Acute leukemia and pregnancy

Case report

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Summary: In this case report we describe a case of acute myeloid leukemia (AML; FAB M4) diagnosed in a 27-year-old female at the 20th week of gestation.

After informed consent, the patient chose to undergo anti-leukemic treatment without therapeutic abortion. Complete remission was obtained following standard chemotherapy for AML (doxorubicin, cytosin-arabinoside, 6-thioguanine). The patient succesively underwent an autologous bone marrow transplant (ABMT). No fetal malformation was observed. Urgent cesarean section was necessary at the 29th gestational week because of the onset of foetal sufference. Fourteen months after diagnosis and seven months after ABMT the patient died due to relapse of AML. The child is presently 3.5 year old and well.

In our opinion, the care of a pregnant woman with acute leukemia is feasible and it needs a multi-specialist effort that is easier to be achieved in a tertiary care institution.

Key words: Acute leukemia; Pregnancy; Chemotherapy.

INTRODUCTION

A 27 year old female at the 20th week of pregnancy was admitted to our Hematology Unit with the suspicion of acute leukemia in January 1992. The patient had a recent history of persisting cough and "flu-like" syndrome. The clinical examination showed gum infiltration and moderate hepatosplenomegaly. No cutaneous haemorrhage nor lymphnode enlargement were present.

The haemocromocytometric values were: Hb 7.3 g/dl, leukocytes 38.5×10^9/L and platelet count 44×10^9/L.

Aperipheral blood smear showed 50% of blast cells with basophilic cytoplasm containing rare azurofilic granules, a kidney-shaped nucleus with one or two nucleoli. The bone marrow (BM) was packed by cells with the same morphological features, exihibiting nonspecific esterase and myeloperoxidase positivity in 40% and 20% of the blast cells respectively.

Cytofluorimetric analysis of cell suspension obtained from the BM aspirate showed an immunophenotype consistent with the diagnosis of acute myeloid leukemia (positivity for CD15, CD11C, CD13, CD33 and negativity for lymphoid markers).

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Seric lysozyme was high (25 μg/L). The cariotype was hyperdiploid (47, XX).

On the basis of clinical, morphological, cytochemical and immunophenotypic features, diagnosis of acute myeloid leukemia (FAB: M4) was made.

The chest radiograph was normal. Abdominal ecotomography showed hepatosplenic enlargement, celiac and hepatic hilus lymphoadenopathy. Pelvic ultrasonography revealed a normal fetus according to the gestational age.

Laboratory tests showed that the patient was an asymptomatic carrier for hepatitis B virus (HBs Ag positive, HBcAb positive, HBsAb negative, HBeAb positive, HBe Ag negative, HBcAb IgM negative).

Having been informed about the diagnosis and the possible maternal and foetal risks of chemotherapy, the patient chose to undergo chemotherapy and to continue the pregnancy.

From the beginning of treatment the foetal biophysical profile was evaluated weekly and birth was planned for the 30th - 32nd week of gestation.

Following the first chemotherapy course (D2AT7 regimen: doxorubicin 35 mg/sqm i.v., 1-2 days; cytosin-arabinoside 100 mg/sqm two hours infusion twice daily, 1-7 days; 6-thioguanine 100 mg/sqm orally twice a day, 1-7 days), which was not associated with major side effects, a complete remission (CR) was obtained.

During the aplasia induced by the second course of chemotherapy (doxorubicin 50 mg/sqm i.v., day 1; vincristine 1.3 mg/sqm i.v., day 2; cytosin-arabinoside 500 mg/sqm 2 hours infusion twice daily, 3-8 days, at the 29th week, before foetal lung maturity (amniotic fluid lecitin/sphingomyelin ratio) could be evaluated, strumental signs of foetal sufferance appeared as documented by ultrasonography and cardiotocography. The patient underwent urgent caesarean section.

