manual Exchange Blood Transfusion with Cytoreduction in the Management of Chronic Myelocytic Leukemia with Hyperleukocytosis: A Case Report

Abstract

Chronic Myelocytic Leukaemia (CML) is a haematological malignancy characterized by granulocytic leukocytosis, splenomegaly, and weight loss. Hyperleukocytosis can lead to leukostasis and hyperviscosity syndrome. Leukapheresis is used to manage hyperleukocytosis, but apheresis machines are expensive and unavailable in most health facilities across Nigeria and other resource-limited countries. Manual Exchange blood transfusion (EBT) can be an alternative to leukapheresis in managing hyperleukocytosis and associated metabolic derangement.

We report a case of a 53-year-old woman who presented to the Jos University Teaching Hospital with granulocytic leukocytosis and massive splenomegaly. Full Blood Count and Bone Marrow Aspiration cytology showed features of CML in the accelerated phase. The patient was commenced on cytoreduction with hydroxyurea but defaulted treatment and re-presented one year after with features of CML in blastic transformation and pulmonary leukostasis. Recommencement of Hydroxyurea and Manual EBT achieved cytoreduction and improvement of pulmonary symptom, while the eventual introduction of imatinib mesylate resulted in the attainment of haematological remission.

Our report found that Manual EBT, combined with cytoreduction, is a reliable alternative to automated leukapheresis in managing hyperleukocytosis in resource-limited settings.

INTRODUCTION

Chronic Myelocytic Leukaemia (CML) is an acquired haematological malignancy resulting from a multipotent haematopoietic stem cell transformation.[1][2] It is characterized by anaemia, granulocytosis, and splenomegaly. In its natural course, the disease is triphasic: a chronic phase characterized by the accumulation of more matured myeloid cells, the accelerated phase, and finally, the blastic phase characterized by an arrest in differentiation, accumulation of primitive cells of the myeloid series and thrombocytopenia.[1][2]

Worldwide, CML is the most common myeloproliferative disorders and represents 15 to 20% of all newly diagnosed leukaemia cases. [1] The age-adjusted incidence rate in the United States is approximately 2.3 per 100,000 persons in men and 1.6 per 100,000 persons in women.[1] The median age at diagnosis in the Western World is 87 years.[1] However, the median age at diagnosis in Nigeria is lower, with most patients presenting in the chronic phase.[3]

Tyrosine Kinase Inhibitors (TKIs) have revolutionized CML management and have become the standard of care.[1][2][3][4] In the absence of treatment, CML patients risk progression to more aggressive phases of the disease, increasing leukocytosis, worsening splenomegaly, cerebrovascular events, and death.[1][2] Leukapheresis, a procedure that reduces white blood cells in patients with hyperleukocytosis, is hardly done in Nigeria and other resource-limited countries because of the cost and, most often, unavailability of the apheresis machine. Manual EBT can serve as an alternative to automated leukapheresis. When combined with hydroxyurea, manual EBT can prevent hyperviscosity syndrome and catastrophic leukostasis and allows cytoreduction before definitive treatment.[5][6] Here, we report a case of a patient diagnosed in the accelerated phase of CML at the Jos University Teaching Hospital but defaulted treatment and re-presented a year later in the blastic phase of CML with respiratory complications. Serial EBT with

hydroxyurea was used in managing leukostasis. The introduction of Imatinib Mesylate resulted in complete haematological remission.

CASE REPORT

Patient K.S is a 53-year-old female Civil servant who presented at the Jos University Teaching Hospital with a three-month history of progressive abdominal swelling, weight loss, night sweat, easy satiety, bone pain, and intermittent low-grade fever. There was no history of bleeding or blood transfusion. The patient was diagnosed with retroviral disease fifteen years before the presentation and has been on antiretroviral drugs since then. Physical examination revealed significant wasting and hepatosplenomegaly with no significant peripheral lymphadenopathy.

Full Blood Count (FBC) was as follows: Packed Cell Volume (PCV):35%, Total Leucocytes Count (TLC): 200 X 10^9/L, Myeloblasts: 13%, Promyelocytes: 8%, Myelocytes: 15%, Metamyelocytes: 6%, Band forms: 10%, Neutrophils: 27%, Lymphocytes: 3%, Eosinophils: 6%, Basophils: 12%, and Platelets: 700 X 10^9/L. (Fig.1)

Bone Marrow Aspiration Cytology revealed a markedly hypercellular marrow, myeloid hyperplasia with a complete spectrum of granulocytic differentiation, marrow basophilia, and eosinophilia. Erythropoiesis was mildly depressed and megaloblastic. The megakaryocytes were adequate and active. (Fig.2)

A diagnosis of Chronic Myelocytic Leukemia in the Accelerated Phase was made. We counselled her on the disease, prognosis, available treatments and likely complications and placed her on hydroxyurea 500mg tds and Allopurinol 300mg once daily. We ordered BCR-ABL transcript analysis and FBC for her next visit to our Haematology Outpatient Clinic.

