Original Article

Leukaemia with pregnancy managed at B. P. Koirala Memorial Cancer Hospital

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ABSTRACT

Abstract: Leukaemia during pregnancy is rare, occurring approximately one in every 75,000 to 100,000 pregnancies annually. Chemotherapeutic agents may have harmful effects to the developing baby though leukaemia itself rarely harms the baby. There is no evidence that pregnancy accelerates the progression of disease or affects the outcome. However, treatment dilemmas often occur.

Aims: To study the clinical presentation, treatment and outcome of leukaemia with pregnancy managed at B. P. Koirala Memorial Cancer Hospital (BPKMCH).

Methods: Descriptive study was conducted at BPKMCH. Case records of women with cancer and pregnancy from January 2006 to February 2013 were analyzed regarding their clinical details, treatment, follow-up and feto-maternal outcome.

Results: Six women, of 20 to 28 years had leukaemia with pregnancy among which four were chronic myeloid leukaemia (CML), one was acute lymphocytic leukaemia (ALL) and acute myeloid leukaemia (AML) each. All four cases of CML had conceived while on oral Imatinib; the three case diagnosed in the first trimester opted for immediate termination of pregnancy while the fourth one diagnosed at 22 weeks of pregnancy continued pregnancy and delivered at 34 weeks by emergency caesarean section for severe oligohydramnios. The ALL case diagnosed at 26 weeks of pregnancy wanted termination of pregnancy and immediate induction chemotherapy. The AML case diagnosed at 32 weeks of pregnancy desired to undergo induction chemotherapy with pregnancy but she defaulted treatment and had intrauterine fetal death and died due to postpartum haemorrhage. The baby, delivered to a mother exposed to Imatinib throughout pregnancy, till date has normal growth and development. Five mothers are in remission.

Conclusions: Leukaemia with pregnancy, more common in younger women is rare and posed treatment challenges. Definitive treatment should be individualized according to the desire of the pregnant woman and should include a multi- disciplinary team.Termination of pregnancy in favour of definitive chemotherapy to mother is better and easier during the first trimester of pregnancy. Because of teratogenic effects of chemotherapy, effective contraception be used during therapy to prevent pregnancy.

Keywords: Chemotherapy, Leukaemia, Pregancy

Introduction

Cancer diagnosed during pregnancy is rare with approximate occurrence of only 0.1% of pregnant women. Common malignancies associated with pregnancy are cervical and breast cancer, melanoma, lymphomas (1:1000–1:6000 pregnancies) and acute leukaemia (1:75,000–1:100,000). [1]

The presentation of acute leukemia in pregnancy is broadly similar to the non pregnant state, although pregnancy may obscure some of the clinical signs. The

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majorities of the leukaemia diagnosed in pregnancy are acute myeloid leukemia (AML). If the disease is left untreated likely to endanger both mother and fetus life[2] and further delay in initiation of chemotherapy negatively impact the outcome of treatment.

AML occurs more frequently with advancing age and treatment can't be delayed due to aggressive behaviors. If the treatment is initiated on time, prognosis for women with pregnancy will be compare to the non-pregnant patients[3]. The long term side effects and infertility should be considered while giving chemotherapy, although recent leukemia remission-induction regimen may not induce infertility. However, existing protocol for treating AML include cytarabibe and daunorubicin, both agents are well recognized to cause fetal abnormalities[4] which warrants cautious use during pregnancy, especially in the first trimester.

During the period of first trimester most of the organogenesis occurs which is associated with adverse effect of traditional chemotherapy. The decision to treat AML in the first trimester with the regime containing anti-metabolites, the most effective therapeutic option, must be accompanied by careful counseling of the mother and that will choose the termination of pregnancy[5]. Exposures after first trimester with chemotherapy result in increase intra uterine growth retardation[5]. Early deliveries may be considered if the leukemia presents sufficiently late in pregnancy.[5] In second and third trimester, the patients should be counseled about the possible adverse events and if not possible chemotherapy can be introduced with regular survilance.[5]

