

Chronic Myeloid Leukemia in Pregnancy

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A forty-two-year-old, Para 5, abortion 4, Bangladeshi woman was a known case of Chronic Myeloid Leukemia (CML). She was diagnosed with CML eight years earlier during her last pregnancy. Termination of pregnancy was advised because the total blood count was suggestive of exacerbation of her condition and due to the teratogenic potential of the therapy she had received in early pregnancy.

The termination was not approved because the current pregnancy advanced uneventfully to 22 weeks, ultrasonographic screening of the baby was normal, her general condition was stable, blood count was restabilized and the patient was hesitant to have a termination. The pregnancy progressed uneventfully and she delivered normally at 38 weeks of pregnancy.

Bahrain Med Bull 2014; 36(1):

Leukemia during pregnancy is a rare condition. In Salmaniya Medical Complex (SMC), which is the main referral hospital in Bahrain, there has been, as far as we are aware of, only one case of leukemia in pregnancy during the last two decades. Chronic Myeloid Leukemia (CML) is one tenth of all leukemias in pregnancy, while the lymphocytic type is extremely rare¹⁻².

The main challenges of dealing with such conditions are: the potential of immediate and long-term hazards of leukemia therapy to the fetus, such as the need for joint supervision by the obstetrician and the hematology oncologist, timing and mode of delivery and the postnatal care^{3,4}.

The aim of reporting this case is to highlight the difficulties encountered in dealing with such cases especially the patient's health needs and treatment guidelines of CML during pregnancy.

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THE CASE

A forty-two-year-old, Bangladeshi woman, Para 5, abortion 4, was referred from the hematology clinic to antenatal clinic in her twentieth week of gestation for urgent consideration of pregnancy termination because of an episode of leukocytosis.

She was diagnosed in 2004, during her last pregnancy, following a bone marrow biopsy, to have a myeloproliferative disorder suggestive of chronic myeloid leukemia (CML). She was also found to have hypothyroidism. The treatment options were discussed with the couple which included bone marrow transplant, interferon and Imatinib mesylate (Glivec®). The patient opted to continue the pregnancy and to be treated with hydroxyurea 500 mg capsules (USP) twice daily and interferon alpha 29 Pegasys 180 mg subcutaneous injection weekly. Complete hematological remission was achieved and there was no evidence of splenomegaly. Patient delivered normally at term.

In 2007, chromosomal analysis showed Philadelphia positive cells line, which is found in 90% of patients with CML. The karyotype was reported as: 46 XY, t (9; 22) (q34; q11.2)⁹.

In 2010, she was put on Glivec 400 mg and Aspirin 81 mg daily. In the interim period, she had been irregular in her therapy because of the cost incurred. From 2007, she was started on Interferon, Imatinib and Aspirin. The patient remained in remission until the fourth pregnancy. In the present pregnancy, her medications included Glivic® (Imatinib mesylate) 400 mg once daily and Aspirin 81 mg (Aspicor®) tab daily. She also received interferon subcutaneous injections weekly. At 24 weeks, she was referred to Obstetrics for termination of pregnancy because of an episode of marked leukocytosis.

Blood group A, Rh positive, Hct. 29.1%, antibodies screening was negative, peripheral blood was normal, liver function tests were normal, prothrombin time and APTT were normal. White blood count, Hb, platelets, urea, electrolytes and creatinine were normal. Dimers, HIV and hepatitis HBsAg were negative.

The fetal ultrasound was normal, WBC count was falling and the pregnancy was proceeding normally. At that time, she was not taking any medicine because of financial reasons. The medications were issued to her free of charge. By then, the pregnancy progressed to 24 weeks and near viability of the fetus. She attended both the antenatal and the hematology oncology clinics regularly. Her blood count returned to normal and fetal well-being was normal.

She went into spontaneous labor at 38 weeks and delivered a live and healthy female baby. The postpartum period was uneventful and the patient was offered a family planning advice.

DISCUSSION

The association of chronic myeloid leukemia (CML) with pregnancy is rare (1/70-100,000) and it approximately occurs in 10% of all leukemias complicating pregnancy^{1,2}. CML is slightly more common in males than in females occurring usually in older age groups. In our patient, the

disease was diagnosed in the second trimester of her fifth pregnancy. The patient was 35 years old, which is relatively young age for CML.

CML is divided into three phases based on clinical symptoms and laboratory investigations. Without treatment, this disease begins with the chronic phase and over the course of several years it progresses to the accelerated phase and eventually to the blast crisis, which is the terminal phase⁵. Treatment usually halts the progress of this disease. Current treatment of CML, without pregnancy, includes antineoplastic preparations such as hydroxyurea, Busulfan, bone marrow transplant, leukapheresis, alpha interferon and Imatinib myselate⁶. The teratogenic side effects of antineoplastic drugs are well-documented. There is an evidence that exposure to Busulfan during pregnancy has teratogenic effects, both in the short and long-term on the new born⁷. Information about the teratogenic side effects of hydroxyurea in pregnancy indicates that it should not be used, but recent studies suggested that the incidence is dose-related and dependent on the duration of exposure. Exposure, however, must not be a justification for termination of pregnancy but a careful follow-up, clinical and ultrasonic examination. Chromosomal analysis of the newborn was suggested because of the findings in animal experiments which indicated that there is teratogenic effect of interferon use in pregnancy⁸⁻¹⁰.

Imatinib is the most promising development in the anti CML drug therapy. In fact, it is the first class of the new drugs that act by specifically inhibiting tyrosine kinase receptor. It is relatively safe in pregnancy than other cytotoxic drugs used in CML^{11,12}.

CONCLUSION

Cases of chronic myeloid leukemia in pregnancy should be evaluated jointly by an obstetrician and gynecologist, hematologist, oncologist and social worker. The patient must also make an informed decision regarding her future fertility and family planning. Economic status of these patients, particularly among migrant workers should not preclude their access to effective and safe anti-cancer drugs.

Author contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential conflicts of interest: None.

Competing interest: None. **Sponsorship:** None.

Submission date: 17 September 2013. **Acceptance date:** 29 December 2014.

Ethical approval: Obstetrics and Gynecology department, SMC, Bahrain.

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