Management of myelofibrosis during pregnancy: A case report

Lečenje mijelofibroze tokom trudnoće

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Abstract

Introduction. Primary myelofibrosis (PMF) is a clonal myeloproliferative neoplasm that occurs most commonly in the decade six of life and it is very rare in the young persons. Case report. We reported a 28-year-old female patient with primary myelofibrosis who had a normal pregnancy and delivery in the week 40 of pregnancy without any complications. Two years before the diagnosis of PMF she had normal pregnancy. The patient was treated with interferon-alpha and low dose aspirin during the whole pregnancy and with low-molecular-weight heparin a week before delivery and 6 weeks after. The patient had no complications during pregnancy. She delivered in term with healthy, normal baby weight. Conclusion. Decision about treatment strategy of pregnancy associated hematologic malignancies should be made for each patient individually.

Key words: myeloproliferative disorders; primary myelofibrosis; pregnancy; interferon-alpha; treatment outcome.

Apstrakt


Key words: mijeloproliferativni poremećaji; primarna mijelofibroza; trudnoća; interferon-alfa; lečenje, ishod.

Introduction

Primary myelofibrosis (PMF) is a clonal myeloproliferative neoplasm characterized by a proliferation of megakaryocytes and granulocytes in the bone marrow, associated with reactive deposition of fibrous connective tissue and with extramedullary hematopoiesis. It occurs most commonly in the decade six of life and it is very rare in the young ones. Pregnancy is a high-risk event in women with thrombocytosis, especially in patients with essential thrombocythemia and PMF. The risk of spontaneous abortion is 2.5-fold higher than in the control population, while the incidence of maternal complications is lower, 3% for major thromboembolic and 2% for major bleeding event. We reported a 28-year-old female patient who had a normal pregnancy and delivery, treated with interferon-alpha, low-dose aspirin and low-molecular-weight heparin (LMWH).

Case report

A 28-year-old woman was sent to the hematologist in November 2011, due to asymptomatic thrombocytosis (platelet count 1,040 × 10^9/L). Her previous medical history was unremarkable, excluding conization of uterine cervix because of cervical intraepithelial neoplasia diagnosed in 2007. Two years before admission she had a normal pregnancy and delivery. Physical examination did not show peripheral lymphadenopathy, hepatosplenomegaly or signs of skin and mu-
cosal bleeding. Laboratory findings (sedimentation rate, biochemistry and hemostatic findings) were normal. Except for elevated platelet count, the rest of the full blood count was within normal limits. Chest radiology was normal, too. Ultrasonography of the upper abdomen showed slightly enlarged spleen (130 × 60 mm in diameter). The bone marrow trephine biopsy showed 60% bone marrow cellularity with moderate proliferation of megakaryocytes, which were mostly enlarged, hyperlobulated, polymorphic, forming clusters of variable size. Reticular fibrosis was moderate, grade I. Karyotype was normal, 46,XX. Janus kinase 2 (JAK2) (V617F) mutation was not identified, as well as bcr-abl rearrangement. Pattern of in vitro growth of hematopoietic progenitors from bone marrow and peripheral blood did not speak in favor of the myeloproliferative disease, so the revision of pathological findings of the marrow trephine biopsy was done in the University of Cardiff, Wales. These findings confirmed the diagnosis of prefibrotic phase of primary myelofibrosis (MF-1) with no evidence of CD34/CD117 blasts. Considering low International Prognostic Scoring System and Dynamic International Prognostic Scoring System (both 0) we decided to follow the patient with low-dose aspirin as the only treatment.

Soon after the diagnosis of PMF, the patient became pregnant. Interferon alpha therapy (3 MIU, 3 times a week) was given immediately, together low-dose aspirin. After three weeks of therapy platelet count was reduced to normal value and sustained within normal limits during the whole pregnancy. Two weeks before delivery low-dose aspirin was stopped and LMWH was given before delivery and 6 weeks after. Fetal safety of interferon-alpha was also confirmed in the study of Yazdani Brojeni et al. 10. Their results suggest that interferon-alpha have a protective effect against pregnancy loss and does not significantly increase the risk of major malformations, miscarriage, stillbirth and pre-term delivery above general population rates.

Having in mind all these studies we decided to treat the presented patient with interferon-alpha and low dose-aspirin during the whole pregnancy and with LMWH two weeks before and six weeks after the delivery. We suggest such therapeutic approach as the best for patients with PMF, although the nature of the disease itself (low DIPSS score and negative JAK2 mutation) maybe contributed to good outcome of pregnancy.

The question of further treatment of our young PMF patient still remains. HLA typing of her sister and brother have been done, but no HLA-matched sibling donor was found. The only curative treatment of PMF is allogeneic hematopoietic stem cell transplantation. According to French authors factors affecting favorable engraftment are splenectomy before HSCT, HLA-matched sibling donor, peripheral blood use as a source of stem cells and the absence of pre-transplant thrombocytopenia. Tefferi 7 modified risk stratification of patients with PMF for further management that could be useful for patients like the presented. However, having in mind that the presented patient is still very young (at this moment 30 years) and in excellent condition with low International Prognostic Scoring System, the risk of allogeneic hematopoietic stem-cell transplantation in the light of the lack of family matched donor remain significant, particularly in innovative drug era. New drugs such as JAK2 inhibitors, mTOR (target of rapamycin) inhibitors, histone deacetylase inhibitors and pomalidomide show encouraging results in treatment of patients with PMF. Interferon-alpha also showed some promising results in reducing the fibrosis in Philadelphia-negative chronic myeloproliferative neoplasms, and it can possibly be used in combination with new drugs.

**Conclusion**

This case is the first reported pregnancy in primary myelofibrosis patient without the previous history of abortions, with no complications during pregnancy and normal, in term delivery with healthy, normal weight baby.

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Decision about treatment strategy of pregnancy associated hematologic malignancies should be made for each patient individually.

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REFERENCES


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