Detection of BCR-ABL-Positive Cells in the Colostrum of a Pregnant Patient with Chronic Myeloid Leukemia

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Abstract

A 31-year-old pregnant woman was diagnosed with chronic-phase chronic myeloid leukemia at gestational week 16. To avoid exposure of the fetus to teratogenic agents, the patient opted for a course of careful observation only for the duration of her pregnancy. We detected 9.1% of BCR-ABL-positive cells in the patient’s colostrum with fluorescence in situ hybridization.

Key words: chronic myeloid leukemia (CML), pregnancy, breast feeding, colostrum, BCR-ABL, cord blood


Introduction

The optimal treatment for pregnant women with chronic myeloid leukemia (CML) has not yet been established. Although imatinib is the gold standard therapy for CML, its use in pregnant patients may cause malformations (1). Imatinib has been found to be damaging to the developing fetus in rats; the use of contraception is therefore recommended in women treated with imatinib (1). Consequently, there is little available information regarding the use of imatinib during pregnancy in humans. Several studies in pregnant women with acute leukemia have suggested that maternal leukemia cells can be transferred to infants (2-4), and because of the immature immune system in the fetus, maternal tumor cells could have a growth advantage over fetal host cells. The fetus and the mother need to tolerate each other’s alloantigens such as noninherited maternal antigens (NIMAs) and inherited paternal antigens during pregnancy (5, 6); exposure of the fetus to NIMAs may induce specific tolerance to maternal alloantigens. A recent study in mice demonstrated that oral exposure to maternal antigens through breast feeding could induce immunological tolerance to NIMAs (7-9). Breast milk contains a number of maternal antigens and leukocytes. Another report in mice showed that oral feeding of tumor fragments could confer a growth advantage on, and induce immune tolerance to, tumor cells (10-12). These findings suggest that breast feeding after delivery could promote a survival advantage for and tolerance to maternal BCR-ABL-positive cells, in the event of their transmission to the infant. We used sensitive molecular methods to detect the presence of BCR-ABL-positive cells or transcripts in umbilical cord blood and milk in a pregnant woman with CML.

Case Report

A 30-year-old pregnant woman was referred to our hospital at 16 weeks of gestation. Peripheral blood showed: hemoglobin, 9.8 g/dL; platelets, 591×10^9/L; and white blood cells (WBC), 18.0×10^9/L (81% neutrophils, 10% lymphocytes, 2% eosinophils, 1% basophils, and 1% monocytes). A bone marrow specimen demonstrated marked myeloid hyperplasia (bone marrow cell counts: nucleated cells, 874×10^9/L; megakaryocytes, 843.8×10^6/L, with 0.4% myeloblasts). Chromosome analysis showed the presence of Philadelphia chromosome (Ph)-positive cells (Mitsubishi Chemical Medience Corporation, Tokyo, Japan). The spleen size was normal. These findings were consistent with low-risk type according to the Sokal score. Fluorescence in situ hybridization (FISH) analysis revealed BCR-ABL fusion in 89% of peripheral blood cells and 93.4% of bone marrow cells (Mitsubishi Chemical Medience Corporation). Qualitative polymerase chain reaction (PCR) detected BCR-ABL transcripts...
The present case represents the first report of a pregnant patient with CML where the colostrum was examined for the presence of BCR-ABL-positive cells. In animal models, the presence of numerous maternal cells or soluble antigens in breast milk could induce tolerance to maternal cells (7, 8, 13), while ingestion of tumor fragments could give the tumor cells a growth advantage (10-12). These results suggest that breast milk containing maternal leukemic cells, as well as normal cells, might facilitate tolerance to and promote growth of maternal leukemic cells transmitted to the infant during pregnancy. Thus examination of breast milk for the presence of tumor cells might provide physicians and patients useful decision-making information regarding breast feeding after delivery. In the present case, the patient did not breast feed. We could not identify BCR-ABL transcripts in the cord blood as in another reported case (13). However, there are few reports on the transmission of maternal BCR-ABL-positive cells to a fetus. Thus we were unable conclusively to rule out the possible presence of BCR-ABL transcripts in the cord blood or in the infant, despite the use of sensitive molecular methods. The role of breast feeding in facilitating tolerance to maternal BCR-ABL-positive cells remains unknown.

Several studies have reported favorable maternal and infant outcomes for pregnant CML patients treated with only observation, leukapheresis (13-16) or interferon alpha (IFN-α) treatment. IFN-α, which has never been associated with teratogenicity in humans, seems to be the only safe treatment of pregnant CML patients (17). However, IFN-α shows a number of adverse effects, but achieves only a small number of complete cytogenetic responses (18). The present patient demonstrated a low-risk type of CML according to the Sokol score at the initial diagnosis. Thus we selected a careful and close observation avoiding adverse events by IFN-α. The present case successfully delivered a healthy baby, and fortunately, there was no progression of CML during pregnancy. Thus, close observation alone could be a preferable and viable treatment option for stable chronic-phase CML during pregnancy.

Pregnancy presents a dilemma to CML patients and physicians; the issue of how best to treat pregnant CML patients during pregnancy and after delivery is unresolved, especially in terms of the advisability of breast feeding. We suggest that extensive examinations should be performed, including identifying the presence of BCR-ABL-positive cells in breast milk, to allow better-informed decision making.

The authors state that they have no Conflict of Interest (COI).

References


Figure 1. BCR/ABL fusion gene-positive cells detected in the patient’s colostrum.


13. Salomon O, Tohami T, Trakhtenbrot L, et al. BCR-ABL transcripts are not detected in cord blood or the peripheral blood of the newborn child whose mother developed chronic myeloid leukemia while pregnant. Leuk Res 34: e78-e81, 2010.


