

# Pregnancy Outcome of Two Patients with Chronic Myelogenous Leukemia Treated with Imatinib

M.A. Mashhadi

## Abstract

Although chronic myelogenous leukemia in pregnancy is rare, its management and treatment is more difficult and complicated.

Treatment of patients with chronic myelogenous leukemia includes bone marrow transplantation, however in less than 30% of patients the donor's organ would be accepted. To this end, cytotoxic therapy is considered as an alternative therapeutic option. This option provides satisfactory hematologic and clinical response, while cytogenetic response is poor.

Imatinib (Gleevec) is a new drug with highly specific efficacy in the treatment of chronic myelogenous leukemia. Prescription of this drug during pregnancy and lactation is not a classic approach and most physicians suggest that this drug should be discontinued during the pregnancy.

Here we report the use of imatinib during the pregnancy in two women with chronic myelogenous leukemia.

**Iran J Med Sci 2008; 33(2): 114-116.**

**Keywords** • Imatinib • chronic myelogenous leukemia • pregnancy

## Introduction

**C**hronic myelogenous leukemia (CML) accounts for 20% of newly diagnosed cases of leukemia in adults.<sup>1,2</sup> The disease has three phases: a chronic phase lasting three to six years that is followed by development of accelerated and/or blastic phases.<sup>1-6</sup> The cause of CML is translocation of regions of the *BCR* and *ABL* genes to form a *BCR-ABL* fusion gene.<sup>1,7-12</sup>

CML can potentially be cured by allogeneic stem-cell transplantation. However, fewer than 30% of patients have matched donors.<sup>1,3,7,13</sup>

Pregnancy accompanied by CML is an uncommon presentation. The management of CML during pregnancy remains a major challenge because of potential side effects on the mother and fetus.<sup>14-16</sup>

Leukapheresis has demonstrated satisfying results in the management of CML. However, this approach has transient effect and does not influence the survival rate and required admission for treatment.<sup>17,18</sup>

Here, we describe the successful management of two patients with CML in chronic phase using imatinib throughout the pregnancy as the sole modality of treatment.

## Case Reports

### Case 1

A 20-year-old woman presented in January 2003 with

Department of Hematology & Oncology,  
Zahedan University of Medical Sciences,  
Ali Ebne Abitaleb Hospital,  
Zahedan, Iran.

### Correspondence:

Mohammad Ali Mashhadi MD,  
Department of Hematology & Oncology,  
Zahedan University of Medical Sciences,  
Ali Ebne Abitaleb Hospital,  
Zahedan, Iran.

**Tel:** +98 0915 341 1445

**Fax:** +98 541 3411252

**Email:** [dralimashhadi@yahoo.com](mailto:dralimashhadi@yahoo.com)

Submitted: 8 April 2007

Revised: 17 July 2007

Accepted: 23 September 2007

abdominal pain, early satiety, weakness, night sweating, bone pain, and mild pallor.

On physical examination, spleen was 10-12 cm below costal margin. White blood cell (WBC) count was over 400000/mm<sup>3</sup>, hemogram and bone marrow aspiration were consistent to CML. The patient was diagnosed as having CML. Cytogenetic study was performed and translocation of 9-22 was documented.

She was managed with hydroxyurea to reduce the WBC count. After decreasing the WBC count to 20000/mm<sup>3</sup> imatinib was administered. She was visited monthly by her physician. After 8 months, she was visited by her local physician to control the hemogram while she was receiving imatinib 200 mg/day (initial dose was 400mg/day and adjusted with leukocyte count). In this visit she was diagnosed to be pregnant. She had not stopped imatinib during pregnancy. The drug had been continued and the fetus had been exposed to imatinib in all three trimesters of pregnancy. The major cause for continue the imatinib during pregnancy in this patient was religious belief and when the patient was referred to hematologist, she had a 32-week fetus. She gave birth to a normal healthy baby in March 2005. The baby is now 21 months old and his growth pattern and development are in the normal range. The mother is in normal situation too. Complete blood cell count and ultrasonography of the abdomen in her baby are normal and he does not have any abnormality.

