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A case of chronic myelogenous leukemia treated with different medication in each of the two pregnancies

Malak Alshammari, Ghazi Sindi, Abdullah Khaled Agabawi, Estabrq Al Hachim, Hassan S.O. Abduljabbar

ABSTRACT

The simultaneous occurrence of pregnancy in case of chronic myelogenous leukemia is relatively uncommon. We describe successful management of chronic myelogenous leukemia (CML) in a 24-year-old woman in her first and second pregnancies using different medications. In her first pregnancy, she was started on PEG-interferon and delivered a baby girl in good condition at 40th week. After seven months she again got pregnant with twin pregnancy and was managed by hydroxyurea. She delivered twin girls in good condition by spontaneous vaginal delivery at 38th week.

Keywords: Chronic myelogenous leukemia, Hydroxyurea, PEG-Interferon, Pregnancy

Malak Alshammari[1], Ghazi Sindi[1], Abdullah Khaled Agabawi[2], Estabrq Al Hachim[3], Hassan S.O. Abduljabbar[4]

Affiliations: [1]MBBCH, Intern in Obstetrics and Gynecology department, King Abdulaziz University Hospital, Jeddah, Saudi Arabia; [2]MBBCH, Abdulaziz University Hospital, Jeddah, Saudi Arabia; [3]MBBCH, ABOG, Assistant Professor and Consultant, Department of Obstetrics & Gynecology, Medical College, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia; [4]MD, FRCS, Professor and Consultant, Department of Obstetrics & Gynecology, Medical College, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia.

Corresponding Author: Hassan S.O. Abduljabbar, MD, FRCS; Professor and Consultant, Department of Obstetrics & Gynecology, Medical College, King Abdulaziz University, P.O. Box 80215 Jeddah 21452, Kingdom of Saudi Arabia; Email: profaj17@yahoo.com

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INTRODUCTION

Chronic myelogenous leukemia (CML), also called chronic granulocytic leukemia, is slowly progressing disease characterize by increased white blood cells which leads to uncontrolled production of granulocytes: neutrophils, basophils and eosinophil. It is a disease of middle age and rarely occurs in children. It is not an inherited disease [1]. Chronic myelogenous leukemia is more common in men and old age.

It is associated with chromosomal translocation called Philadelphia chromosome. It is a chromosome 22 genetic defect unusually of short arm; because of reciprocal translocation of genetic material between chromosome 9 and chromosome 22. Producing a fusion gene called BCR-ABL. It has a biphasic or triphasic, which are chronic, accelerated, and blast phase [2].

There are different options for treatment which includes tyrosine kinase inhibitors (TKI), stem cell transplantation and chemotherapy. During pregnancy, the major concern is from the therapeutic effect that affects the fetus and stopping it may allow CML to relapse [3].

We discuss a successful uneventful case of CML in a female patient, who had two pregnancies, each of which was treated with different regimen and the newborn were normal.

CASE REPORT

A 24-year-old Ethiopian female para 2+0 was a known case of chronic myelogenous leukemia which was diagnosed about three years ago as an incidental finding during her first pregnancy. She came to emergency room at her 20 weeks gestation by her last menstrual period which was confirmed by early ultrasound; after being recently diagnosed with chronic myelogenous leukemia in a private hospital after incidental finding of a high WBC reading in her first antenatal visit confirmed by a bone marrow biopsy. Afterwards, she was referred to our center for more evaluation.

The patient was asymptomatic except for mild fatigue which she had attributed this to her pregnancy. In the emergency room on initial assessment, she was vitally stable with twenty weeks pregnant uterus and no organomegaly.

Laboratory finding were white blood cell (WBC) counts 122.6 K/UI (neutrophils 111.8 K/UI) (lymphocytes 4.3 K/UI) (monocytes 4.4 K/UI) (eosinophils 0.8 K/UI) (basophils. 1.3 K/UI). Her hemoglobin was 10.6 g/dl and platelets were 243x10^3/mm^3. The patient was admitted to our hospital for evaluation and BCR-ABL testing.

Based on the clinical findings and microscopic analyses of her peripheral blood and genetic study (BCR-ABL) detected and previous bone marrow, CML was diagnosed (Figures 1–3).

Informed consent was obtained for therapeutic PEG-interferon. The patient was started on PEG-interferon 120 μg SC Q week, clexane 40 mg SC OD and allopurinol 100 mg PO daily and hydroxyurea 500 mg PO BID temporarily till WBC count reduced then stop and continue with PEG-interferon alone.

The patient was discharge after one month when her value were WBC 12.13 K\UI, platelet 174x10^3/mm^3. The patient remains on PEG-interferon once a week until the time of delivery. She went into labor when she was at 40th week of gestation. A healthy baby girl was delivered vaginally.

