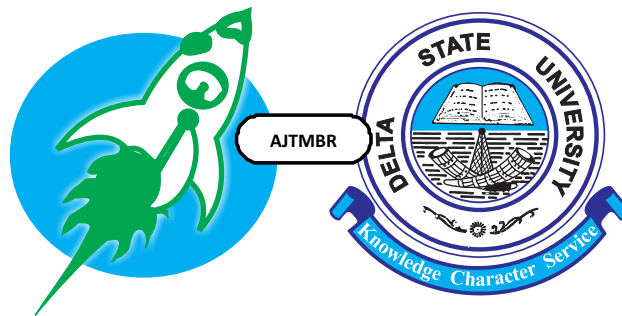


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Case Reports

Chronic Myeloid Leukaemia in Pregnancy – A Case Report

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ABSTRACT

Introduction: Chronic myeloid leukaemia is a Haematological malignancy characterized by the accumulation of monoclonal myeloid cells in peripheral blood and bone marrow. CML in pregnancy presents an intriguing scenario as first line therapy with tyrosine kinase inhibitors (TKI), are contraindicated due to fetal complications. Major presentations include features of hypermetabolism and bleeding complications such as antepartum and postpartum hemorrhages. CML is rare in pregnancy, occurring in about 1 in 75,000 pregnancies with the prevalence in Nigeria not documented.

Case Report: An unbooked 37 year old woman with markedly increased absolute neutrophil count with basophilia who had hysterectomy done on account of severe postpartum haemorrhage prior to a diagnosis of chronic myeloid leukaemia being made. This case report describes the delayed presentation and clinical management of the patient with CML and challenges associated there with.

Conclusion: CML in pregnancy is rare and is associated with several challenges in terms of presentation and management.

Keywords: Chronic Myeloid Leukaemia, Pregnancy, Nigeria

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INTRODUCTION

Chronic myeloid leukaemia is a haematological malignancy characterized by the accumulation of monoclonal myeloid cells in peripheral blood and bone marrow usually with associated infiltration of the spleen by the malignant cells. The diagnosis of CML is rarely difficult and is assisted by the characteristic presence of the Philadelphia (Ph) chromosome. This results from the t(9;22)(q34;q11) translocation between chromosomes 9 and 22 resulting in the chimeric BCR-ABL1 gene.¹ CML is the second most common of the leukaemias in the Niger Delta region of Nigeria, representing 11% of all

haematological malignancies² with a mortality rate of 13.6%.³ It occurs in either sex with equal sex distribution. Majority (62.5%) of cases occur between the ages of 30 and 49 years.² In up to 50% of cases the diagnosis is made incidentally from a routine blood count.¹

CML is rare in pregnancy, occurring in about 1 in 75,000 pregnancies.⁴ The prevalence of CML in pregnancy in Nigeria is not documented.. However, it is estimated to occur in about 10% of pregnancies.⁵ The challenges and complications of CML in pregnancy, such as antepartum and postpartum haemorrhagic phenomenal and

intrauterine foetal growth restrictions, as well as the potential effects of its treatment on maternal and foetal health, ranging from infertility to foetal malformations, are well documented.^{6,7}

CASE REPORT

Mrs OA, a 37 year old secondary school teacher first presented at a general hospital in a remote area with complaints of generalized body weakness of a week duration and bleeding per vaginal of two days duration. She was then an unbooked G3P3+0 lady presenting at 31+2 estimated gestational age (EGA). She was placed on bed rest while some medications were administered to her. No investigation was carried out. On day two on admission she was referred to the Mother and Child Specialist Hospital in the nearby town due to persistent bleeding. There, obstetric ultrasound scan revealed antepartum haemorrhage and liver and splenic spans of 18cm and 22cm respectively. Total white cell count (WBC) was 117,300/uL with a absolute neutrophil count (ANC) of 107,000/uL. Hematocrit (HCT) was 33% while platelet count was 387,500/uL. She was placed on intravenous antibiotics while being worked up for a emergency caesarean section. Patient however, had a spontaneous vaginal delivery while on the operating table in the theater. A live born neonate weighing 1.8kg with an apgar score of 7.8 was delivered. She was discharged third after delivery but represented two weeks later due to postpartum haemorrhage and fever. A Full Blood Count (FBC) done showed a WBC of 240,000/uL, ANC of 236,000/uL and basophil count of 1,100/uL. HCT was 28% while platelet count was 435,000/uL. She was placed on heavier intravenous antibiotics and evacuation of retained products of conception (ERPC) was done with minimal yield. Due to persistent vaginal bleeding and clinical decompensation, an hysterectomy was

eventually carried out. Post operative FBC done showed a WBC of 170,000/uL, ANC of 162,000/uL, platelet count of 373,000/uL and HCT of 30%. She was stabilized and later discharged a week later with a referral to see a haematologist.

