Use of hydroxyurea and α-interferon in chronic myeloid leukemia during pregnancy: a case report

C. Baykal[1], N. Zengin[2], F. Coşkun[3], N. Güler[2], A. Ayhan[4]

[1]Department of Obstetrics and Gynecology; [2]Department of Medical Oncology; [3]Department of Anesthesiology; [4]Hacettepe University, School of Medicine, Ankara (Turkey)

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Introduction

Chronic leukemia is rarely noted in women of reproductive age. Chronic myeloid leukemia (CML) represents 90% of chronic leukemia cases complicating pregnancy [1]. Various therapy methods have been used in the management of this disease during pregnancy. Cytotoxic drugs, interferon and leukapheresis are all reported to have different success rates [2-4]. Hydroxyurea (HU) which effects by inhibiting deoxyribonucleic acid synthesis in proliferating cells is useful in the treatment of CML. Also α-interferon (α-IFN) is known to possess anti-proliferative and immunoregulatory effects and is being used in the treatment of both chronic and accelerated phases of CML [5]. In this case report successful management with HU and α-IFN in a case of CML throughout the patient's pregnancy is described.

Case Report

A 30-year-old woman (gravida 1, para 0) was referred to our clinic at the 18th week of her pregnancy. She was diagnosed as CML during a routine pregnancy visit due to leucocytosis found in an automated blood count. When she was admitted to our clinic she had no complaints; the white blood cell count (WBC) was $174x10^9$/L with 60% neutrophils, 12% metamyelocytes, 7% myelocytes, 8% promyelocytes, 8% monocytes, 1% lenfocytes. The hemoglobin level was 11.2 g/dl and platelet count was $296x10^9$/L. Philadelphia chromosome was found to be positive. The patient was informed about the disease and she and her family decided on continuing the pregnancy. HU was started at a dose of 1500 mg/day together with allopurinol 600 mg/day. WBC count was decreased progressively and at the end of the 28th week of pregnancy it was $17x10^9$/L. α-IFN ($3x10^6$ U/day) was added to HU at the 28th week. The drug therapy and the WBC levels are summarized in Figure 1. She received these combined therapies until the 31st week of pregnancy when her platelet count was found to be $70x10^9$/L. Drugs were stopped because of thrombocytopenia and she was not given any of the drugs for three weeks. Her white blood cell count began to increase afterwards and HU was started again at the 34th week. She was also taking steroids from the 28th week to the 34th week for fetal pulmonary maturation because of the possibility of premature labor or any emergency decision before term. The fetus was known to be in breech presentation. At the 37th week she had regular uterine contractions; tocolysis was not useful, therefore a cesarean section was performed. A normal, physically healthy 2450-g female infant with normal blood counts was delivered with no perinatal complications.

Conclusion

The concomitant occurrence of CML with pregnancy is uncommon [2]. There are two sides affected in the therapy of this phenomenon. On one hand there is the mother who needs optimal cancer therapy, and on the other hand there is the fetus that must be protected from both the disease of the mother and also cytotoxic and other types of drugs that are used. The course of the disease is not affected in most cases. However, if the disease is uncontrolled, it may result in placental insufficiency and increased fetal prematurity and mortality [6]. Approximately 96% of pregnant women with CML survive delivery. Fetal survival throughout the gestation is 84% [1]. Widely used treatment modalities in such patients are cytotoxic agents, interferon, and leukapheresis. Busulfan has been reported as a chemotherapeautic agent and pregnancy outcome with this drug was found to be favorable [7]. Another therapeutic modality, being also the newest one is leukapheresis. Leukapheresis rapidly reduces high leukocyte counts, but a risk of hemodynamic instability, which may be harmful for the pregnancy, still exists. Other disadvantages of this method are the cost and time and moreover it is not available at every center.

Cytotoxic therapy is still the mainstay of therapy and some drugs are known to be well tolerated and cause less

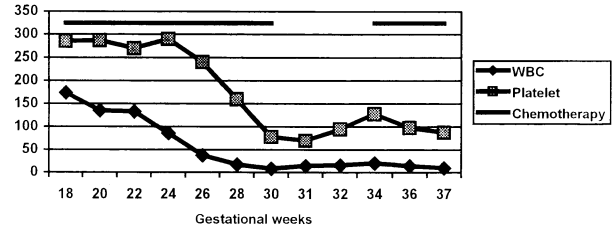

Figure 1. — WBC and platelet counts during chemotherapy from the 18th to the 37th gestational week.

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teratogenic effects. HU and busulfan are the leading drugs in this area and their usage in pregnant patients has been reported from different centers [8, 9]. Their mechanism of action is by inhibiting DNA synthesis and because of this they have the potential to result in abortion, intrauterine growth retardation, premature deliveries and possible congenital malformations [10]. α-interferon is another alternative drug which does not inhibit DNA synthesis and has no side-effects on fetus and pregnancy outcome [11]. α-IFN can also be used during the first trimester, which includes the organogenesis period. Here we report the combined usage of hydroxyurea and a-interferon in chronic myelogenous leukemia with a successful pregnancy outcome. It seems that hydroxyurea and α-interferon may be well tolerated in pregnant patients with CML.

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Address reprint requests to:
A. AYHAN, M.D.
Hacettepe University Tip Fak.
Kadin - Doğum
Sihhiye 06100
Ankara (Turkey)