CASE REPORT

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Pregnancy After Liver Transplantation

Mehmet KULHAN,[a,b]
Nur Gözde KULHAN,[a,b]
Ümit NAYKI,[c]
Cenk NAYKI,[c]
Paşa ULUĞ,[c]
Hülya TOKLUCU[a]

[a]Clinic of Gynecology and Obstetrics, İzmir Tepecik Training and Research Hospital, İzmir
[b]Clinic of Gynecology and Obstetrics, Erzincan Üniversitesi Mengücek Gazi Training and Research Hospital,
[c]Department of Gynecology and Obstetrics, Erzincan University Faculty of Medicine, Erzincan

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Correspondence:
Mehmet KULHAN
Erzincan Üniversitesi Mengücek Gazi Training and Research Hospital, Clinic of Gynecology and Obstetrics, Erzincan, TURKEY
mehmet_kulhan@yahoo.com

ABSTRACT Liver transplantation has become an available and successful option for treating numerous congenital and acquired hepatic disorders. Studies have shown that when the prepregnancy recipient graft function is stable and adequate, pregnancy is normally well tolerated with favorable neonatal outcomes. However, several reports exist showing increased incidences of hypertension and preeclampsia, as well as lower birth weights, prematurity, preterm labor, anemia, diabetes, and intrauterine growth retardation. These patients should be monitored with a multidisciplinary approach to achieve optimal maternal and fetal outcomes. In this case report, pregnancy follow-up and the results of the patient who underwent liver transplantation approximately 12 months before pregnancy are discussed.

Keywords: Liver transplantation; pregnancy

At present, liver transplantation is one of the usable option to treat advanced stage liver failure.[1] Menstrual irregularities or amenorrhea has been associated with the decreased fertility in women who have an anovulatory cycle with liver failure.[2] However, the rapid recovery of libido, menstrual cycle, and fertility has been reported in the several patients of reproductive age after successful transplantation.[3] In the past 25 years, studies on liver transplantation and pregnancy have revealed that pregnancy is well tolerated and the neonatal outcome is satisfactory if the prepregnant recipient graft functions are normal.[4] However, hypertension, preeclampsia, preterm birth, low birth weight, anemia, diabetes mellitus, and some infections are more common in these patients.[4] In these patients, acute graft rejection and considerable graft dysfunction were not observed, and no specific malformation was observed in neonates.[1-4] Another possible problem in pregnancies after transplantation is fetal anomalies, which may be secondary to immunosuppressive agents used. Therefore, such patients, when pregnant, are in the high-risk pregnancy category that should be closely monitored against the possible pregnancy complications. In this case report, a patient who underwent liver transplantation approximately 12 months before pregnancy was presented.

CASE REPORT

Type 1 autoimmune hepatitis disease was diagnosed in a 26-year-old primiparous patient at the age of 19. The patient received steroid monotherapy