#### Case 2

A 21-year-old woman was visited in July 2005. She complained of abdominal pain. On physical examination, her spleen was 10 cm below costal margin and her WBC count was 280/000/mm<sup>3</sup>. She was referred to hematologist for management of splenomegaly and leukocytosis.

Hemogram and bone marrow aspiration showed chronic myeloid leukemia. Cytogenetic study was performed and Philadelphia chromosome was confirmed.

The treatment started by hydroxyurea to reduce the WBC count. Imatinib was administered afterward (400mg/day that was adjusted by leukocyte count). During the treatment with imatinib, she was diagnosed to be pregnant. The hematologist recommended to discontinuing imatinib and terminating the pregnancy but the patient and her husband refused the recommendations. The cause of this decision was religious belief. She continued using imatinib during pregnancy.

She had a normal delivery and her baby was normal after birth. The baby is now 9 months old with normal growth and development. The mother shows complete hematologic remission.

#### Discussion

Management of CML during pregnancy has not completely been evaluated. The pregnancy dose not compromise the behavior of CML.<sup>19</sup> Bone marrow transplantation is the best and curative approach for CML, however the best pharmacological treatment is imatinib. The therapeutic options for patients with CML and pregnancy are leukapheresis, hydroxyurea, and interferon therapy.<sup>15,17,20-24</sup>

The administration of imatinib for treatment of CML during pregnancy has not been evaluated clinically and the scientific reports on this issue are limited to animal studies. In animal studies, the side effects of imatinib during pregnancy were reported to be decreased weight of testicles and epididymis in male offspring and teratogenicity and postimplantation loss of the fetus.<sup>19</sup>

The best clinical report of pregnancy among patients with chronic myeloid leukemia treated with imatinib has been published by Ault et al.<sup>19</sup> The researchers reported 10 female pregnant patients who consumed imatinib. In their report, the average time of exposure to imatinib was 4 weeks (range 2-9 weeks) and the longest time of exposure was nearly one trimester (<2 months). In our report the exposure time was all the three trimesters of pregnancy. In Ault et al report two spontaneous abortions occurred which were not due to any pathologic condition or family history for pregnancy loss. They reported that the babies had weight loss and one of them had hypospadias with small intestinal malrotation. We did not observe such problems and the two babies had normal growth and development and did not have any abnormalities.

#### Conclusion

The beneficial effects of treatment with imatinib in pregnant patients with CML should be balanced with the risk of teratogenicity and congenital abnormality in fetus. Similar reports in other countries show that the risk of teratogenicity has been variable and in most cases it is low and is not well established. A more extensive surveillance is needed for better decision making in treating pregnant women with CML.

**Conflict of Interest:** None declared

#### References

- 1 Sawyers CL. Chronic myeloid leukemia. *N Engl J Med* 1999; 340: 1330-40.
- 2 Faderl S, Talpaz M, Estrov Z, Kantarjian HM. Chronic myelogenous leukemia: biology and therapy. *Ann Intern Med* 1999; 131: 207-19.

