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Case Report

Successful outcome of pregnancy with chronic myeloid luekamia with preterm premature rupture of membranes

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ABSTRACT

The concomitant occurrence of pregnancy and chronic myeloid luekamia (CML) is uncommon and hence its management often poses a dilemma due to limited data available for the same. There is also very sparse data available with respect to the use of imatinib in pregnancy (which is usually the mainstay in the management of CML with few case reports suggesting congenital anomalies in the fetus. We presented a case report of a known case of CML who was in the chronic phase on tablet imatinib 300 mg OD. She presented with preterm premature rupture of membranes (PPROM) at 28 weeks and was given conservative management for the same, she went into preterm labour at 32 weeks and delivered vaginally a healthy 1.8 kg male baby without any intrapartum or postpartum complications. Both mother and baby were in good health at six month follow up. We had to weigh carefully the risks of immune-compromised state of the patient versus the complications of preterm delivery and tread through the management of this particular case. Use of imatinib did not cause any obvious congenital malformations in the baby.

Keywords: Chronic myeloid leukaemia, Imatinib, Preterm premature rupture of membranes, Hydroxyurea

INTRODUCTION

Chronic myeloid leukaemia (CML) is a myeloproliferative disorder with clonal expansion of transformed primitive haematopoietic progenitor cells in which there is an exchange of genetic material between chromosome 9 and 22.[1]

The incidence of CML in pregnancy is rare and occurs in 1 in 10000 cases, this is because CML commonly presents in the older age groups.[1] Thus, the management of such a case poses a definite therapeutic dilemma.

CASE REPORT

A 23 year old lady was referred to our hospital at 28 weeks. She presented with complaints of leaking per vagina since 4 hours and abdominal discomfort. Antenatally she was following up in a primary health care center. She was diagnosed of CML two years back and was following up in Tata Memorial Hospital for the same and presently she was in the remission phase. She had conceived on tablet imatinib 300 mg (once daily) which had been continued in pregnancy.

She was admitted in the antenatal ward and given conservative management with injectable antibiotics to prevent ascending infections and steroids for fetal lung maturity. Regular ultra sonographies and non-stress test were performed to assess fetal well-being. Weekly complete hemograms were done to detect blast crisis. Serial total and differential count assessments were done to rule out leukocytosis. Daily clinical monitoring was done to rule out any signs of impending chorioamnionitis.

Patient was thereby conservatively managed for 4 weeks, however at 32 weeks she spontaneously went into preterm labor. The course of labor was uneventful and she delivered vaginally a healthy 1.82 kg male baby with an Apgar score of 7, 9. Baby did not have any congenital anomalies and was shifted to neonatal intensive care unit in view of low birth weight and prematurity.

Puerperal course was uneventful, imatinib was continued postnatally in view of which breast feeding was avoided. She was discharged on the ninth postnatal day on hematinics and subsequent follow-up at 6 weeks showed the mother and baby in good health.

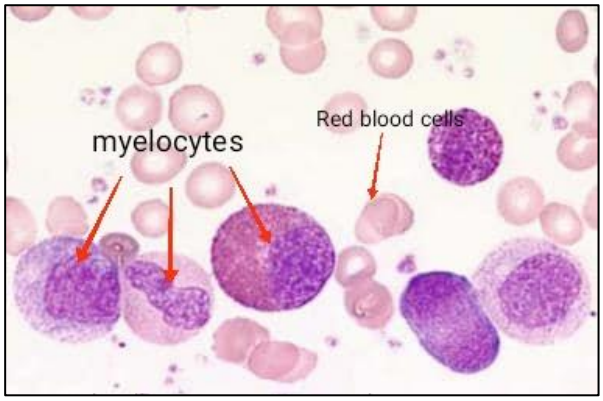

Figure 1: Peripheral smear in patient with CML (chronic phase).

