HIGH RISK PREGNANCY OF A WOMAN WITH LIVER TRANSPLANT FAILURE – CASE REPORT.

Karolina Kuczborska1, Jolanta Gozdowska1, Marek Pachołczyk2, Olga Tronina1, Bronisława Pietrzak3, Magdalena Durlik1

1. Department of Transplantation Medicine, Nephrology and Internal Medicine, Medical University of Warsaw, Warsaw, Poland
2. Department of General and Transplantation Surgery, Medical University of Warsaw, Warsaw, Poland
3. First Department of Obstetrics and Gynecology, Medical University of Warsaw, Warsaw, Poland

#Corresponding author: Jolanta Gozdowska, e-mail: jgozdowska@wum.edu.pl, Department of Transplantation Medicine, Nephrology and Internal Medicine, Medical University of Warsaw, Nowogrodzka Street 59, p.o. box 02-006 Warsaw, Poland; phone number: +48 605 532 525

RUNNING TITLE High risk pregnancy during liver transplant failure.

KEYWORDS high risk pregnancy; liver failure; pregnancy after liver transplantation

WORD COUNT 1038

CONFLICT OF INTERESTS no conflicts of interest

ABSTRACT

Along with the progress of transplantation medicine, the number of liver transplant recipients has gradually increased in the last decade. Among different indications and clinical run, also some young females have been given a chance to live, become pregnant and give birth to a healthy child. However, pregnancy in liver recipients is associated with increased risk in the post transplant run, both in respect of graft failure and the fetus. A 22-year-old woman after two liver transplantations: first due to the secondary biliary cirrhosis induced by biliary atresia, and second for multiple complications (acute rejections, recurrent cholangitis and the development of AIH), was considered for the third liver transplantation. Shortly after four-month hospitalization, during the outpatient visit, the patient informed about being 7 weeks pregnant. Despite high risk for her and child, the woman did not consent to abortion. Throughout the pregnancy the patient was hospitalized several times because of cholangitis, cholestasis, deepening anemia and thrombocytopenia. Due to the worsening condition of the patient, a decision was made to terminate the pregnancy in 29th week with cesarean section. A healthy son was born, 1320/41, 8 points APGAR score. The described case report shows that with proper cooperation of gynecologist and transplantologist, as well as determination of the recipient it is possible to monitor the pregnancy even during liver transplant failure.
BACKGROUND

Orthotopic liver transplantation (OLTx) has become a method of choice in management of patients with end stage liver failure [1]. Due to the intense development of transplantation medicine, the number of recipients is growing, including young women. Owing to allograft they have the chance not only to live, but also to become pregnant and give birth to a healthy child. It is calculated that female constitute more than 30% of patients undergoing liver transplantation, about 8% are of reproductive age, and 5% are girls who will most probably survive into adulthood and consider becoming pregnant [2].

However, pregnancy after liver transplantation is considered high risk and especially in the period of deterioration of the graft function even a threat both to the mother and the fetus [3]. Therefore, the decision on conception should always be consulted with transplantologist who should assess the allograft function and withdraw potentially teratogenic treatments if necessary. Most transplant centers recommend conception 1 year after transplantation, only with optimal liver function and on stable immunosuppression [2].

CASE REPORT

A 22-year-old woman, that became pregnant in 2012, underwent two liver transplantations: first in 2001 due to the secondary biliary cirrhosis induced by biliary atresia and the second in 2003 due to biliary strictures and recurrent cholangitis. In the post-transplant run multiple complications were observed: five episodes of acute rejections, poor bile drainage (cholestasis) and development of AIH. The patient also suffered from recurrent cholangitis. For the last reason, the woman was hospitalized for over four months in the pre-pregnancy period. Numerous antibiotics were administered, including carbapenems (meropenem), however every drug withdrawal was associated with recurrence of inflammation and cholestasis. Out of thirteen blood cultures no one has detected the pathogen. Fungal and CMV infections were also excluded. Liver histopathology revealed extensive fibrosis and suspicion of cirrhosis. Therefore, patient run the pre-transplant assessment for the third transplantation. There were no contraindications, however, during surgical consultation the patient was qualified for endoscopic dilatation of the biliary tract and stenting. During the procedure, a biliary lodgment obstructing the biliary anastomosis was removed. The suspicion of biliary cast syndrome was set. The bile culture revealed Pseudomonas aeruginosa infection. After administration of ciprofloxacin the patient was discharged home. However, two months later, during the outpatient visit, the patient informed about being 7 weeks pregnant presenting with cholestasis, leucopenia and thrombocytopenia. Hemoglobin and albumins were within normal limits. Due to the medical history, the abortion was recommended but the patient did not consent to it, fully aware of existing threat.

