Therapeutic Management in a Patient with Homozygous Sickle Cell Disease and Prior Pulmonary Embolism during the Pregnancy - A Case Report

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Introduction

Pregnancy in patients with sickle cell disease (SCD) is associated with high risk of maternal and fetal morbidity and mortality [1-4]. SCD patients have a significantly higher risk of infections, thromboembolism including deep vein thrombosis, pulmonary embolism and stroke, preeclampsia, preterm labor, placental abruption, fetal growth retardation and maternal death. SCD patients are also more likely to have sickle cell crises during the pregnancy [1].

SCD itself seems to be an important hypercoagulable condition, which include activation of the endothelium, platelet activity, coagulation and fibrinolytic systems. The exact pathophysiology of this not yet fully understood and needs further research [5-7]. This leads to an higher risk of thromboembolic events in patients with SCD. As pregnancy and the post-partum period itself (in patients without SCD as well) carry a higher risk of thromboembolism, SCD patients have due to the combination of both factors as well as other factors (e.g. more use of central venous catheters, more likely to have surgery, more hospitalizations) an especially high risk of thromboembolic events during pregnancy and post-partum with a significantly elevated risk of both maternal and fetal morbidity and mortality [8,9].

There are still unresolved issues regarding the optimal management of pregnancy in SCD as there is few evidence available on the subject. No recommendations were found concerning the management of anticoagulation in patients with prior PE, pregnancy and SCD, a particular high risk combination [4,10,11]. The objective of our paper is to describe one possible approach to patients with SCD, pregnancy and prior PE using a case description.

Case Description

This is the case description of successful pregnancy of a 30-year-old patient with homozygous sickle cell disease with chronic hemolytic anemia. In her personal history, she has functional asplenism, status after two miscarriages and had suffered a subsegmental pulmonary embolism eight months before the pregnancy. She has had hip replacement on both sides due to osteonecrosis of the femoral head. Other than that, she had not suffered from many sickle cell crises.
Due to the pulmonary embolism she was under a therapeutic dosage of low molecular weight heparin (LMWH; Dalteparin). Other medication included hydroxyurea and paracetamol if needed. The patient did not receive any preconception care as the pregnancy wasn’t planned with support from medical specialists. The patient stopped taking the hydroxyurea herself approximately two months before conception.

After confirmation of the pregnancy, folic acid was added to the regimen. Aspirin 100mg was added at the beginning of the second trimester to reduce the risk of preecampsia and the LMWH was reduced to a prophylactic dosage to reduce the risk of bleeding under the combination therapy while still reducing the risk of another thromboembolism. The pregnancy was monitored closely with regular obstetric and hematological checks.

The hemogram showed signs of the known chronic hemolytic anemia with a macrocytic, hyperchromic erythrocytes and a hemoglobin of 103g/l (see table 1 and graph 1). In the peripheral blood smear distinct anisocytosis and poikilocytosis with sickle cells, target cells, spherocytes, tear drops and fragmentocytes could be detected. The HbS was 70% and the HbF 18%. A screening for red cell-antibodies was negative (anti-F-antibodies had been detected in the patient 4 years earlier). There was no sign of an iron overload. TSH levels were normal. Screening for HIV, Syphilis, Hepatitis B and C was negative. The vaccination status was completed with H. influenzae, pertussis and influenza vaccination prior to the birth. The meningococcal and pneumococcal vaccination status was current.

Prenatal ultrasounds of the fetus showed a normal growth with no signs of abnormalities. Testing of the haemoglobinopathy status of the father’s child was normal.

An echocardiography did not show any signs of pulmonary hypertension. A lung function test showed a minimal gas exchange dysfunction but with no radiological indication of any structural abnormalities. The patient had proteinuria and microalbuminuria during the pregnancy as early signs of renal failure or preecampsia but with normal renal parameters in the serum and with no substantial increase during the course of the pregnancy. Blood pressure levels were normal.

During the second trimester the patient showed increasing liver enzymes (Table 1). An abdominal ultrasound showed no signs of intrahepatic cholestasis, gall stones or other abdominal pathologies. The increased liver enzymes were either interpreted to the therapy with dalteparin or pregnancy-induced. Dalteparin was switched to Enoxaparin and the liver enzymes were decreasing during the rest of the pregnancy.