DISCUSSION

Pregnancy as such does not affect the course of CML. However obstetric complications like low birth weight, fetal prematurity, increased perinatal and maternal mortality can be seen in some patients, and the common denominator could be attributed to uteroplacental insufficiency which results due to haemostasis from the uncontrolled myeloproliferation seen in CML.[2]

CML presents in three phases. A chronic stable phase, accelerated phase and a blast crisis in which it transforms into AML or ALL.[3] It commonly presents in the 4th or 5th decade of life, hence its occurrence is rare in pregnancy.[3] Symptoms are generally non-specific like abdominal distension, post prandial fullness, gastric reflux, fever, weight loss, fatigue and malaise.[3]

The management of CML during pregnancy is a difficult problem because of the potential adverse effects of therapy on the mother and fetus.[4]

Management options include: (a) luekapheresis: can be considered as early as in the first trimester because of lack of teratogenic and other adverse effects; (b) hydroxyurea: it is a cytotoxic drug that inhibits DNA synthesis. It rarely results in attaining cytogenetic response. Risk of minor anomalies (hip dysplasia, pilonidal sinus) is present and hence avoided in first trimester, however in second and third trimester it is relatively safe; (c) interferon: this drug inhibits cell proliferation by its effect on protein synthesis by causing RNA degradation and possibly by immune system modulation. It however doesn't inhibit DNA synthesis. It doesn't cross the placental barrier due to its high molecular weight. No mutagenicity/teratogenicity is noted and hence is relatively safe in pregnancy; (d) imatinib: it is a tyrosine kinase inhibitor (TKI) which induces a dramatic haematological and cytogenetic response in patients with CML. It acts by inhibiting BCR-Abl and also other related proteins such as c-KIT, PDGF (alpha and beta) and other related proteins.[4-7]

It's safety in pregnancy is limited to a few case reports. A risk of possible congenital anomalies like skeletal malformations (premature closure of skull sutures, craniosynostosis, absent hemivertebrae and shoulder anomalies), renal malformations (duplex kidney, renal agenesis, hypoplastic kidneys) and gastrointestinal anomalies (exomphalos, omphalocoele).

When a patient conceives on TKI the difficulty lies in balancing the risk to the foetus v/s risk to the mother of treatment interruption and disease progression.[8] According to limited data available it is still questionable whether patients who conceive while on imatinib should discontinue treatment because of the high risk of disease progression following imatinib cessation.[8] Most studies have reported disease progression following imatinib discontinuation.[8]

Numerous studies have been performed to assess the safety of imatinib. Studies done by Ault et al, Pye et al showed that most women had a successful outcome however exposure was still associated with increased risk of fetal malformations.[9,10] Russel et al described two patients exposed to imatinib in third trimester, imatinib was found to be in higher concentrations in maternal blood and placenta and lower concentrations in fetus and cord blood suggesting that it crosses placenta poorly.[11] A recent study by Irrappa et al studied 10 patients who took imatinib in pregnancy.[12] 7 patients had normal term deliveries, one had a preterm delivery, two had congenital malformations (omphalocoele and craniosynostosis).[12]

Interferon alpha seems to be the only safe treatment during pregnancy and is the treatment of choice in all trimesters. Also some case reports have been there where in plasmapheresis was done in pregnancy and chemotherapy was discontinued which also met with favourable outcome.

In our patient we continued imatinib throughout pregnancy and there were no structural or functional defects in the baby which may suggest its safety in pregnancy. There was no disease progression/exacerbation in the mother .This case was made further precarious due to simultaneous occurrence of PPROM. No case reports are available yet of such simultaneous occurrence for comparative analysis. It can be suggested that PPROM can be managed with

similar guidelines as that followed in uncomplicated pregnancies as was done in our case weighing the potential risks of prematurity and maternal infection trying to attain an interim balance between the two.

CONCLUSION

The risk of CML in pregnancy is a challenge owing to limited data with respect to modality of therapy. This case was further complicated with simultaneous occurrence of PPROM considering the immune-compromised condition of the patient, however we satisfactorily dealt with the uphill task of delivering a healthy baby with no maternal complications.

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