Chronic Myeloid Leukemia with Pancytopenia in a 30-year Old Male: Challenges in Care

Mwansa Bwalya[1], John Bukole[1], David M Chabala[1], Nicollin B Chalapa[1], Bumba N Halucha[1], Kennedy Gondwe[2], Samuel Phiri[3], Christopher Nyirenda[1*]

[1]Department of Internal Medicine, Ndola Teaching Hospital/Copper Belt University, Ndola, Zambia.
[2]Department of Internal Medicine, Kitwe Teaching Hospital/Copper Belt University, Kitwe, Zambia.
[3]Arthur Davison Children's Teaching Hospital/Copper belt University, Ndola, Zambia.

ABSTRACT

We report a case of chronic myeloid leukemia (CML) in a 30-year-old man who presented to a University Teaching Hospital with a history of spontaneous epistaxis associated with generalized body weakness and on and off right-sided chest pains, palpitations, fatigue, hyperhidrosis, and loss of weight. He is a known patient who had been on treatment for a period of 7 months with 400mg of imatinib. He presented with a nasal pack, pallor of grade 2, and splenomegaly. His labs showed pancytopenia, with severe thrombocytopenia and had a working diagnosis established through examination of a bone marrow aspirate. A more definitive diagnosis could not be attained though due to the unavailability of molecular techniques such as reverse transcription PCR (RT-PCR) for the demonstration of the BCR-ABL gene. The case also presented a management dilemma in terms of its progression and the deterioration of the patient despite being fairly compliant and receiving appropriate treatment.

Keywords: Chronic Myeloid Leukemia, Pancytopenia, Thrombocytopenia, Diagnosis, Treatment.

Address for Corresponding Author
Dr. Christopher Nyirenda; Department of Internal Medicine, Ndola Teaching Hospital/Copper Belt University, Ndola, Zambia.
E-mail: kelvinyirenzm@gmail.com
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Introduction

Chronic myeloid leukemia CML) is a myeloproliferative neoplasm (MPN). Myeloproliferative neoplasms are relatively rare hematological neoplasms characterized by marked leukocytosis, myelocyte bulge, basophilia, and eosinophilia in peripheral blood with presence of underlying Philadelphia chromosome as a cytogenetic abnormality or BCR-ABL transcriptase as a molecular abnormality.[1]

CML is associated with reciprocal translocation of the Philadelphia chromosome which is detected in about 95% of CML patients.[2] Reciprocal translocation of the Philadelphia chromosome results in the production of an activated BCR-ABL protein tyrosine kinase which is the causative oncogene of this disease. CML has three phases namely chronic phase, accelerated phase, and the blast phase.[2] The chronic phase has a good response to treatment and is easily controlled. The accelerated phase is not always seen and the disease is not easily controlled at this phase. The blast crisis phase is frequently the cause of death in the majority of patients. In this phase, the disease transforms into acute leukemia, either myeloid (70%) or lymphoblastic (30%).

Imatinib has been widely accepted as the first-line treatment in chronic myeloid leukemia. It is a BCR-ABL tyrosine kinase inhibitor. The side

effects of this drug include pancytopenia, nausea, headache, and rashes.[3]

We report a case of a middle-aged male patient who was diagnosed with CML in 2019. Prior to the diagnosis, he had been experiencing fatigue, weight loss, and general body weakness for some time for which he went to seek medical attention at a teaching hospital where he was attended to. Investigations done including a full blood count revealed extremely elevated white cell count at the time. From there it was suspected that the patient could have leukemia. Further, a peripheral blood film and bone marrow aspirate were done and it was confirmed that the patient had CML. He was then referred to the Cancer Diseases Hospital (CDH) where he was prescribed imatinib. Following treatment, the patient was in a fair state of health for 7 months until he presented to the hospital again with a history of epistaxis and general body weakness.

Clinical Assessments

History: A 30-year old male, a known chronic myeloid leukemia patient on imatinib for 7 months who presented with epistaxis associated with general body weakness and dizziness for 1 day. The bleeding was unprovoked with no history of trauma. Three days prior patient experienced on and off episodes of right-sided chest pains which were relieved by taking diclofenac. He also reported experiencing palpitations, fatigue, increased sweating, and had lost weight in the course of his illness. There was no history of fever, cough, orthopnea, paroxysmal nocturnal dyspnea, or wheezing. The patient had 3 episodes of epistaxis during his stay in the hospital. He had no diabetes, epilepsy, asthma, hypertension, or tuberculosis and was HIV non-reactive.

Physical Examination

On examination, the patient was stable, oriented to time place, and person, and was not in any obvious respiratory distress. His nose was packed with blood-stained cotton wool. On closer examination, he had moderate conjunctiva pallor (++). His BP was 104/71 mmHg with a full volume tachycardia pulse rate of 106 beats/min, respiratory rate of 20 breaths/min, and a temperature of 36.5. He had no axillary, cervical, or inguinal lymphadenopathy. Abdominal examination revealed a palpable spleen about 3 finger breadths below the left costal margin.