In Acute promyloblastic leukemia there is fear of further complication with coagulopathy in pregnancy, labour and delivery. Standard treatment in addition with coagulation support is treatment with ATRA and idarubicin both could pose problem in pregnancy. There are many fetal malformations with ATRA; therefore European Leukemia net recommended avoidance of ATRA in the first trimester and women are best counselled for termination.[6]

Acute lymphoblastic leukemia (ALL) is more common in early age. Management of ALL involves longer course of induction, consolidation and maintenance phase with intrathecal chemotherapy and even prophylactic cranial radiotherapy. The regular regime with curative intent contains high dose methotrexate regime which may not be possible to be given during pregnancy due to its known adverse events. Patients diagnosed at later weeks of pregnancy may be given modified treatment without methotrexate.[5] A brief period of prednisolone alone during the early gestation period till 20 weeks and less intensive chemotherapy till delivery to less aggressive disease could be safer treatment option.[7]

Chronic Myeloid leukemia (CML) accounts for 15% of adult leukaemias. Only small populations are diagnosed during child bearing age. Therapeutic approach for CML in pregnancy have included supportive care in the form of leukopheresis and chemotherapy like hydroxyarbamide , interferon Alpha and Imatinib.[5] In early pregnancies Imatinib may cause serious fetal anomalies which raises serious concerns. For the women with CML in first trimester with less than 100000/mm^3 WBC counts and Platelets counts less than 500,000/mm^3 treatment may be postponed till the second trimester. Frequent leucopheresis, a low dose heparin as well as aspirin can be used once platelets more than 1000000/mm^3. [5] Chronic lymphocytic leukemia and Hairy cell leukemia are rare in pregnancy and are indolent in nature, requiring only supportive care till the safe confinement.[5] However, there could be problem in caring these patients with antibiotics and anti fungal agents.

Breast feeding during chemotherapy is associated with increased toxicities to neonate due to the general fact that (less that 5% of weight adjusted maternal daily dose) most medicines are excreted in breast milk. It is advisable not to breast feed during chemotherapy or begin breast feeding only two weeks after chemotherapy.[7]

Diagnosis of leukaemia during pregnancy creates a difficult situation to the patient, her family and the treating medical team due to the concerns of the patient's health and that of the baby. The involved treatment could raise the chances of birth defects or even fetal demise.[8] The treatment decision and execution should involve multidisciplinary team consisting of haemotologist, obstetrician, pediatrician, pathologist, psychiatrist, counsellor, nurses and family members for the desired and optimal outcome of the woman and her baby.

Aims

To study the clinical presentation, treatment and outcome of leukaemia with pregnancy managed at B. P. Koirala Memorial Cancer Hospital.

Methods

Descriptive study was conducted at B. P. Koirala memorial cancer hospital. Case records of women with cancer and

pregnancy from January 2006 to February 2013 were analysed regarding their clinical details, treatment, follow-up and feto-maternal outcome. The treatment plan and decision involved medical oncologist, obstetrician-gynecologic oncologist, pediatric oncologist, pathologist, nurses, social service staff and family members. The treatment with chemotherapy was commenced after the informed written consent of the patient and her family member. Termination of pregnancy (induced abortion or delivery) was done in institute; either in our center or university hospital. The delivered babies were assessed and followed up by the pediatrician for any defects or deviation from normal developmental milestone.

Results

Six women, of 20 to 28 years had leukaemia with pregnancy among which four were chronic myeloid leukaemia (CML), one was acute lymphocytic leukaemia (ALL) and acute myeloid leukaemia (AML) each.

Women in our study were young ranging from 20 to 31 years of age all gravida second or third as shown in table below.

