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Case Report

Successful pregnancy outcome in a patient of chronic myeloid leukemia on imatinib therapy

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ABSTRACT

Pregnancy and cancer is a complex situation. The coincidence chronic myeloid leukemia (CML) and pregnancy is an uncommon event, in part because CML occurs mostly in older age group. The management of CML, during pregnancy is a difficult problem because of potential effects of therapy on the mother and foetus. Imatinib, a tyrosine kinase inhibitor induces dramatic hematologic and cytogenetic responses in CML, but it is not recommended for use in pregnancy or if the patient plans to conceive. In literature there are very few reports of successful outcome of pregnancy while on imatinib. In this report we describe a successful pregnancy and labor under treatment with imatinib in a known case of CML.

Keywords: CML in pregnancy, Imatinib in pregnancy, Safety of imatinib

INTRODUCTION

Pregnancy and cancer is a complex situation. Treatment cannot be delayed and cytotoxic treatment often requires termination of pregnancy.¹ Chronic myeloid leukaemia (CML) is a myeloproliferative disorder with clonal expansion of transformed primitive hematopoietic progenitor cells. The management of CML during pregnancy is a difficult problem because of potential effects of therapy on mother and foetus¹. Pregnancy does not appear to affect the course of CML, there is still a risk of leukostasis as well as risk of placental insufficiency with consequent below normal fetal birth weight, increased prematurity, and increased mortality if CML left untreated for the duration of pregnancy.²

Imatinib mesylate (ST1571, Gleevec, Novartis) entered clinical trials in 1998 and has since been shown to induce dramatic hematologic and cytogenetic response in CML.³ Imatinib has been found to be antiangiogenic in animal models. The antiangiogenic effect is mediated by platelet derived growth factor receptor (PDGFR); however it does not affect human umbilical vein endothelial cells as they

do not express PDGFR. Imatinib has been found to be teratogenic in rats at doses above 100 mg/kg but not at doses up to 60 mg/kg. The teratogenic effect observed are encephalocele, anencephaly, and reduced or absent parietal bones in animal studies.⁴

Imatinib is not recommended for used during pregnancy or if patient plans to conceive. There are very few reports of successful outcome of pregnancy conceived while on imatinib. We report a case of successful pregnancy outcome in patient with CML while on imatinib.

CASE REPORT

A 24 year old primigravida attended antenatal clinic of Zenana hospital attached to S.M.S. Medical College at 20 weeks of gestation. The patient was married for 1 year. In her past she attended local physician for dragging pain in the left upper abdomen 2 yrs back and was found to have moderate splenomegaly. Subsequent peripheral blood smear and bone marrow examination confirmed it to be a case of Philadelphia chromosome positive CML. She was prescribed imatinib 400mg once daily by haemato-

oncologist. She had her routine check-up by hematologist every 6 months. This was her spontaneous conception and before conception she was in complete remission of haematological and major molecular phase. On general physical examination no abnormality was detected. Uterus was 18 weeks size. Opinion of the haematologist was immediately sought. Complete hemogram showed Hb-10.3 gm%, Hct-28.2%, MCV-94.3 fl, MCH-33.4 pg/ml, WBC-13490/mm³, platelets-242×10³/L, and differential count showed N 81 L15 M03 B04 E01, PBF showed RBCs were normocytic normochromic, neutrophilic leucocytosis, platelets were adequate no abnormal cells were seen. Blood biochemistry revealed normal liver function tests, and blood sugar, urea, creatinine and uric acid levels were 133 mg%, 24 mg%, 0.8 mg%, 11 mg%, respectively. No gross congenital malformation was noted on level 2 scan. As she reported at 20 weeks of gestation and was anxious for issue decision to continue pregnancy on imatinib was taken after counselling regarding potential threat to her and risk of teratogenicity associated with imatinib. The patient was kept under close monitoring till term her monthly antenatal and haematological controls were within normal limits. Her Hb% remained around 10 gm%, WBC count varied between 15000-20000/mm³, blood biochemistry remained normal. She had leaking at 37 weeks and delivered vaginally a healthy female child of 2.3kg. Counselling was done regarding contraceptive measures. After 1 week, she was discharged from hospital on imatinib as advised by the haematologist and was asked to attend haematology outpatient department and well baby clinic regularly.