Two weeks later, she returned to the clinic with a TLC of 109 X 10^9/L and a platelet count of 700 X 10^9/L, having stopped hydroxyurea, citing body swelling and pruritus as reasons. She was prescribed

Chlorpheniramine maleate 2mg bid and advised to recommence hydroxyurea. After clinic visits for four months, the TLC and Platelets count dropped to 32.5 X 10^9/L and 525X10^9/L, respectively, but the patient was subsequently lost to follow-up.

The patient presented at the emergency unit of our hospital a year later with chest pain, difficulty breathing, cough, epistaxis, hematochezia, bone pain, and massive splenomegaly of 20cm below the left costal margin with oxygen saturation of 86%. Further review revealed that she discontinued hydroxyurea and had been on nutritional supplements. She also visited several prayer houses in search of a cure. A review of her haemogram showed the following: TLC: 400 X 10^9/L, Myeloblasts: 30%, PCV: 20%, and Platelets: 150 X 10^9/L. We made a diagnosis of Chronic Myeloid Leukemia in the Blastic phase. A decision was taken to manage as acute myeloblastic leukaemia. However, we opted for manual exchange blood transfusion for three consecutive days and cytoreduction using hydroxyurea due to her performance status. After the first session of manual EBT, the TLC dropped to 350X10^9/L. After the second and third sessions, a repeat haemogram showed the following: TLC: 100X10^9/L, Myeloblasts: 20%, PCV: 36%, Platelets: 300X10^9/L. Bone pain and bleeding also ceased. The oxygen saturation increased to 97%. The liver and Spleen sizes decreased to 8 and 16cm, respectively. She was counselled on the risks involved in taking nutritional supplements with her condition and advised to do the BCR-ABL transcript analysis urgently.

At follow –up, the patient came with a BCR-ABL transcript generated using the Real-Time PCR-Taqman Chemistry as follows: ABL quantity: 1.98 X 10^5 copies per 10 µl of cDNA; BCR-ABL quantity: 1.99 X 10^5 copies per 10 µl of cDNA, and BCR-ABL ratio: 1.00. As a result, she enrolled in the GLIVEC® program offered by the Norvatis/Max foundation. She started imatinib at a dose of 600mg OD but developed pruritus three days later that was resistant to Chlorpheniramine maleate. We advised her to take the drug with food and plenty of water; the pruritus eventually stopped. Four weeks later, she came to the clinic with the following haemogram: TLC: 2.8 X10^9/L, PCV: 36%, Neutrophils: 28%, Lymphocytes: 65%, Eosinophils:

01%, Basophils: 02%, and Platelets: 180 X10^9/L. There was no splenomegaly. We reduced the dose of imatinib to 400mg OD. She had been on the adjusted dose for six months with normalization of her blood counts (Fig.2).

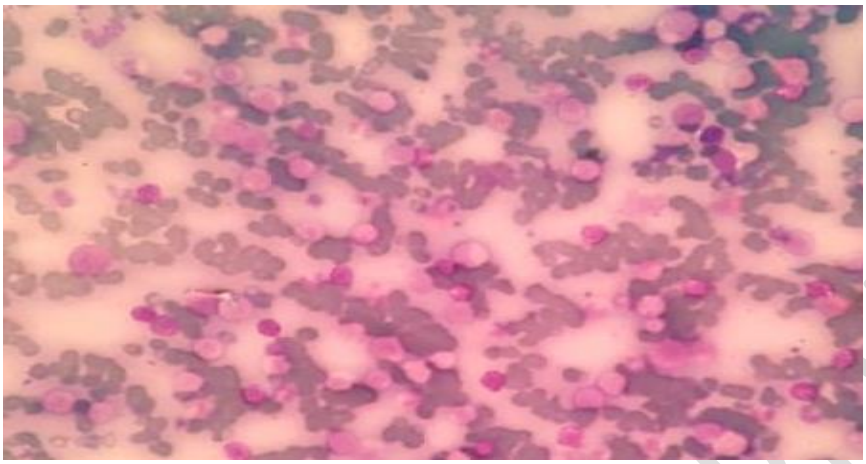

Fig. 1. Bone Marrow Aspiration film (X40) stained with Leishman stain showing hypercellular marrow for age with granulocytes at different stages of maturation and basophilia.

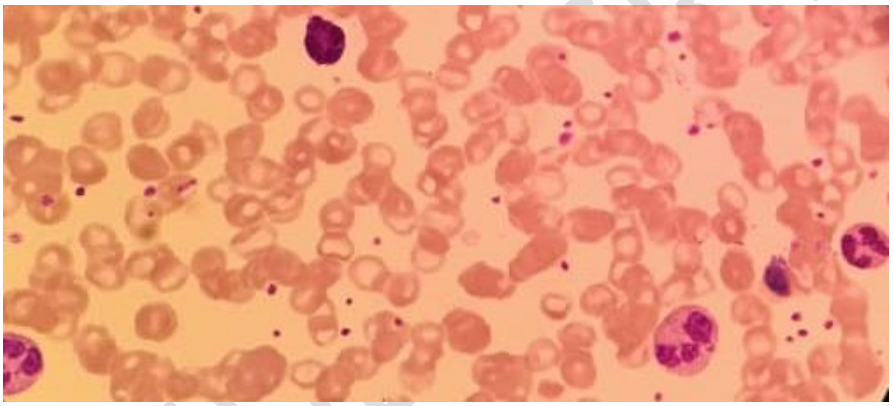

Fig 2. Peripheral Blood Film (X100) of the patient stained with Leishman stain showing normal white cell count. The film was made six months after the commencement of imatinib mesylate (Glivec®).