(prednisone 20 mg) for immunosuppression but subsequently developed hepatic insufficiency. Approximately 12 months before her pregnancy, the liver from her sister was transplanted to her. The patient approached our clinic for the first time with secondary amenorrhea and was reported to have a fetal heartbeat-positive pregnancy for approximately six weeks. In addition, she was taking 4 mg tacrolimus and 5 mg prednisone every day for immunosuppression. The patient was taken to the center where the transplant was performed. On consultation, it was stated that the first year after liver transplantation is dangerous to the patient for pregnancy, and it is appropriate to postpone the pregnancy to the following years in these patients. The patient even after knowing these risks, accepted all of them and desired the continue the pregnancy. The liver function tests (LFTs) were normal in the patient's antenatal follow-up [Aspartate aminotransferase (AST): 24 U/L, Alanine aminotransferase (ALT): 6 U/L, Alkaline phosphatase (ALP): 90 U/L]. The patient had a hemoglobin value of 13.7 g/dL and a platelet count of 228,000. In the TORCH panel, toxoplasma immunoglubulin G (IgG) was negative and rubella and cytomegalovirus (CMV) IgG were positive. Other biochemical test results showed that the prothrombin time (PT), international normalized ratio, and active partial thromboplastin time were within the normal range. The blood group of the patient was B Rh-positive. The patient was followed by antenatal follow-up with folic acid. The patient was treated with 4 mg tacrolimus and 5 mg prednisone every day for immunosuppression. Nuchal translucency measurement was 1.6 mm in the 12th gestational week, and nasal bone was detected positive. The fetal risk in the combined test was in the normal range. The second level ultrasonographic examination performed during the 20th gestational week and fetal echocardiography performed in the 22th week showed no pathological findings. In the laboratory studies of the patient who presented with complaints of nausea and abdominal pain during the 28th gestational week, infections such as CMV, human immunodeficiency virus, hepatitis markers, toxoplasmosis, and rubella were found to be negative. The hemoglobin level was 10.1 mg/dL. LFT and renal function tests were normal. No abnormality was observed in obstetric ultrasonography, and no contraction was observed in a non-stress test. The patient was hospitalized and symptomatic treatment was initiated for pain. After two days, all the routine tests were repeated and no pathology was observed in the patient; the patient was discharged and the routine pregnancy follow-up was continued. Blood pressure, weight gain, the presence of edema, fetal biometry, amniotic fluid index, and LFT were assessed at each visit. The patient was treated with folic acid for the first three months and then with iron supplementation until birth. For immunosuppression, 4 mg tacrolimus and 5 mg prednisone were continued throughout pregnancy. The patient had no clinical complaints and no pathology was found in fetal antenatal evaluations. The patient was admitted to our hospital at the 41st week of pregnancy on the onset of delivery pain. As the estimated fetal weight was over 4000 g and cephalopelvic incompatibility was observed, the birth was performed by cesarean section; 4720 g male baby was delivered live with the Apgar score of 8 in the first minute. No complications were observed in the mother and newborn in the postoperative period. The postoperative LFTs were normal.

DISCUSSION

Approximately at 20 years ago, it was nearly impossible to think about transplantation, pregnancy, and immunosuppression together. However, the use of safe immunosuppressive regimens, as well as clinical and surgical developments, have increased the number of successful transplantations. The modern technology has opened up new perspectives for saving a life in such cases.[4] When the literature is reviewed, it has been observed that hepatic failure is the most common autoimmune hepatitis in young women.[5,6] Thus, autoimmune hepatitis is the leading cause of three of four liver failures in the reproductive age. In our case, the transplantation was performed because of liver failure caused by type 1 autoimmune hepatitis. Contraception has become a crucial part of medical

counseling in the post-transplant women of reproductive age who have regained ovulation functions. In general, several centers recommend the postponement of pregnancy by a year after transplantation. This recommendation is supported by the National Transplant Pregnancy Registry (NTPR) so that the number of live births will be high and organ rejection will be less.[4] In case of pregnancy in the early stages of transplantation, the chances of opportunistic infections such as CMV are high because of the use of a high-dose immunosuppressive agent that may adversely affect pregnancy outcomes.[7] In our case, pregnancy occurred in the early stages of transplantation. However, no complications were developed.

The patients planning post-transplant pregnancy may face various obstetric complications. After organ transplantation, pregnancy should be evaluated in terms of maternal and fetal outcomes, as well as effects on transplanted organs and other systems. Patients who are planning a pregnancy after solid organ transplantation should be followed up with a multidisciplinary approach. This follow-up should include information on which immunosuppressive agent is to be used during pregnancy, the time between pregnancy and transplantation, cervical cytology, infection screening (CMV and urine cultures), and which liver and kidney function tests should be performed. The most frequently used immunosuppressive agents after liver transplantation are corticosteroids, cyclosporin A, tacrolimus, mycophenolate mofetil (MMF), and azathioprine, and their categories in the FDA guidelines are B, C, C, D, and D, respectively. MMF and azathioprine are generally not preferred during pregnancy. Another possible problem in pregnancies after transplantation is fetal anomalies, which may be secondary to immunosuppressive agents used. A small membranous ventricular septal defect was detected in the babies of two of the three mothers using tacrolimus.[8] Investigations emphasize that maternal-fetal toxicity is dose-dependent. Due to the development of cardiomyopathy in the infants of tacrolimus-receiving mothers, fetal echocardiography is recommended during the 20th to 22nd week of pregnancy.[8,9] After transplantation, fetal cardiac anomalies may be the maternal systemic effect of the pregnancy itself or the drugs used. Hypertension and preeclampsia are more common in these pregnancies than in the normal population.[10,11] This may be because of the vasoconstrictive effects of cyclosporin A and tacrolimus.[12] According to NTPR data, the rate of rejection after liver transplantation is approximately 8%.[13] In one study, out of 57 patients who underwent transplantation under the age of 21 years, 5% of them experienced organ loss during pregnancy and 11% within 2 years.[14]