DISCUSSION

The coincidence of CML and pregnancy is an uncommon event CML occurs mostly in older age group. In contrast this patient presented at younger age.¹ In this case patient reported in second trimester and wanted to continue pregnancy even after counselling. CML has been treated during pregnancy with busulfan, alpha-interferon, hydroxyurea and leukapheresis. Unfortunately, the potential teratogenic effects of chemo-therapy on the fetus make their use during pregnancy much less attractive. Hydroxyurea is a cytotoxic drug, which inhibits DNA synthesis and is capable of crossing the placenta. Hydroxyurea treatment should be avoided in first trimester and could be given to patients who cannot tolerate interferon therapy during second or third trimester.⁵

Interferon-alpha (IFN- α), an immune modulator, does not cross the placenta to a great extent due to its high molecular weight (19 kda) and does not inhibit DNA synthesis in the fetus. No fetal malformations were reported when interferon was administered as monotherapy. All reported cases of pregnant women with CML, treated with interferon, resulted in healthy babies and normal maternal outcomes. Given the available preclinical and clinical data, interferon can be safely

administered throughout pregnancy and it is the treatment of choice for patients diagnosed with CML in pregnancy.⁶

Administration of imatinib mesylate, a Bcr-Abl tyrosine kinase inhibitor, during the first trimester is associated with a considerable risk of congenital anomalies and spontaneous abortions, while late exposure does not have the same impact. It has been reported that the concentration of imatinib mesylate and its active metabolites were higher in the placenta than in the maternal blood, while they were low or undetectable in the umbilical cord.⁷ Although these findings suggest limited placental transfer of imatinib mesylate in late pregnancy it should not be the treatment of choice because of the high risk for malformations during first trimester.⁸ Fortunately in our case no potential side effects were observed on mother and foetus and pregnancy was uneventful on imatinib therapy.

CONCLUSION

In conclusion, like the other successfully treated cases reported in literature and our own, we would suggest that the use of imatinib can be considered for treatment of CML as early as first trimester of pregnancy and that it may be successfully continued throughout the pregnancy. Further studies may be needed to prove the safety profile of imatinib during first trimester with the main aim of a healthy mother and a healthy infant in both the short and long term.

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REFERENCES

1. Peleg D, Ben-Ami M Lymphoma and leukemia complicating pregnancy. *Obstet gynecol clin North Am.* 1998;25:365-81.
2. Buekers TE, Lallas TA. Chemotherapy in pregnancy. *Obstetgynecolclin North Am.* 1998;25:323-9.
3. Ali R, Ozkalemkas F, Ozcelik T. Pregnancy under treatment of imatinib and successful labor in a patient with chronic myelogenous leukemia (CML). Outcome of discontinuation of imatinib therapy after achieving a molecular remission. *Leuk Res.* 2005;29(8):971-73.
4. Prabhash K, Sastry PS, Biswas G. Pregnancy outcome of two patients treated with imatinib. *Ann Oncol.* 2005;12:1983-4.
5. Thauvin-Robinet C, Maingueneau C, Robert E, Elefant E, Guy H, Caillot D. Exposure to hydroxyurea during pregnancy: a case series. *Leukemia.* 2001;15:1309-11.
6. Rizack T, Mega A, Legare R, Castillo J. Management of haematological Malignancies during pregnancy. *Am J Hematol.* 2009;84:830-41.
7. Russell MA, Carpenter MW, Akhtar MS, Lagattuta TF, Egorin MJ. Imatinibmesylate and metabolite

concentrations in maternal blood, umbilical cordblood, placenta and breast milk. *J Perinatol.* 2007;27:241-3.

8. Shapira T, Pereg D, Lishner M. How I treat acute and chronic leukemia in Pregnancy. *Blood Rev.* 2008;22:247-59.

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