CASE REPORT

Pregnancy with Polycythemia Vera: A Case Report and Review of Literature

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Abstract

Polycythemia vera is a form of myeloproliferative disease common in sixth and seventh decade and more in males than in females. Occurrence of MPD with pregnancy is rare. Hence, this case is reported. She was diagnosed as polycythemia vera at the age of 28 years and platelet count was 1082 x 10^9L. She was under treatment and needed phlebotomy 2 to 3 times a year. Pregnancy was natural 2 years after diagnosis of MPD. During pregnancy, platelet count remained 8 to 9 x 10^9L with aspirin. LMWH was started at 28 weeks of gestation. Although, she was advised elective LSCS at 37 weeks; 2 days prior to LSCS, she went into spontaneous labor. Last dose of aspirin and LMWH was given just 18 hours before labor. She was delivered by emergency LSCS. Fortunately, there was no excess bleeding during surgery. The lactation was suppressed.

All cases of polycythemia vera with pregnancy should be monitored by joint care of hematologist and obstetrician. In high risk cases, drug therapies like Interferon, Hydroxy urea, Busulfan and Anagrelide can be used.

Since unexplained fetal loss is known, elective LSCS is recommended at 34 and 37 weeks of gestation. Modern therapy has significantly extended the life expectancy. The discovery of JAK2V617F mutation has revolutionized the field of MPDs. Furthur research is necessary.

Keywords: Myeloproliferative diseases, Polycythemia vera, Pregnancy.

INTRODUCTION

Polycythemia vera (PV) is a form of myeloproliferative diseases (MPDs). Other such disorders include essential thrombocythemia (ET) and idiopathic myelofibrosis (MF). In 2001, WHO included in the classification of MPDs, chronic neutrophilic or eosinophilic leukemia and chronic myclomonocytic leukemia. But these conditions are relatively rare.

The MPDs are commonly seen in 6th and 7th decades of life and also more in males than females. Therefore, the occurrence of pregnancy with MPD is a relatively rare occurrence. Hence, there is a paucity of literature on the subject. Mostly there are single case reports or small series.

Barbui and Finazzi[1] pooled the outcomes of 461 pregnancies reported in 2006. Robinson, Bewley, Hunt et al[2] reported the management of pregnancy in 18 women with PV. Guidelines for the management were published from Italy in 2004 and UK in 2005.

We present herewith our case.

CASE

Mrs. CD aged 30 years was referred to us with early pregnancy and a history of polycythemia vera.

She had an apparently healthy childhood and was asymptomatic till 2007. However, whenever she had a blood test, the counts were always on the higher side of normal. In 2007, she started getting migraines and was fully investigated. In November 2007, she was diagnosed as a case of polycythemia vera and started treatment with a hematologist. Her Hb was 12.3 gm%, PCV was 41.5, and platelet count was 1082 × 10^9 L. She needed therapeutic phlebotomy twice to thrice a year to maintain hematocrit under 45. She never had any attack of thrombosis or embolic episodes.

She was a working lady married since 4 years and had not planned a pregnancy. The hematologist assured her that though risky, pregnancy and child bearing was possible.

She conceived in August 2008. The pregnancy was managed as a high-risk case with close cooperation with the hemologist. Her Hb was 12 gm%, PCV was 41 and platelet count remained between 8 and 9 lakhs. She was put on 100 mg aspirin daily from the day pregnancy was diagnosed. Pregnancy was uneventful. Although, she was watched closely for occurrence of thromboembolism, there were no episodes. Weight gain was moderate.

Patient was allowed to continue her job. In the 28th week of pregnancy, low molecular weight heparin (Enoxoparin) was started as a subcut injection of 60 mg daily. Apart from local bruising, it was well tolerated.

She was informed that LMWH was a category C drug in pregnancy and that lactation will not be permitted as the drug would have to be given 6 weeks postpartum. She was agreeable.

USG with color Doppler was performed at 26 weeks and 36 weeks of gestation. The blood flow in placenta, cord and fetal circulation was normal. The baby's weight was slightly low.

An elective LSCS was planned on the completion of 37 weeks. She had a therapeutic bloodletting 1 week earlier and the blood was preserved for transfusion if required. It was planned that enoxoparin would be stopped 48 hours before delivery and aspirin 72 hours before delivery.

However, she ruptured membranes, had show and mild contraction 2 days before the scheduled date. She had taken enoxoparin and aspirin just 18 hours before onset of labor.

An emergency LSCS was planned, two-packed cell transfusions were arranged and platelet transfusions were kept ready, in case of profuse bleeding. It was also decided that upto 1000 cc blood loss would be tolerated by the patient and that human albumen was to be used in case of fall of blood pressure.

General anesthesia was given. Lower segment cesarean section was performed. A female baby weighing 2.6 kg was delivered. There was no excess bleeding at surgery. Placenta separated easily and was fully calcified. Patient tolerated the surgery well.