Diagnostic and therapeutic focus, assessment, follow-up and outcome

Patient presented with shortness of breath, dizziness, and headache. A full blood count was done and it revealed low Hb and a high white cell count. A peripheral smear was done and revealed eosinophilia, basophilic and immature granulocytes. A bone marrow aspirate was done and according to the patient, he was told that the results revealed findings consistent with chronic myeloid leukemia.

He was referred to the cancer disease hospital where he was started on treatment. He reported full compliance to the treatment. After about 7 months of treatment, he developed epistaxis which was lasting for hours without stopping. He then presented to the teaching hospital due to the same symptoms. A full blood count with differential (FBC/DC) and a cross match was done and showed the following:

- White blood cell count 0.72 X10^9/L
- Red cell count 3.52 X 10^12/L
- Hemoglobin 9.4 g/dl
- Platelets 14 X 10^9/L
- Blood group O positive

He was then started on Tranexamic acid 1g bd iv, Folic acid 5mg od po., and received Fresh frozen plasma (FFP). He was then admitted to an isolation ward due to the low white cell count. The following day Ceftriaxone 1g od iv was started. A repeat hemogram was ordered and blood transfusions were administered. There was no improvement in the parameters even as suggested in the following results:

- WBC 0.65 X 10^9 L
- Hb 8.9 g/dl
- Platelet 11 X 10^9 L
- Red cell distribution width 22.9%.

Discussion

CML is a myeloproliferative disorder that generally progresses in 3 distinct phases (chronic, accelerated, and blast). It presents with fatigue, weight loss, loss of energy, decreased exercise tolerance, low-grade fever and excessive sweating from hyper-metabolism, elevated white blood cell (WBC) count or splenomegaly on routine assessment, early satiety, and decreased food intake from encroachment on the stomach by the enlarged spleen, left upper quadrant abdominal pain from spleen infarction and hepatomegaly. The bleeding, petechiae, and ecchymosis occur during the accelerated phase, bone pain and fever in the blast phase and increasing anemia, thrombocytopenia, and basophilia with a rapidly enlarging spleen in blast crisis.[4] Most of the signs and symptoms were present in our patient, but of note was the progression from the diagnosis, and in the presence of adequate treatment, to the blast crisis. Essentially, our patient had all three stages of disease progression. Although a peripheral smear was done to hint a diagnosis of CML and a bone marrow aspirate was done, demonstration of the BCR-ABL by reverse transcription PCR (RT-PCR) is essential for the diagnosis of CML and effective management because, in its initial stages, the disease mimics essential thrombocytosis (ET) and the two entities have different management approaches. A case study done in 2014 emphasized the need for this definitive diagnosis by demonstration of the said mutations.[5] Another study done in 2010 further pointed out the different additional tests that needed to be done to arrive at a definitive diagnosis; Philadelphia chromosome, a specific marker of CML, and routine cytogenetical and molecular biological analysis the latter which is not readily available in our setting.[6]

Although the advent of tyrosine kinase inhibitors has increased the survival rate to more than 90%, the demonstration of the specific mutation is important because there are variants of the mutation against which the common drug imatinib may not be effective.[7]

Conclusion

CML is a rare hematological neoplasm in our setting. Despite the proper diagnosis and commencement of treatment to which the patient said he was compliant, he ended up having pancytopenia as a likely complication of imatinib which made him prone to prolonged bleeding, anemia, and infection. According to the European Leukemia Net 2020 recommendations for treating chronic myeloid leukemia, the first-line treatment is a TKI with the exception of cases of CML newly diagnosed during pregnancy. A further recommendation is that a short course of hydroxyurea may be given in symptomatic patients with high white blood cell or platelet counts while molecular and cytogenetic confirmation of the CML diagnosis is pending.[8] Although imatinib emerged as the standard treatment for chronic myeloid leukemia (CML) in the International Randomized Study of Interferon vs. STI571 (IRIS) trial[9], some studies have revealed superior efficacies associated with the use of second-generation TKIs such as Nilotinib and dasatinib.[10] These may be resorted to especially where patients develop resistance or are intolerant to imatinib and also depending on availability.

Emphasis on how changing daily habits and diet can improve the outcome of disease should be emphasized on patients diagnosed with leukemia as not only compliance of medication can guarantee good outcome. Educating patients on the side effects of the drugs and how best they can be managed should be mandatory.

The lesson to learn from this write up is that demonstration of the specific mutation in patients suspected of having CML is important, in addition, the differentiation from Essential thrombocytosis is equally essential as both disease entities have different management and treatment approaches, none of which could be definitively done in our patient due to unavailability of the required equipment and material to do the exhaustive tests.

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