# Acute myeloblastic leukemia in pregnancy: a case report and review of the literature

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**Summary**

Leukemia is a rare event during pregnancy. The presence of leukemia during pregnancy raises several concerns about the effect of pregnancy on the prognosis of leukemia, the effect of the disease on pregnancy outcome and the teratogenic and mutagenic effect of chemotherapeutic agents on the fetus. We report a case of acute myeloblastic leukemia diagnosed during the third trimester of gestation and treated with chemotherapeutic agents before delivery. The duration of pregnancy was able to be prolonged for four weeks after clinical diagnosis of the disease and then terminated by cesarean section due to the presence of signs of fetal distress.

*Key words:* Acute myeloblastic leukemia; Pregnancy; Preterm delivery.

## Introduction

Because of its ability to threaten the life of both the mother and fetus, and its potential curability with modern therapy, acute myeloblastic leukemia complicating pregnancy remains an important consideration in obstetric practice. Acute leukemias tend to affect the younger population so they are much more commonly seen in pregnant patients than are chronic leukemias. The incidence of leukemia in pregnancy is estimated to be one per 75,000 pregnancies [1-3]. Acute myeloblastic leukemia (AML) accounts for 60% of leukemias that are seen in pregnancy [4, 5]. Given the clearly dismal prognosis of leukemia if not treated, because of good response to therapy and the lack of documented side-effects in children exposed to chemotherapy in utero, aggressive therapy should be started promptly, even in the first trimester of gestation [6].

A case of acute myeloblastic leukemia diagnosed during the third trimester of pregnancy and treated with chemotherapy before delivery is reported.

## Case

A 27-year-old, gravida 6, para 4 woman, was referred to our clinic at 33-34 weeks' of gestation because of severe thrombocytopenia and signs of fetal distress. A month before, with the complaint of weakness, fatigue, loss of appetite, fever and a mild sore throat she had been admitted to another medical center. At that time, laboratory analysis revealed 180,000/mm$^3$ white blood cells (WBC), 23,000/mm$^3$ platelets and 6.5 g/dl hemoglobin and 20.3% hematocrit level. Routine biochemical analysis was in normal range. Bone marrow aspiration materials revealed the diagnosis of acute myeloblastic leukemia French-American-British (FAB) type M1 with 95% of myeloblasts. Immunophenotypic analysis of the acute leukemia panel showed positive reactivity for CD13, CD33, CD34. One cycle of idarubicin and cytarabine (7+3) chemotherapy was given to the patient. Three weeks after the chemotherapy she was referred to our university clinic because of the presence of severe thrombocytopenia and signs of fetal distress.

Obstetric history included four term-births at home without any complications, and one miscarriage at 16 weeks' gestation. She had not attended regular antenatal follow-up in the previous pregnancies. She had unremarkable medical and family histories.

On admission to our clinic, the patient was pale, mildly icteric, dyspneic and tachycardic. Physical examination revealed blood pressure of 150/100 mm Hg, heart rate 110 beats per minute, and an axillary body temperature of 37.1°C. The gravid uterus was palpable at the level of four centimeters above the umbilicus. Abdominal sonographic examination showed a live, single fetus, appropriate for 33-34 weeks' gestation with normal fetal growth. At presentation, her blood WBC, platelet counts, hemoglobin and hematocrit values were 84,000/mm$^3$, 14,000/mm$^3$, 8.9 g/dl and 25.4%, respectively. There were no remarkable abnormalities in her routine biochemical analysis and bleeding profile. Assessment of a peripheral smear by the hematologist revealed 97% blast cells in which 26% showed positive reactivity with myelo-peroxidase staining. Supportive measures were initiated with erythrocyte and thrombocyte transfusion. Bone marrow aspiration showed an increase in cellularity with low megakaryopoietic, erythropoietic and myelocytic activity and presence of 90% myeloblasts revealed that she was not in remission.

Obstetric examination performed during admission to our clinic revealed an unripened cervix that was unfavorable for vaginal delivery. Mild uterine contractions accompanied by severe late decelerations with decrease in beat-to-beat variability were observed on external fetal monitoring. Four hours after admission the patient underwent cesarean section with great hematological supportive care including platelet and erythrocyte transfusions. A baby boy weighing 2,200 g was born with Apgar scores of 2 and 6 at one and five minutes, respectively. Amniotic fluid was meconium stained. The operation was uneventful and the patient was administered antimicrobial pro-

Revised manuscript accepted for publication July 9, 2003

phylaxis with first generation cephalosporin intravenously. The baby was later transferred to another neonatal care unit immediately after stabilization.

On postoperative day 2, a fever of 38.8°C lasting more than one hour developed in the patient. At physical examination, bilateral diffuse rales were detected on pulmonary auscultation and mild pneumonic infiltration was observed in the lower zone of the right pulmonary at chest X-ray. An empiric broad-spectrum antimicrobial regimen, due to febril neutropenia, of aminoglycoside, fourth generation cephalosporin and teicoplenin was instituted intravenously for polymicrobial coverage after the cultures were taken. She became afebrile 24 hours after the beginning of therapy. After the infectious problems and postoperative complications were under control she was transferred to the department of internal medicine in order to continue chemotherapy for AML on postoperative day 4. The patient was scheduled for remission-induction chemotherapy and the baby was still in the neonatal care unit at another center.