Immunosuppressive treatment - based on prednisone and tacrolimus - remained unchanged. The course of pregnancy was not uneventful – the patient was hospitalized several times due to cholangitis, cholestasis, deepening anemia (concentration of hemoglobin decreased to 8 mg/dl) and thrombocytopenia (PLT decreased to 29\(^{10^3}/\mu l\)). Throughout the pregnancy 12 units of PRBCs, 2 units of PLT concentration and 2 of FFP were transfused. Considering the risk of bleeding from esophageal varices the patient was also given prophylaxis with propranolol in the pre-labor period. On 14.08 the woman was hospitalized again because of cholangitis. On admission, the patient presented with significant leucopenia, anemia, hypoalbuminemia and cholestasis. Due to the worsening condition of the patient, on 17.08 dexamethason was administered, on 21.08 the patient was transferred to high-risk pregnancy department and on the following day a decision was made to terminate the pregnancy in 29th week with cesarean section. A healthy son was born - 1320g, 41 cm in length, 8 points APGAR score. The mother was discharged home after 9 days in good general condition, while the child was transferred to neonatal intensive care unit. Currently, 4,5-year-old boy develops properly, whereas the patient underwent third transplantation one year after labor.

DISCUSSION

Pregnancy in liver recipient is associated with multiple complications. Firstly, it can lead to deterioration of the allograft function, acute rejections and even loss of the graft [4, 5]. These problems occur more often in recipients getting pregnant less than 1 year after transplantation [6]. However, pregnancy related death is uncommon [5]. There is also increased risk for cholestasis that can be difficult to distinguish from graft failure [7, 8]. Liver function deterioration manifested by hematological disorders, mainly thrombocytopenia (40%), also play in important role [4]. The coagulation disorders increase the risk of perinatal hemorraghe - observed twice more often than among non-transplanted women. Also because of anemia and leucopenia blood transfusions are required more often [9].

After liver transplantation, patients also have a four-fold risk of perinatal complications comparing to standard population, such as gestational hypertension and pre-eclampsia [9]. However, there is no clear data about increased frequency of gestational diabetes. These women more often give birth prematurely (up to 30%) and by cesarean section, percentage of which amounts to 50% [4]. It is not caused by liver graft itself – which is not contraindication to vaginal delivery – but by obstetric complications and rapid deterioration of graft function, when occurring at the beginning of the third trimester [4].

The neonates are often born with low birth weight (1500 - 2500g) – up to 20% - and very low (<1500g) amounting to 50% [5]. It is not only caused by preterm delivery, but also by intrauterine growth restriction observed in about 5% [9]. Some studies stress the impact of the acute rejection on low birth weight [6]. Nevertheless, congenital anomalies are rare [3].

Another concern of the recipients is frequent inability to become pregnant. Severe chronic liver disease leads to
the amenorrhea in up to 50% of women of childbearing age (10). Hormonal imbalances, elevated level of estrogens and hypogonadotropic hypogonadism are common due to the dysfunction of the hypothalamic-pituitary-ovary axis. Consequently, successful conception is uncommon in these patients [10, 11].