When evaluated in terms of obstetric complications, hypertension, preeclampsia, cesarean delivery, intrauterine growth retardation, diabetes mellitus, anemia, infection, and preterm delivery are more common in pregnancies after liver transplantation than in a normal pregnant population. Pregnancy after organ transplantation should be evaluated in terms of effects on transplanted organs and other systems, as well as maternal and fetal outcomes, and these events should be closely monitored for possible pregnancy complications, which should be considered in high-risk pregnancy category.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Paşa Uluğ;* ***Design:*** *Mehmet Kulhan;* ***Control/Supervision:*** *Can Türkler;* ***Data Collection and/or Processing:*** *Hülya Toklucu;* ***Analysis and/or Interpretation:*** *Nur Gözde Kulhan;* ***Literature Review:*** *Cenk Naykı;* ***Writing the Article:*** *Ümit Naykı;* ***Critical Review:*** *Mehmet Kulhan;* ***References and Fundings:*** *Mehmet Kulhan;* ***Materials:*** *Nur Gözde Kulhan.*

REFERENCES

1. Jabiry-Zieniewicz Z, Kamiński P, Pietrzak B, Cyganek A, Bobrowska K, Ziółkowski J, et al. Outcome of four high-risk pregnancies in female liver transplant recipients ontacrolimus immunosuppression. Transplant Proc 2006;38(1):255-7.
2. Miller JC, Mastrobattista JM, Katz AR. Obstetrical and neonatal outcome in pregnancies after liver transplantation. Am J Perinatol 2000;17(6):299-302.
3. Riely CA. Contraception and pregnancy after liver transplantation. Liver Transpl 2001;7(11 Suppl 1):S74-6.
4. Armenti VT, Herrine SK, Radomski JS, Moritz MJ. Pregnancy after liver transplantation. Liver Transpl 2000;6(6):671-85.
5. Czaja AJ, Carpenter HA. Distinctive clinical phenotype and treatment outcome of type 1 autoimmune hepatitis in the elderly. Hepatology 2006;43 (3):532-8.
6. Bermas BL, Hill JA. Effects of immunosuppressive drugs during pregnancy. Arthritis Rheum 1995;38(12):1722-32.
7. Heneghan MA, Sylvestre PB. Cholestatic diseases of liver transplantation. Semin Gastrointest Dis 2001;12(2):133-47.
8. Armenti VT, Moritz MJ, Davison JM. Drug safety issues in pregnancy following transplantation and immunosuppression: effects and outcomes. Drug Saf 1998;19(3):219-32.
9. Vyas S, Kumar A, Piecuch S, Hidalgo G, Singh A, Anderson V, et al. Outcome of twin pregnancy in a renal transplant recipient treated with tacrolimus. Transplantation 1999;67(3):490-2.
10. Scantlebury V, Gordon R, Tzakis A, Koneru B, Bowman J, Mazzaferro V, et al. Childbearing after liver transplantation. Transplantation 1990;49(2): 317-21.
11. Ville Y, Fernandez H, Samuel D, Bismuth H, Frydman R. [Pregnancy after hepatic transplantation. 17 pregnancies]. J Gynecol Obstet Biol Reprod 1992;21(6):691-6.
12. Textor SC, Taler SJ, Canzanello VJ, Schwartz L, Augustine JE. Posttransplantation hypertension related to calcineurin inhibitors. Liver Transpl 2000;6(5):521-30.
13. Armenti VT, Radomski JS, Moritz MJ, Gaughan WJ, Hecker WP, Lavelanet A, et al. Report from the National Transplantation Pregnancy Registry (NTPR): outcomes of pregnancy after transplantation. Clin Transpl 2004;103-14.
14. Coscia LA, Constantinescu S, Moritz MJ, Frank A, Ramirez CB, Maley WL, et al. Report from the National Transplantation Pregnancy Registry (NTPR): outcomes of pregnancy after transplantation. Clin Transpl 2009;103-22.