Patient presented at our facility ten weeks after she was discharged from the Mother and Child Specialist Hospital with complaints of fatigue, malaise, vertigo, headaches, fever, excessive sweating and anorexia. She was acutely ill looking with a temperature of 38.6°C, mildly pale and dehydrated. There were no palpable peripheral lymph nodes. Her abdomen was mildly uniformly distended with a healed pfannenstiel scar. The liver and spleen were palpably enlarged measuring 8cm and 12cm from the right and left subcostal regions respectively. They were firm and non-tender. She was conscious but lethargic and could barely sit up in bed due to vertigo.

FBC showed a HCT of 30%, WBC 178,000/uL, ANC 168,000/uL, basophil count 1,000/uL, platelet count 324,000/uL. Peripheral blood film revealed markedly increased myeloid cells with a complete spectrum of the granulocytic series, basophilic and adequate platelet. Bone marrow cytology revealed a hypercellular marrow with hyperplastic myelopoiesis and active megakaryopoiesis. Blast cells were less than 5%. Therefore, a diagnosis of CML in chronic phase was made. Patient was commenced on hydration, allopurinol, haematinics and hydroxycarbamide (hydroxyurea) at 20mg/kg (1.5g) once daily. Day five on admission WBC had dropped to 79,000/uL, platelet count was 220,000/uL and HCT was 26%. She was now able to get out of bed without tripping over, appetite was returning, fever had subsided and she felt stronger. She was discharged on request after samples for BCR-ABL 1 transcript was taken.

Two weeks into therapy, there was resolution of all initial presenting complaints, but she had developed neutropenia (ANC 800/uL). Hydroxycarbamide was discontinued and recommenced a week later at 1g daily following resolution of neutropenia. Patient is strongly being encouraged during each clinic check to visit the foundation where the targeted therapeutic agent, Imatinib mesylate is freely given. But she is yet to do so due to financial constraints.

DISCUSSION

Chronic myeloid leukaemia, BCR::ABL1 rearrangement positive is a clonal disorder of a pluripotent haemopoietic stem cell. The diagnosis of CML is rarely difficult and is assisted by the characteristic presence of the Philadelphia (Ph) chromosome.¹ However, diagnosis during pregnancy is usually delayed as early symptoms of CML are nonspecific.⁶ Up to 50% of cases of CML diagnosis are incidental from a routine blood count. In those cases where the disease presents clinically, symptoms related to hypermetabolism, such as weight loss, lassitude, anorexia or night sweats are seen. Splenomegaly is nearly always present and may be massive. Features of anaemia may include generalized body weakness, shortness of breath and easy fatigability. Some may have features related to thromboembolic events and these are particularly exaggerated in pregnancy.^{6,8} Haemorrhagic phenomena such as antepartum and postpartum haemorrhages (as witnessed in this index patient) are a particularly common presenting complaints in pregnancy related CML.⁶

Tyrosine kinase inhibitors (TKIs) are the mainstay of the treatment of CML and several different drugs are now available.¹ However, these are contraindicated in pregnancy due to their teratogenic complications.^{8,9,10} The drug of

choice for CML in pregnancy is interferon-alpha as studies have assured of its safety throughout pregnancy.^{8,11} Hydroxycarbamide can also be used except in the first trimester as it is associated with IUGR and stillbirth as well as preeclampsia. Leukapheresis has also been documented to effectively reduce highly elevated white cell counts with associated symptoms of hyperviscosity syndrome^{8,11}

This patient first presented at two peripheral hospitals where the diagnosis and associated complications of chronic myeloid leukaemia in pregnancy could not be made. Hence appropriate and timely interventions were not instituted leading to inappropriate administration of antibiotics and conduct of hysterectomy. Furthermore, there was delay before patient presented at our facility with consequent clinically deteriorating state. Fortunately, she was still in the early stage of the disease when diagnosis was made and treatment commenced. Of note and in keeping with a previous study on the acceptability and use of molecular targeted therapy¹² is the patient's delay in seeking the use of Imatinib therapy.

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