She was kept in surgical intensive care unit for 24 hours after surgery. There was no bleeding from any site and patient was very comfortable. From the next day, enoxoparin and aspirin were started. Lactation was suppressed by administration of cabergolin 2.5 mg twice a day for 3 days. Baby was given formula feeds and full immunization was carried out.

DISCUSSION

Any woman of PV, who contemplates pregnancy, should be under the joint care of a hematologist and obstetrician experienced in high-risk obstetrics. Any teratogenic drugs should be stopped atleast 3 months before the start of pregnancy. After a detailed personal and family history, the woman should be classified as per risk factors into low- or high-risk.

1. Low-risk
   a. First pregnancy with no previous complications
   b. Platelet count below 1500×10^9/L.
2. High-risk—at least one of the following:
   a. Previous major thrombotic or bleeding complication
   b. Previous severe pregnancy complication, i.e. still birth, pre-eclampsia, thrombosis or IUGR
   c. Platelet count above 1500×10^9/L.

Therapeutic options are limited to the following three:

1. Aspirin
2. LMWH
3. Cytoreductive therapy
   a. Phlebotomy
   b. Drugs – IFN (Interferon)
      – Hydroxy urea
      – Busulfan
      – Anagrelide.

The case should be managed in an institute, where a good hematology laboratory, blood bank and high-risk pregnancy unit exists for round the clock service.

In addition to routine care, patient should have hematologic fremount and obstetric checkup after every 15 days.

For a low-risk case, the target hematocrit should be 45%. Aspirin 100 mg should be started prior to pregnancy atleast as soon as pregnancy is detected. Low molecular weight heparin (LMWH) is recommended in the third trimester and should be continued 6 weeks postpartum.

For high-risk pregnancy in addition to the above treatment LMWH may be given throughout pregnancy. Aspirin may have to be stopped, if bleeding complications occur.

If platelet count is above 1500, interferon may be considered. Bloodletting is of value to maintain hematocrit and platelet count.

Aspirin

According to Harrison and Griesshammer,[3] all patients of PV and ET should be given 75 to 100 mg aspirin daily from before conception to 6 weeks postpartum. Placental and fetal development is, thus, facilitated. Bleeding complications are rare, but if they occur, aspirin has to be stopped and LMWH to be started.

In a meta-analysis published by Kozer E, Nikfar S et al[4] in 2003, it is stated that aspirin given in early pregnancy is not associated with an increased risk of congenital anomalies. However, there may be increased risk of gastroschisis and cleft lip and palate. Hence, these patients should be kept under close observation for the above defects.

LMWH

It is indicated as a prophylaxis and reduces fetal morbidity. 40 mg of enoxaparin daily may be started. In high-risk cases, it can be started in early pregnancy and dose increased to twice daily in the later part of pregnancy. The live birth rate in aspirin and LMWH is reported to be 71 to 80% as compared to 40% in aspirin alone (Robertson 2005).[5]

Cytoreductive Therapy

No clear cut guidelines are available on this issue and literature is very limited. According to Robinson, venesection may be resorted to maintain a hematocrit at 45%.

Drugs should definitely be avoided in the 1st trimester. According to Italian guidelines,[6] drug use should be restricted to high-risk cases with major thrombosis and H/O fetal loss. Interferon is probably the safest option.

Options for Delivery

Very careful observation with frequent USG scans and color Doppler to access placental function are required especially after 30 weeks.

Since fetal loss after 34 weeks of gestation is likely, it is the best to plan a delivery at about 34 to 36 weeks depending on other obstetric conditions. Induction of labor may be considered, if cervix is favorable. Patient may also go into spontaneous preterm labor.

Since unexplained fetal loss is known, an elective LSCS at 37 weeks after stopping enoxoparin and aspirin is a safe option.

Harrison[7] reported a series of 18 patients with polycythemia vera who had 36 pregnancies with a live birth rate of 58%. There were 3 early neonatal deaths. Thus, surviving neonates were only 50%. First pregnancy loss was 22%, preterm delivery was 13.8%. Maternal morbidity was even more significant. There was one mortality due to DIC and thromboembolic phenomenon. Maternal morbidity included pulmonary emboli, one large postpartum hemorrhage and four patients with severe pre-eclampsia. Hence, it is recommended to plan aggressive management from early pregnancy in collaboration with hematologist.

Long-term Prognosis

In the mean time, it is important to emphasize that the modern therapy has significantly extended life expectancy in PV with median survival estimates of more than 15 years.

The combination of cytoreductive and antiplatelet therapies have managed to keep the diseases specific risk of thrombosis below 10% in most patients.

The discovery of JAK2V617F mutation has revolutionized the field of MPDs and identified JAK2 as a legitimate drug target (Wolanskyj AP).[8]

Accordingly specific JAK2-inhibiting small molecules are currently under development and hold the long anticipated promise of molecularly targeted therapies in PV.

Quantitative JAK2V617F allele burden measurement assays are currently available and should serve as a useful function during laboratory correlative studies of anti-JAK2 clinical trials.

However, the ultimate concern is the development of leukemia and fibrotic transformation. For this, further research is necessary and hopefully a therapy will emerge, which can prevent these changes.

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