The foetus, female sex, weighing 1000 g, Apgar index at 1 minute of 6, and macroscopically normoformed, was admitted to the Neonatology Unit. Hyaline membrane disease and moderate meningeal haemorrhage were diagnosed. Haemogram was normal.

No leukemia infiltration was documented at the placenta histological examination.

Subsequently, with appropriate therapy, the child's clinical condition improved and she survived without damage.

Ten days after delivery the patient was discharged from CR and readmitted two weeks later to complete the induction treatment by a consolidation course.

After subsequent aplasia, BM harvesting was performed in view of the autologous BM transplant (ABMT) as a consolidation treatment, since the patient had no identical HLA sibling for allogenic BM transplant.

Soon after the BM collection, marked elevation of serum transaminase was observed; bilirubin, alkaline phosphatase, cholinesterase and gamma-glutamyl transpeptidase were normal. No further chemotherapy was administered for three months until transaminase normalized.

In September 1992, ABMT was performed while the patient was in CR. Conditioning treatment (BAVC protocol; *BCNU, ARA-C, VP16, CTX*) and BM reinfusion were performed and full BM recovery was observed 20 days later and the patient was discharged. She was revaluated with clinical and laboratory controls every month until the seventh month when a leukemia relapse was documented followed by sudden death due to CNS hemorrhage.

Her daughter is presently 3.5 years old. She is well and her weight is in the normal range. No neurological damage residued. Haematological parameters are normal.

DISCUSSION

Acute leukemia during pregnancy is a very rare event, occurring in one per 75,000 - 100,000 pregnancies (8.5). Its poor prognosis requires immediate, specific treatment, which has two requirements, i.e. to be optimal to possibly cure the mother and safe for the foetus.

As for the foetus, if the foetal age is compatible with labor induction, the best choice is probably to induce delivery, although there is no general agreement about it ([1]).

There is concern about the potential dangerous effects of chemotherapy on the developing foetus, although the incidence of congenital malformations in infants born from mothers treated for acute leukemia in pregnancy is infrequent ([3]). According to the literature, potential foetal damage due to chemotherapy largely depends on foetal age.

During the first trimester chemotherapy is associated with 17% - 23% of fetal malformations, mainly in patients with diverse malignancies treated with antifolates or alkylating agents ([5,12]). On the contrary, exposure to single or combination antimytotic drugs during the second or third trimesters is not reported to be associated with gross fetal abnormalities ([6, 7, 10, 11]).

On the other hand, a higher incidence of premature births or abortions has been reported for patients who underwent chemotherapy ([3, 5]).

Hovewer, if acute leukemia is not treated, pregnancy outcome is generally unfavorable ([4]).

Although many infants born to mothers undergoing chemotherapy during pregnancy are described as being normal, due to the rarity of this event, there are few reports with long term follow-up about these children ([2, 11]).

Long term studies about offspring will be important in assessing the risk of *in utero* exposure to the antineoplastic drugs.

According to the available data ([3, 9, 11]), there is no evidence that pregnancy itself makes the course of leukemia worse.

Considering that with combination chemotherapy maternal death is uncommon and foetal survival approaches 90% ([5]), even in early pregnancy, it is important to consider the mother's clinical status and her wishes before recommending therapeutic abortion.

In conclusion, according to our observation, the care of pregnant woman with acute leukemia is feasible and it needs a team effort (haematologist, gynaecologist, neonatologist) that is more easily achieved in a tertiary care istitution.

In our case, after giving adequate information, we complied with the mother's wish to continue the pregnancy.

Our chemotherapy approach to AML was not changed because of pregnancy. Indeed, the subsequent relapse appears more related to the natural history of the disease than the cohexistence of pregnancy.

The foetus in utero exposure to antileukemic drugs probably caused foetal sufference and the subsequent caesarean section; in spite of that, damage to the child has not been documented until the present age of 3.5 years. This observation is in agreement with other reports ([3, 11]) about the need for careful management of fetal complications.

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