Leukemia in Pregnancy and Fetal Outcome After Multi-Agent Chemotherapy

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Introduction

Pregnancy complicated with leukemia is rare. Validated data from which conclusions may be drawn regarding management of pregnancy with leukemia are sparse. We report a case of pregnancy with leukemia with an overview of published literature.

Case Report

A 24 year old gravida 2, para 1, presented at 28 weeks with gradually increasing weakness and breathlessness since one month. On examination, marked pallor was noted with pulse 100 / min, respiration 19/min and BP 100/60mm Hg. No pedal edema was noted. A soft systolic murmur was present over the precordium. On abdominal examination, the fundal height corresponded to 28 weeks of gestation with fetus in cephalic presentation. Mild hepatosplenomegaly was present. On investigation, hemoglobin was 7.2 gm%; total lucocyte count 20200 per cu mm; differential lucocyte count – N_{35} L_{21} E_{0} M_{0}, myeloblasts 1, metamyeloblasts 9, blasts 33, packed cell volume 23%; bleeding time 01'30"; and clotting time 07'10". Platelet count was 60000 / cu mm. General Blood picture revealed a reduced RBC mass with normoblasts and few polychromatophilic cells. Bone marrow biopsy confirmed the diagnosis of acute lymphoid leukemia(L2). Three units of fresh blood were transfused. Multiagent chemotherapy was planned after counseling the patient's relatives. Chemotherapy was, however, delayed by one month on account of reluctance of the patient. The patient returned with hemoglobin 4.1gm% and platelets reduced to 25000/ cu mm. There units of fresh blood were transfused prior to the chemotherapy. The patient successfully completed three cycles of chemotherapy before she started premature labour at 34 weeks gestation. Ultrasonography revealed a single live fetus with mild growth retardation. Liquor was adequate. She delivered vaginally a normal female infant weighing 2.05 kg. No congenital anomaly was identified. The patient had mild post-partum hemorrhage despite oxytocics and prostaglandins. No evidence of genital tract injury was seen. She needed a transfusion of fresh blood. Broad spectrum antibiotics were given. The patient completed two cycles of chemotherapy during the puerperium on the 22nd and 29th postpartum days. After the last chemotherapy her Hb was 13.1. gm % lucocyte count 3800/cumm, differential count – P_{68}, L_{32}, Blasts 0 and platelets 150000 / cu mm. By the 35th day of her last chemotherapy, she was in remission and no blast cells were seen. Breast feeding was withheld during chemotherapy.

Placenta and cord blood were sent for histopathological and hematological examination which revealed no evidence of maternal leukemic cells.

Discussion

One in 1000 pregnancies is complicated by malignant disease[1]. Adult leukemia is invariably fatal and without aggressive treatment with cytotoxic drugs, the disease is characterized by rapid deterioration and death within weeks of diagnosis.

There is no objective evidence that pregnancy has a deleterious effect on leukemia. Survival times in pregnant women with leukemia do not differ statistically from those in non-pregnant women[2].

Diagnosis during pregnancy is made most frequently in the second and third trimester although the disease may have been present earlier. This is because the early symptoms are nonspecific, commonest being fatigue, which is often attributed to the pregnancy by the patient and physician alike. This emphasizes the importance of carrying out proper investigations including bone marrow examination for unexplained anemia in pregnancy.

Acute leukemia in pregnancy offers a unique management dilemma in the absence of clear guidelines. Clinical problems result from the disease process itself and its treatment. There is an increased risk of infection, hemorrhage and abortion consequent to neutropenia, anemia and thrombocytopenia. Fetal loss occurs in approximately 33% of women with acute leukemia[3].

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The diagnosis demands prompt institution of cytotoxic chemotherapy to maximize the chances of maternal survival. Current management of acute leukemia has improved maternal and fetal survival. With supportive therapy alone, 20 to 30 % of women did not survive the gestation period and fetal mortality was 50%[4]. With combination chemotherapy, most mothers survive through delivery with concomitant improvement in fetal survival. Thus pregnant leukemic women should be treated with aggressive chemotherapy until a remission is achieved. The risk of malformation in first trimester is as high as 17% especially with folate antagonists[5]. Termination should be considered once she is in remission and this can be performed with safety[3]. Treatment beyond the first trimester is generally safe if appropriate monitoring and obstetric care are available. Termination of pregnancy when therapy is started in the second or third trimester has to be carried out on moral and medico-social grounds, as the fetus is likely to develop normally[3].

The powerful cytotoxic drugs often used to achieve remission in acute leukemia include cytosine arabinoside, daunorubicin, thioguanine and more recent derivatives. Other published data support the view that cytotoxic drugs can be given safely in the second and third trimesters[3,5,6,8]. Greenlund et al[6] reviewed medical records of 17 consecutive pregnant leukemic women. They conclude that pregnancy per se may not affect the outcome of chemotherapy and suggest that treatment delays may compromise maternal outcome without improving pregnancy outcome. Treatment of leukemia during pregnancy does not appear to have a significant impact on the future growth and development of the child[5].

Leukemia in the newborn infant of a mother suffering from the disease has not been reported. Recently Van der Velden et al[7] have reported on the clearance of maternal leukemic cells in a neonate of a mother diagnosed with acute lymphoid leukemia at 36 weeks where delivery was initiated prematurely and a healthy child was born. Cord blood and peripheral blood samples from the neonate (obtained at six weeks, three months and six months) were analyzed for the presence of minimum residual disease. Their data indicate that the maternal leukemic cells did not engraft in the neonate. In the present case cord blood and placenta did not show evidence of leukemic cells. Hansen et al[8] observed transient oligohydraminos during treatment with multiagent chemotherapy. No other side effects were noted. They conclude that fetal concerns should not delay therapy. No adverse fetal effect was found in the present case except for mild growth retardation. Preterm labor and postpartum hemorrhage were other significant features of the present case. The woman successfully survived the pregnancy and delivered a healthy female child. Long term follow up should be carried out on the offsprings of mothers treated with cytotoxic drugs for late development of neoplasm and possible adverse drug effect such as daunorubicin-induced cardiotoxicity.

Pregnant women with newly diagnosed leukemia should not delay treatment until delivery, for fetal concerns and that multiagent chemotherapy can be given safely after first trimester.

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