All of the measurements were normal in comparison to other neonates with a body weight of 2.989 kg, length 51 cm and a head circumference 35 cm. Afterwards, patient was discharged in a normal satisfactory condition with normal CBC readings. She again used oral contraceptives for three months post-partum. Her WBC was 4.46x10^3/mm^3 and platelet was 148. She refuses any family planning methods.

After seven-month, she got pregnant again, this time it was twins. She was on hydroxyurea during the pregnancy. The patient was induced and delivered by spontaneous vaginal delivery. Both twins are well and alive at 38th week.

Twins A: Weight: 2.865 kg, length: 53 cm, head circumference: 34 cm.

Twin B: Weight: 2.910 kg, length: 31 cm, head circumference: 35 cm.

The patient was discharged on hydroxyurea 500 mg PO BID, clexane 40 mg SC OD for six weeks, ferrous sulfate 200 mg PO BID. Her WBC count was 17.8 K/UI, and platelets were 145x10^3/mm^3 and hemoglobin was 13.9 g/dl.

This woman did not have surgical history and never had a history of blood transfusion. There was no family history of such disease or any cancer of any type. She did not have any known allergies to drugs or medications. She was not working, and she had never smoked. She used oral contraceptives before her first pregnancy for four months and before her second pregnancy for three months. None of her pregnancies was planned.

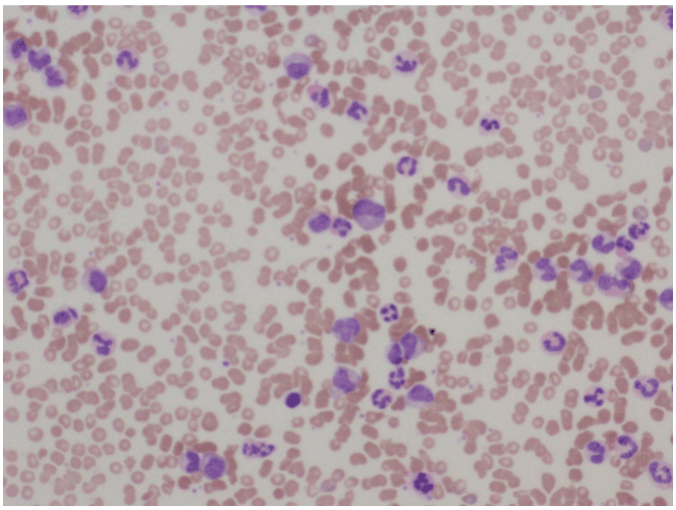

Figure 1: Blood film.

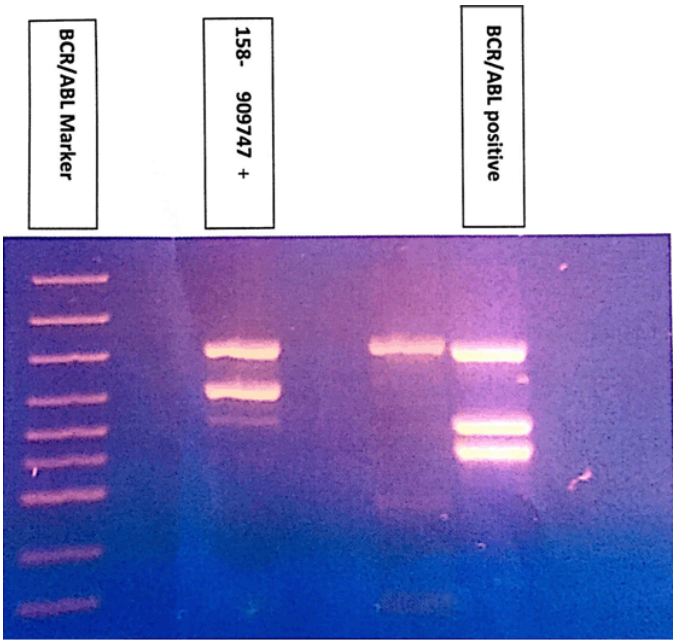

Figure 2: Chronic myelogenous leukemia.

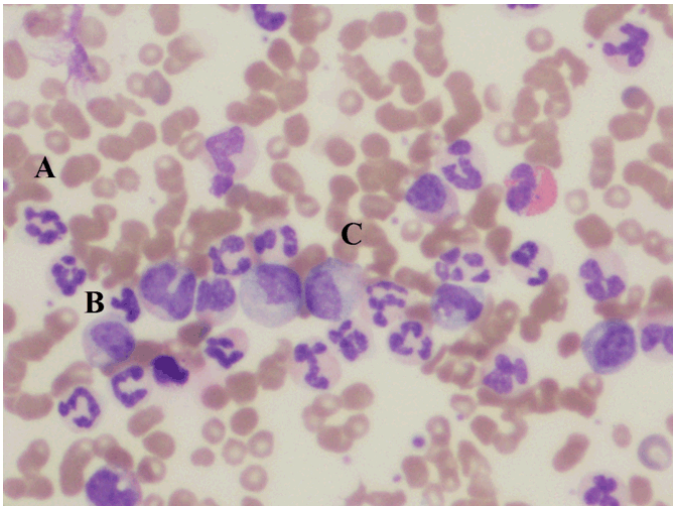

Figure 3: Peripheral blood (A) Neutrophil, (B) Metamylocyte, and (C) Mylocytcte.