The patient suffered four sickle-cell crises during the pregnancy which required hospitalization. In two a possible infection was suspected which required antibiotic treatment with amoxicillin and clavulanic acid. During one hospitalization due to increased hemolytic activity and decreasing hemoglobin levels two blood transfusions were necessary. Other management of the sickle cell crises included analgesics, hydration and oxygen therapy. The patient was able to return home after each episode and did not need prolonged hospitalizations.

The aspirin was stopped at the beginning of the 36th week to reduce birth-related bleeding. Before delivery, one exchange transfusion was conducted to minimize bleeding during the planned C-section and a generous hydration was maintained through the C-section to minimize the chance of a sickle-cell-crisis. A healthy baby girl was delivered full term. The peri- and postnatal phase was uneventful without any major complications.

The LMWH was discontinued 3 months after delivery after a screening for thrombophilia was negative and a repeat chest CT showed no signs of a recurrent pulmonary embolism. The liver enzymes almost normalized after the discontinuation of the LMWH. The patient and baby are in a good condition one year after the delivery.

**Conclusion**

This case report demonstrates that a successful pregnancy in a high-risk patient with SCD, prior miscarriages and pulmonary embolism is possible. As it is a high-risk pregnancy regular obstetric and hematological checks are necessary to be able to detect possible complications as early as possible. An assessment for chronic diseases and its complications should be performed. In this case, we followed the British recommendations of the Royal College of Obstetrics and Gynecology [10], which include screening for pulmonary hypertension, measuring blood pressure, urine-analysis for proteins, screening of liver and renal function, screening of iron-overload and of red-cell-antibodies in addition to the regular screening procedures during any pregnancy. The haemoglobinopathy status of the partner should also be checked. Those screening-tests should preferably take

| Table 1: Chemogram and hematogram of the patient before, during and after the pregnancy. |
|---|---|---|---|---|
| **Reference** | **Pre-pregnancy** | **2nd Trimester** | **3rd Trimester** | **10 months post-pregnancy** |
| AST | < 41 U/l | 32 | 109 | 37 |
| ALT | < 41 U/l | 34 | 141 | 27 |
| GGT | < 40 U/l | 126 | 485 | 202 |
| AP | 35-110 U/l | 57 | 148 | 277 |
| Bilirubin | < 20 µmol/l | 15 | 22 | 18 |
| Creatinine | 45-84 µmol/l | 60 | 47 | 56 |
| Hemoglobin | 120-154 g/l | 113 | 103 | 103 |
| Hematocrit | 0.30-0.46 | 0.32 | 0.30 | 0.31 |
| MCV | 80-99 fl | 130 | 110 | 89 |
| MCH | 27-34 pg | 46 | 38 | 30 |
| MCHC | 315-360 g/l | 351 | 348 | 336 |
| WBC | 3.9-10.2 x 10⁹/l | 4.1 | 10.8 | 8.5 |
| Thrombocytes | 150-370 x 10⁹/l | 268 | 291 | 662 |

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place before the pregnancy in order to enable a well-balanced risk assessment. This was not possible in our case as the patient did not seek preconception-counselling.

Another important factor in the management of a pregnant SCD patient is a close interdisciplinary collaboration, especially between obstetricians and hematologists. The monitoring of such a pregnancy might be done preferably at a larger hospital that has all the necessary subspecialties (including obstetrics with experience in high-risk pregnancy and hematologists) available to guarantee an optimal communication between the specialties and optimal patient care. The treating physicians should be aware of the potential unique risks a pregnancy in a SCD patient carries and actively look for complications.

The use of LMWH and Aspirin describes one approach to the risk minimization of thromboembolisms and preeclampsia in patients with SCD. Unfortunately, there are no prospective studies available that specifically look at the use of LMWH or other anticoagulants in pregnant patients with SCD. In our case, the patient had also suffered a previous pulmonary embolism. We did not find any clear guidelines on the optimal management of such a constellation, even though do to the higher rates of thromboembolisms in SCD patients, we assume that our patient is not an exception and that there is not an insignificant number of pregnant SCD patients with the same constellation. Therefore, we would like to encourage further prospective studies in order to optimize the management of such patients and to reduce the fetal and maternal morbidity.

References


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