Table 1. Characteristics of patients with cancer during pregnancy (n=6)

SN	Age in Years	Parity	Leukaemia Type	Gestation at Diagnosis	Definitive Treatment	Fetal Outcome	Maternal Outcome
1	20	G2P1+0	CML	8 weeks	Gleevac (Imatinib)	Induced Abortion	Remission
2	20	G2P1+0	CML - CP	9 weeks	Gleevac (Imatinib)	Induced Abortion	Remission
3	31	G2P1+0	CML - CP	22 weeks	Gleevac (Imatinib)	Em. LSCS at 34 weeks; 1900 gms, female with good APGAR	Remission
4	25	G3P1+1	AML-M2	32 weeks	Induction Chemo-therapy (Left against medical advice)	Intra-uterine Fetal Death	Mortality due to Post Partum Hemorrhage
5	26	G3P2+0	CML	12 weeks	Gleevac (Imatinib)	Induced Abortion	Remission
6	28	G3P2+0	ALL	26 weeks	Induction Chemo-therapy	Induced Abortion	Remission

Three cases (50%) were diagnosed to have leukaemia during the first trimester and all of them had opted for termination of pregnancy and definitive treatment then after. Among the two women diagnosed to have leukaemia during the second trimester, one with ALL had immediate termination of pregnancy as per her wish of undergoing induction chemotherapy. The woman with CML on Imatinib therapy wished to continue treatment with co-existing pregnancy and she had an emergency caesarean delivery for severe oligohydramnios at 34 weeks of pregnancy.

All four cases of CML had conceived while on oral Imatinib; the three case diagnosed in the first trimester opted for immediate termination of pregnancy while the fourth one diagnosed at 22 weeks of pregnancy desired for continuation of pregnancy. The ALL case diagnosed at 26 weeks of pregnancy wanted termination of pregnancy and immediate induction chemotherapy. The AML case diagnosed at 32 weeks of pregnancy desired to undergo induction chemotherapy with pregnancy but she defaulted treatment and had intrauterine fetal death and died due to postpartum haemorrhage.

The baby, delivered to a mother exposed to Imatinib throughout pregnancy, till date has normal growth and development. Five mothers are in remission.

Discussion

Leukaemia with pregnancy is rare, occurring approximately one in every 75,000 to 100,000 pregnancies annually.[1] There is no evidence that pregnancy accelerates the progression of disease or affects the outcome. However, leukaemia often presents as a medical emergency and induction of appropriate therapy must be initiated promptly, irrespective of the gestational age. The treatment could yield poor outcome if delayed.

The majority (90%) of cases of leukaemia during pregnancy are acute leukaemia, of which two-thirds are AML and one-third ALL.[9] In our study, CML was reported more often (66.6%).

Leukaemia can itself or chemotherapy given may complicate pregnancy. The timing of fetal exposure to the chemotherapeutic agents is one of the most

important determinants of pregnancy outcome. In the first trimester, exposure to chemotherapy can result in congenital malformations or abortion. The risk of congenital malformations like cranial anomalies, cleft palate, anencephaly, and micrognathia has been reported to be as high as 17%.[10] Women diagnosed to have leukaemia in early pregnancy, are better managed with termination of pregnancy which was followed in our cases to avoid teratogenic effects and also begin definitive treatment without undue delay.

Chemotherapy can be safer to women during the second and third trimesters of pregnancy[11] though there could be a greater risk of stillbirth, growth retardation, premature birth and maternal and foetal myelo-suppression. Two of our cases in later half of pregnancy underwent chemotherapy. The AML case diagnosed at 32 weeks of pregnancy desired to undergo induction chemotherapy with pregnancy. Later she defaulted treatment and had intrauterine fetal death and died due to postpartum haemorrhage.

The treatment during pregnancy does not appear to have a significant impact on the future growth and development of the child which were observed in our case of CML who continued Imatinib throughout pregnancy as well.

Conclusions

Leukaemia with pregnancy, more common in younger women is rare and posed treatment challenges. Definitive treatment should be individualized according to the desire of the pregnant woman. The therapeutic decision should involve a multi- disciplinary team including medical oncologist, obstetrician-gynecologic oncologist, pediatric oncologist, pathologist, nurses, social service staff and family members also. Termination of pregnancy in favour of definitive chemotherapy to mother is better and easier during early pregnancy. Because of teratogenic effects of chemotherapy, effective contraception be used during therapy to prevent pregnancy.

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