CONCLUSIONS

Pregnancy after liver transplantation should always be regarded high-risk and in the period of deterioration of the graft function even as a threat both to the recipient and the fetus. Described case report shows, however, that with proper cooperation of gynecologist and transplantologist, as well as determination of the recipient, it is possible to monitor the pregnancy and give birth to a healthy child even during liver transplant failure. Yet the woman should be under strict supervision with frequent evaluation of the allograft function [4]. This report also proves that conception is achievable despite liver cirrhosis, associated hormonal disorders and expected abnormal ovulation.

CITE THIS AS


ABBREVIATIONS

AIH – autoimmune hepatitis
OLTx – orthotopic liver transplantation
CMV – cytomegalovirus
PRBCs – packed red blood cells
PLT – platelet
FFP – fresh frozen plasma

REFERENCES


LIST OF THE TABLES

Tab. 1. Selected laboratory test results of patient at the beginning (7-16.03), in the middle (16.05, 21.06) and at the end of the pregnancy (15-22.08)
### TAB. 1. SELECTED LABORATORY TEST RESULTS OF PATIENT AT THE BEGINNING (7-16.03), IN THE MIDDLE (16.05, 21.06) AND AT THE END OF THE PREGNANCY (15-22.08)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>7.03</th>
<th>13.03</th>
<th>16.03</th>
<th>16.05</th>
<th>21.06</th>
<th>15.08</th>
<th>17.08</th>
<th>22.08</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC [G/L]</td>
<td>2.59</td>
<td>3.46</td>
<td>2.15</td>
<td>3.66</td>
<td>2.68</td>
<td>2.58</td>
<td>2.66</td>
<td>3.02</td>
</tr>
<tr>
<td>RBC [G/L]</td>
<td>4.37</td>
<td>4.55</td>
<td>3.88</td>
<td>3.22</td>
<td>2.85</td>
<td>2.76</td>
<td>2.69</td>
<td>2.87</td>
</tr>
<tr>
<td>HGB [g/dl]</td>
<td>13.3</td>
<td>11.9</td>
<td>11.8</td>
<td>10.4</td>
<td>9.5</td>
<td>9.3</td>
<td>8.9</td>
<td>9.5</td>
</tr>
<tr>
<td>PLT [G/L]</td>
<td>49</td>
<td>39</td>
<td>39</td>
<td>51</td>
<td>40</td>
<td>38</td>
<td>45</td>
<td>41</td>
</tr>
<tr>
<td>ALT [U/L]</td>
<td>65</td>
<td>174</td>
<td>141</td>
<td>49</td>
<td>36</td>
<td>49</td>
<td>59</td>
<td>45</td>
</tr>
<tr>
<td>AST [U/L]</td>
<td>51</td>
<td>157</td>
<td>107</td>
<td>49</td>
<td>46</td>
<td>71</td>
<td>89</td>
<td>67</td>
</tr>
<tr>
<td>Bilirubin [mg/dl]</td>
<td>1.23</td>
<td>1.38</td>
<td>1.64</td>
<td>1.71</td>
<td>2.78</td>
<td>5.15</td>
<td>4.81</td>
<td>4.67</td>
</tr>
<tr>
<td>ALP [U/L]</td>
<td>330</td>
<td>839</td>
<td>739</td>
<td>378</td>
<td>279</td>
<td>473</td>
<td>471</td>
<td>368</td>
</tr>
<tr>
<td>GGTP [U/L]</td>
<td>157</td>
<td>441</td>
<td>444</td>
<td>290</td>
<td>96</td>
<td>129</td>
<td>125</td>
<td>135</td>
</tr>
<tr>
<td>Albumin [g/dl]</td>
<td>3.9</td>
<td>4.1</td>
<td>4.16</td>
<td>3.5</td>
<td>3.2</td>
<td>2.2</td>
<td>2.2</td>
<td>2.7</td>
</tr>
<tr>
<td>INR</td>
<td>1.1</td>
<td>1.2</td>
<td>1.2</td>
<td>1.1</td>
<td>1.2</td>
<td>1.1</td>
<td>1.2</td>
<td>1.1</td>
</tr>
</tbody>
</table>