Caring for Two: Pregnancy and Chronic Myeloid Leukemia

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A 27-year-old Australian-born woman named Mrs. B presented to her general practitioner in December 2010 with a three-month history of excessive tiredness. She has a supportive husband, and they have four children aged four months to five years old. Mrs. B was breastfeeding her youngest child and had initially attributed her fatigue to her busy home life. A blood test revealed an elevated white blood cell count (WBC) of 43.7 x 10^9/L (reference range: 4–11 x 10^9/L); hemoglobin and platelets were within normal range. Mrs. B was subsequently referred to a specialist hematology service.

Mrs. B had no significant past medical history. She denied a history of fevers, infections, night sweats, or unintentional weight loss. Her vital observations on examination were unremarkable. No palpable lymphadenopathy or hepatosplenomegaly were noted. A repeat complete blood count (CBC) and film assessment confirmed high WBC of 55.3 x 10^9/L with a marked left shift in the myeloid series in addition to basophilia and eosinophila, raising suspicion of chronic myeloid leukemia (CML). Mrs. B was told to wean her child from breastfeeding in preparation for treatment. A bone marrow biopsy confirmed a diagnosis of chronic phase CML with 100% cytogenetic evidence of the Philadelphia chromosome. She was prescribed imatinib 400 mg daily and was educated on the management of potential side effects and importance of adherence. During this time, Mrs. B discussed her desire to have more children. She was counseled about the potential teratogenic risk associated with treatment, the need to use adequate contraception, and the risk of blast phase transformation in poorly managed CML. Mrs. B was advised to attain at least a major molecular response (MMR) (BCR-ABL transcript $\leq$ 0.1%) for two years before considering pregnancy.

Mrs. B attained hematologic remission (HR) with normalization of CBC within four weeks of starting imatinib. She initially experienced issues with fatigue and nausea. At three and six months after starting imatinib, Mrs. B was achieving an ideal molecular response with BCR-ABL transcripts of 2.9% and 0.12%, respectively.

In August 2011, Mrs. B admitted during clinic review that she had stopped imatinib therapy six weeks earlier with the goal of becoming pregnant. Her hematologist and nurse reiterated the potential loss of disease response with this course of action. Mrs. B demonstrated understanding of the potential risk but was undeterred. Two months later, Mrs. B was approximately four weeks pregnant. Her BCR-ABL transcript was rising (39%), and she had lost HR. She was started on aspirin 100 mg daily for anticoagulation prophylaxis, given the rise in her platelet count (440 x 10^9/L) (reference range: 150–400 x 10^9/L), and was referred to a specialist obstetric service. At eight-weeks gestation, treatment with interferon-alfa (IFN-α) 3 million IU, three days per week, was started in response to rising WBC (16.8 x 10^9/L). Mrs. B experienced the expected side effects of IFN-α, including fevers, myalgia, headache, and fatigue. By December, she regained HR and maintained this until early May 2012 when, at 37-weeks gestation, her WBC had risen to 20 x 10^9/L. Two weeks later, Mrs. B delivered a healthy baby girl weighing 3.3 kg.

Following the birth, Mrs. B was advised to resume imatinib; however, she elected to breastfeed and remained off treatment. By September 2012, her WBC was 80 x 10^9/L. Mrs. B weaned breastfeeding, resumed imatinib 400 mg daily, and HR was achieved within four weeks. Despite attaining HR, Mrs. B was experiencing side effects to imatinib, which limited her adherence. A repeat bone marrow biopsy confirmed a minor cytogenetic response of 50%, and BCR-ABL transcripts of 11%. She was switched to second-line treatment with dasatinib 100 mg daily in December 2012 with the anticipation of better adherence and tolerance to therapy. Surprisingly, her BCR-ABL transcript rose to 22% in February 2013, raising questions of nonadherence, which Mrs. B denied.

One month later, Mrs. B contacted her specialist nurse and reported delayed menses. Blood work subsequently revealed an unexpected pregnancy with fetal exposure to dasatinib during the first two to four weeks of gestation. She was advised that limited information was available to inform on fetal risks. Mrs. B and her husband chose to continue the pregnancy, and her dasatinib was stopped. She was started on IFN-α three days per week once again. Reassuringly, fetal development appeared normal. Again, IFN-α was poorly tolerated and, at 17-weeks gestation, with a rising WBC, her IFN-α dose was increased to five days per week. This did not halt the rising of WBC (52 x 10^9/L) and BCR-ABL transcript (110%). After careful deliberation, Mrs. B was advised to switch to imatanib therapy in the third trimester. This was significantly better tolerated than IFN-α. She again achieved HR and reduction in BCR-ABL transcripts by 32-weeks gestation. In October 2013, at 36-weeks gestation, a healthy 3 kg boy was born.

Again, Mrs. B declined her imatinib to breastfeed, against medical advice. Four weeks later, she remained in HR

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