DISCUSSION

Slowly progressing increase in white blood cells characterize the chronic myelogenous leukemia. It is a disease of middle age and rarely occurs in children [1].

Bones are either compact or spongy bone, and the center of bone (red and yellow) is called bone marrow. The red narrow responsible for blood stem cells produces RBC's, WBC's, and platelets; the yellow is responsible for fat. Leukemia affects the bone marrow in which spongy, red tissue fills the bones, provide the stem cells which is the derivative of red cells, white cells, and platelets. The stem cell is either a myeloid stem cell or a lymphoid stem cell. The lymphoid stem cell becomes white blood cell. However, the myeloid stem cell becomes mature red blood cells, platelets or granulocytes.

In chronic myeloid leukemia, many blood stem cells become white blood cells (granulocytes) and these are leukemic cells. Chronic myelogenous leukemia is a genetic but not inherited diseases with a defect in the chromosome 22 (abnormally short chromosome) (Philadelphia chromosome). This exchange of genetic information is BCR-ABL [2]. Our patient had a high count of WBC with BCR-ABL detected.

Clinical presentation is either asymptomatic or may present with general symptoms of weakness, tardiness, weight loss, fever and night sweats and pain [4].

Diagnosis includes history and physical examination, blood tests including complete blood count with differential, hemoglobin, and blood chemistry studies (bone marrow aspiration and biopsy). To examine the cytogenetic analysis: A test for the Philadelphia chromosome using either (fluorescence in situ hybridization) FISH or reverse transcription polymerase chain reaction test (RT–PCR).

The prognostic factor is age, the patient's general health, the size of the spleen, the phase of CML and the number of blasts in the blood or bone marrow. It is a reciprocal translocation between the long arms of chromosomes 9 and 22. The results is the Abelson (ABL) on chromosome 9 oncogene to an area of chromosome 22 (BCR) lead to the production of an abnormal tyrosine kinase protein that causes the disordered myelopoiesis found in CML [5].

Chronic myeloid leukemia in pregnancy is very rare disease, with an incidence of one per 100,000 pregnancies [6]. Pregnancy does not affect chronic myeloid leukemia leukapheresis, interferon, and hydroxyurea [7] used in the management of the initial chronic phase. The efficacy and safety of therapy during conception have not been adequately evaluated [8], because it is rare.

The management is a dilemma mainly if stay on medication may carry the risks of congenital defects and if it stops the medications and risk relapse [9]. The animal experiments have suggested an embryo-toxic effect of these agents; so during conception, targeted molecular therapies are not recommended [10]. It remains uncertain how these results apply to humans.

The diagnosis of CML is occasionally an incidental finding found in antenatal routine blood investigations during pregnancy [11]; as it happened in this case. Literature has no definitive consensus in the treatment of CML in pregnancy though some of the several different options are used [12].

PEG-Interferon (interferon-alpha; IFN-α), is the treatment of choice (non-transplant) for most patients with CML in pregnancy because it does not completely cross the placental barrier. The degree of response ranges from no 'hematologic' response to complete suppression. The mechanism is results of enhancement of 'immune' regulation and its selective toxicity against the leukemic cells and modulation of bone marrow [13].

Animal studies have shown that in high dose, it might lead to abortion in rhesus monkeys, and the small dose has no teratogenicity effects in rats and rabbits resulting in normal offspring.

Note; "the potential benefit justifies the potential risk to the fetus" [14].

Hydroxyurea is a cytotoxic drug that inhibits DNA synthesis by decreasing the production of deoxyribonucleotides by inhibition of the enzyme ribonucleotide reductase [15]. Up to 90% of CML patients treated with hydroxyurea may experience clinical and hematological remission. This treatment is not curative, does not prolong overall survival and only rarely results in attaining cytogenetic response [16].

This case is a fascinating case of a patient with who CML got pregnant twice, treated in her first pregnancy with interferon and the second pregnancy with hydroxyurea, and fetal outcome was excellent.

CONCLUSION

The diagnosis of chronic myelogenous leukemia during pregnancy is easy and different treatment regimen can result in a good prognosis.

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Author Contributions

Malak Alshammari – Substantial contributions to conception and design, Revising it critically for important intellectual content, Final approval of the version to be published
Ghazi Sindi – Substantial contributions to conception and design, Drafting the article, Final approval of the version to be published
Abdullah Khaled Agabawi – Substantial contributions to conception and design, Drafting the article, Final approval of the version to be published
Estabrq Al Hachim – Substantial contributions to conception and design, Revising it critically for important intellectual content, Final approval of the version to be published
Hassan S.O. Abduljabbar – Substantial contributions to conception and design, Drafting the article, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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