DISCUSSION

Chronic Myeloid Leukemia as a disease was rarely diagnosed in the past.[1] With the availability of specialists with improved diagnostic skills, an increasing number of cases are seen and cared for; our patient adds to the growing list of these cases.

Clinically, CML presents in most cases with splenomegaly, weight loss, fever and drenching night sweats, as were seen in our patient.[1][2] In most cases, splenomegaly is massive, contributing to easy satiety. Fever and drenching night sweats are consequences of hypermetabolism. Approximately 15% of patients with CML presents with hyperleukocytosis (TLC over 300 X 10^9/L in Chronic Leukemias). [2]The high plasma viscosity caused by leukocytosis impedes blood circulation to the lungs, brain, retina, vestibulocochlear apparatus, and penis.[1][2] Thus, it is not uncommon for CML patients to present with loss of consciousness, stroke, hearing loss, blindness, venous thrombosis, coronary syndrome, and or priapism. On the other hand, markedly elevated TLC may present with bleeding because of capillary and venous congestion.[1][2] Thrombocytosis in CML can cause acquired von Willebrands disease leading to a bleeding phenotype.[1] Patients presenting with hyperviscosity syndrome and unexplained cytopenias or elevated blood cell counts need a consultative Haematologist review to exclude haematological disorder as a cause.

Initial management of hyperleukocytosis is with hydration, leukapheresis, and cytoreduction with hydroxyurea. [1][2]The dose of hydroxyurea must be adjusted to minimize overt tumour lysis syndrome (TLS).[1] Leukapheresis was associated with metabolic, thrombotic and haemorrhagic complications in some studies.[5][7][8] It was also associated with extracorporeal volume loss of red blood cells and platelets.[5]The evaluation of leukapheresis' efficacy also yielded conflicting results, with some studies reporting no significant long term benefit in reducing mortality. [7][8][9] In our patient's case, we used serial manual EBT as an alternative to leukapheresis, while hydroxyurea served as the cytoreductive agent. Exchange blood transfusion is inexpensive compared to leukapheresis and can be performed over a

relatively short period in adults but longer and often cumbersome in paediatric patients. The addition of Serial EBT to the patient's management minimizes the risk of TLS and volume overload that may be seen when hydroxyurea is used in combination with hydration. EBT offers the benefit of improving the haematocrit and oxygen-carrying capacity without circulatory overload that may be seen with the traditional simple top-up transfusions. Manual EBT alone may not achieve the desired fall in TLC. When combined with hydroxyurea, the simultaneous reduction in circulating white blood cells and correction of metabolic abnormalities may be achieved.[10]Exchange Blood Transfusion has been used for cytoreduction in acute and chronic leukaemias with troublesome hyperleukocytosis, but the procedure varies.[11][12][13] In our case, we obtained units of ABO and Rh compatible whole blood screened by a fourth-generation ELISA at the regional National Blood Transfusion Service (NBTS) for the EBT. At each session, the donor unit was set and transfused slowly while the patient is undergoing phlebotomy. After each phlebotomy, the speed of transfusion was increased. Thus, we effectively removed the patient's blood containing the excess malignant cells and replaced it with fresh donor blood.

One of the many problems encountered with managing malignant diseases and other chronic illnesses in Nigeria is the default on prescribed drugs and their substitution for dietary supplements and unorthodox medicines. In most cases, the supplements contain amino acids, folates, vitamins and minerals that serve as nutrients required by the malignant cells to thrive. Furthermore, such drugs are often expensive, causing an additional financial burden on patients and their families. In our patient's case, she defaulted on cytoreduction therapy with hydroxyurea and instead opted for supplements. The result was the progression of her condition to the terminal phase of the disease. Therefore, Healthcare workers must adequately counsel cancer patients on the dangers of concomitant use of non-prescribed medications and nutritional supplements to manage their condition.

CONCLUSION

Our study showed that the use of Manual Exchange Blood Transfusion in combination with cytoreduction is a cheaper alternative to leukapheresis in managing leukaemia associated with hyperleukocytosis in resource-limited settings. It should be considered for patients with high count leukaemias to prevent catastrophic metabolic, cerebral, cardio-pulmonary, and thrombotic complications of hyperleukocytosis.

LIMITATIONS

Our study did not compare biochemical parameters before and after the manual EBT; therefore, we did not assess the impact of EBT on metabolic abnormalities.

ETHICAL CONSIDERATION

The consent of the patient was obtained that permitted us to write this case report.

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