- 3 Kantarjian HM, Deisseroth AB, Kurzrock R, et al. Chronic myelogenous leukemia: a concise update. *Blood* 1993; 82: 691-703.
- 4 Savage DG, Szydlo RM, Goldman JM. Clinical features at diagnosis in 430 patients with chronic myeloid leukemia seen at a referral centre over a 16-year period. *Br J Haematol* 1997; 96: 111-6.
- 5 Speck B, Bortin MM, Champlin R, et al. Allogeneic bone-marrow transplantation for chronic myelogenous leukaemia. *Lancet* 1984; 1: 665-8.
- 6 Sokal JE, Baccarani M, Russo D, Tura S. Staging and prognosis in chronic myelogenous leukemia. *Semin Hematol* 1988; 25: 49-61.
- 7 Rowley JD. A new consistent chromosomal abnormality in chronic myelogenous leukaemia identified by quinacrine fluorescence and Giemsa staining. *Nature* 1973; 243: 290-3.
- 8 Nowell PC, Hungerford DA. A minute chromosome in human chronic granulocytic leukemia. *Science* 1960; 132: 1497-1497.
- 9 Heisterkamp N, Jenster G, ten Hoeve J, et al. Acute leukaemia in bcr/abl transgenic mice. *Nature* 1990; 344: 251-3.
- 10 Daley GQ, Van Etten RA, Baltimore D. Induction of chronic myelogenous leukemia in mice by the P210bcr/abl gene of the Philadelphia chromosome. *Science* 1990; 247: 824-30.
- 11 Kelliher MA, McLaughlin J, Witte ON, Rosenberg N. Induction of a chronic myelogenous leukemialike syndrome in mice with v-abl and BCR/ABL [published erratum appears in Proc Natl Acad Sci U S A 1990;87:9072]. *Proc Natl Acad Sci USA* 1990; 87: 6649-53.
- 12 Elefanty AG, Hariharan IK, Cory S. bcr-abl, the hallmark of chronic myeloid leukaemia in man, induces multiple haemopoietic neoplasms in mice. *EMBO J* 1990; 9: 1069-78.
- 13 Silver RT, Woolf SH, Hehlmann R, et al. An evidence-based analysis of the effect of busulfan, hydroxyurea, interferon, and allogeneic bone marrow transplantation in treating the chronic phase of chronic myeloid leukemia: developed for the American Society of Hematology. *Blood* 1999; 94: 1517-36.
- 14 Baer MR. Normal full-term pregnancy in a patient with chronic myelogenous leukemia treated with alpha-interferon. *Am J Hematol* 1991; 37: 66.
- 15 Strobl FJ, Voelkerding KV, Smith EP. Management of chronic myeloid leukemia during pregnancy with leukapheresis. *J Clin Apher* 1999; 14: 42-4.
- 16 Buekers TE, Lallas TA. Chemotherapy in pregnancy. *Obstet Gynecol Clin North Am* 1998; 25: 323-9.
- 17 Bazarbashi MS, Smith MR, Karanes C, et al. Successful management of Ph chromosome chronic myelogenous leukemia with leukapheresis during pregnancy. *Am J Hematol* 1991; 38: 235-7.
- 18 Juárez S, Cuadrado Pastor JM, Feliu J, et al. Association of leukemia and pregnancy: clinical and obstetric aspects. *Am J Clin Oncol* 1988; 11: 159-65.
- 19 Ault P, Kantarjian H, O'Brien S, et al. Pregnancy among patients with chronic myeloid leukemia treated with imatinib. *J Clin Oncol* 2006; 24: 1204-8.
- 20 Celiloglu M, Altunyurt S, Undar B. Hydroxyurea treatment for chronic myeloid leukemia during pregnancy. *Acta Obstet Gynecol Scand* 2000; 79: 803-4.
- 21 Patel M, Dukes IA, Hull JC. Use of hydroxyurea in chronic myeloid leukemia during pregnancy: A case report. *Am J Obstet Gynecol* 1991; 165: 565-6.
- 22 Baer MR, Ozer H, Foon KA. Interferon-alpha therapy during pregnancy in chronic myelogenous leukaemia and hairy cell leukaemia. *Br J Haematol* 1992; 81: 167-9.
- 23 Baykal C, Zengin N, Coskun F, et al. Use of hydroxyurea and alpha-interferon in chronic myeloid leukemia during pregnancy: A case report. *Eur J Gynaecol Oncol* 2000; 21: 89-90.
- 24 Kuroiwa M, Gondo H, Ashida K, et al. Interferon-alpha therapy for chronic myelogenous leukemia during pregnancy. *Am J Hematol* 1998; 59: 101-2.