## Discussion

Hematologic malignancies complicating pregnancy remain a challenging problem in obstetric practice. Fortunately these malignancies are rare during pregnancy [1-3]. Acute myeloblastic leukemias are among the most common malignant neoplasms in young women of childbearing age. Acute lymphoblastic leukemia is generally seen in childhood whereas chronic myeloblastic leukemia is usually a disease of patients beyond reproductive age [2].

Studies have shown that the presence of pregnancy does not appear to influence either the development or the course of the disease [7, 8]. The immunosuppressive effect of pregnancy, illustrated by the immunotolerance of fetal tissue by the mother, is thought to increase the risk of cancer development during pregnancy or to allow a more fulminant course. However, this was not demonstrated and the immunotolerance was found to be specific for the fetus only [9].

Pregnancy in leukemic patients is said to be at jeopardy. A review of the literature showed that, even in the face of treatment, leukemia in a pregnant patient increases the risk of abortion, fetal wastage and perinatal mortality as a result of preterm delivery [4, 5, 18]. Fetal growth restriction and spontaneous preterm delivery have been reported to occur in approximately 40-50% of cases with leukemia and were said to be multifocal in origin [10]. Improvement in perinatal outcome has been reported to be attributed to the use of chemotherapy for remission-induction during pregnancy. However, good pregnancy outcomes are largely influenced by maternal response to therapy [11-17]. Despite this, perinatal outcomes in pregnant women with leukemia are generally poor [4, 5, 18]. Although metastasis of maternal leukemia to the placenta has been reported, metastasis to the fetus and congenital leukemia are extremely rare [20-22].

In untreated patients, maternal mortality is significantly high and the mean survival is reported to be two months after the initial diagnosis [23]. Remission and cure rates of 65-75%, similar to that of non-pregnant women, can be achieved with aggressive therapy and delay in therapy may comprise maternal outcome without improving pregnancy outcome [24]. Long-term disease-free survival of leukemic pregnant patients ranges from 25% to 50% in some reports [5-7, 13-17]. However the possibility of mutagenic and teratogenic effects of cytotoxic agents on the fetus raise several concerns. Although most studies in the literature revealed that surviving fetuses showed little risk of teratogenesis, it is evident from the animal models that the first trimester is the time of greatest risk. Hence, many authors recommend against the use of cytotoxic agents during this period because of the mother's health [17, 19, 25-27]. Nevertheless, given the rapid progressive nature of AML, it is prudent to institute appropriate therapy immediately when the diagnosis is established regardless of gestational age. Long-term follow-up studies [6, 7] reported no abnormalities regarding birth weight, growth, development, hematological, cytogenetic, neurological and psychological learning, and reproductive performance in children who were exposed to chemotherapy in utero. The risk of fetal malformations associated with chemotherapy during the first trimester was reported as 10-20% [16, 17], whereas later in pregnancy it was no higher than that of the general population (3%) [25-30]. Morishita *et al.* [30] investigated the effects of cytotoxic agents in the fetuses of women treated with multiagent chemotherapy for the treatment of AML at the third trimester of gestation and found that fetal hematopoiesis was not adversely affected and no malformations were observed [30]. However, transient myelosuppression and increased risk of low birth weight, prematurity and stillbirth in fetuses of women treated with multi-agent chemotherapy during pregnancy were demonstrated [16, 18].

Because it is not discernible that pregnancy poses a risk for leukemia patients or that pregnancy by itself affects the course of the disease, termination of pregnancy is not recommended to improve prognosis. In the first trimester in order to avoid teratogenesis chemotherapy may be delayed. However, treatment delay may lead to poor maternal and fetal outcome. There is a rare case of spontaneous remission of acute leukemia after termination of pregnancy in the literature [31]. Management options are based on the stage of pregnancy at the time of diagnosis of leukemia. In the first trimester the patient should be offered termination of pregnancy because of the likely potential fetal consequences of chemotherapy and the maternal complications of leukemia. If abortion is refused, the patient should be treated with chemotherapy immediately, because maternal prognosis is dismal without treatment of leukemia. Methotrexate is particularly deleterious to the fetus and should be avoided, if possible. Late in pregnancy consideration can be given to a slight delay in treatment to allow for delivery before institution of chemotherapy. If the patient has acute symptoms and the possibility of a viable fetus is remote, then chemotherapy should be offered promptly. During therapy fetal survillance should be carried out and monitored for adequate growth since intrauterine growth

restriction is common. Supportive therapy including adequate nutrition, even total parenteral nutrition, and erythrocyte and thrombocyte transfusion when indicated, should be maintained [32]. Because of the risk of bleeding and infection, active disease makes labor hazardous for both mother and fetus. With great supportive care, the delivery route should be based on obstetric indications.

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