

# Cesarean Delivery and Anesthetic Management of Pregnancy after Liver Transplantation: Case Report

## Karaciğer Nakli Sonrası Gebelikte Sezaryenle Doğum ve Anestezik Yaklaşım

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**ABSTRACT** Successful liver transplantation not only recovers the underlying liver disease, but also re-establishes fertility in the pre-menopausal recipients. That provides a chance of pregnancy likely causing challenges to recipients as well as clinicians. An 18-year-old patient underwent liver transplantation at our hospital due to liver failure related  $\alpha$ -1 antitrypsin deficiency. She became pregnant nine months after the liver transplantation. She received tacrolimus treatment throughout the pregnancy with normal fetal development during follow up. Beginning of ninth month of pregnancy, tacrolimus dose was increased due to elevated liver enzymes. Upon the start of labor at 36<sup>th</sup> week, cesarean delivery was performed via administration of spinal anesthesia. No hypotension or the requirement of ephedrine was observed during the operation. An improvement was determined in liver functions by the second post-operative day. The patient was discharged with recommendations of tacrolimus treatment and not to breast-feed at the third post-operative day. The timing of pregnancy, usage of immunosuppressive agent and to provide safety of mother and fetus during delivery seems to be essential points concerning pregnancies following liver transplantation. Anesthetic management with regional block can be preferred in patients with normal coagulation profile and better hemodynamic parameters.

**Key Words:** Liver transplantation; pregnancy; anesthesia, spinal

**ÖZET** Başarılı karaciğer nakli sadece altta yatan karaciğer hastalığını tedavi etmekle kalmaz; premenopozal kadın alıcılarda fertilitiyi de düzeltir. Bu da, nakil yapılmış hastalar ve klinisyenler için birtakım zorluklara neden olabilecek gebelik şansını gündeme getirir.  $\alpha$ -1 antitripsin eksikliğine bağlı karaciğer yetmezliği nedeniyle 18 yaşında hastaya hastanemizde karaciğer nakli yapıldı. Nakil sonrası 9. ayda gebelik gelişti ve hasta hamileliği boyunca takrolimus kullandı. Takipte fetüs gelişimi ile ilgili herhangi bir sorun ile karşılaşılmadı. Gebeliğin 9. ayına girerken karaciğer enzimlerinde yükselme olması üzerine takrolimus dozu artırıldı. Doğum sancuları 36. haftada başladı; acil sezaryene alındı ve spinal anestezi uygulandı. Operasyon boyunca annede hipotansiyon gelişmedi ve efedrin ihtiyacı olmadı. Postoperatif dönemde karaciğer fonksiyon testlerinde 2. günden itibaren düzelme gözlemlendi. Üçüncü günde anneye takrolimus kullanması, bebeğe anne sütü vermemesi önerilerek taburcu edildi. Nakil sonrası gebelikte; gebeliğin zamanlaması, kullanılan immüno-supresif ajan, anne ve fetüs güvenliğinin sağlanması önemli noktalarlardır. Koagülasyon profili normal olanlarda, iyi bir hemodinami ile rejyonel blok tercih edilebilecek anestezi yöntemi olabilir.

**Anahtar Kelimeler:** Karaciğer transplantasyonu; gebelik; anestezi, spinal

Successful liver transplantation not only recovers the underlying liver disease, but also restores fertility in the pre-menopausal recipients.<sup>1</sup> That provides a chance of pregnancy, which causes a risk for recipients and also some troubles for clinicians.<sup>2</sup>

Pregnancy after liver transplantation is in a group of high risk due to increased materno-fetal morbidity. Augmentation on obstetric complications like hypertension, preeclampsia, renal dysfunction, premature birth and low birth-weight were reported as the possible problems.<sup>1</sup> The risk of graft rejection and the possible side effects of immunosuppressive agents on mother and fetus were indicated as other problems to be concerned in pregnancies after the transplantations.<sup>2</sup>

Although guidelines for the follow up of pregnancy in kidney recipients are available, there is no guideline specific to patients having pregnancy after the liver transplantation.<sup>2,3</sup> There is need more data about the safety of recipient and fetus as well as the perioperative management despite of increased amount of successful pregnancy outcomes after liver transplantation.

In this regard, this paper reports the successful anesthetic management and perioperative follow up of a patient who has pregnancy after liver transplantation, underwent emergency cesarean delivery at 36<sup>th</sup> week of the pregnancy.

## CASE REPORT

An 18-year-old female patient had living donor liver transplantation in our hospital due to liver failure related  $\alpha$ -1 antitrypsin deficiency. Patient with no postoperative problems was decided to be follow-up with administration of tacrolimus (2x1 mg/day) as an immunosuppressive agent. Hemogram, hemostasis panel, liver and renal function tests and tacrolimus level were evaluated monthly. During her controls at 9<sup>th</sup> month, post transplantation pregnancy was recognized and the patient was consulted by Obstetrics and

Gynecology Department. Patient was recommended to receive tacrolimus treatment at 2x1 mg/day dose throughout the pregnancy. There were no problems related to fetal development during her controls. In the beginning 9<sup>th</sup> month of pregnancy, tacrolimus dose was increased to 2x2 mg/day due to elevated liver enzymes without jaundice. Upon onset of labor pains after one week, patient was referred to our hospital and was decided to undergo emergency cesarean section at the 36<sup>th</sup> week of the pregnancy. At preoperative assessment, physical examination revealed no abnormal findings. Laboratory analysis revealed Hb level of 8.9 g/dL, Htc of 27.6, PLT of 171.10<sup>3</sup>/mL, prothrombin time of 11.6 sec, aPTT of 21.6 sec, INR of 1, glucose of 78 mg/dL, BUN of 14 mg/dL, creatinine of 0.6 mg/dL, total bilirubin of 2.13 mg/dL, direct bilirubin of 1.52 mg/dL, AST of 149 U/L, ALT of 219 U/L and ALP of 320 U/L. Patient was taken into operation at IIE risk classification according to American Society of Anesthesiology (ASA) classification.

Monitorisation of noninvasive blood pressure, ECG and pulse oximetry was performed in the operation room. Initial measurements of blood pressure, pulse and sPO<sub>2</sub> were 163/84 mmHg, 111 beat/min and 92%; respectively. Due to appropriateness of hemodynamic parameters and normal hemostasis panel; spinal anesthesia was decided after the consent of the patient. Rapid intravenous infusion of ringer lactate and colloids were given via large peripheral line. Lumbar puncture was performed at L3-L4 level in sitting position and 12 mg hyperbaric bupivacaine+12.5 µg fentanyl were administered intrathecaly. After the procedure patient was returned to the supine position with left lateral tilt in order to avoid supine hypotension.

Operation was allowed upon identification of the sensory block at T5 dermatome level assessed by pin-prick test. Within 5 minutes of skin incision, a healthy, 3050 g weigh baby was born; 1<sup>st</sup> and 5<sup>th</sup> minute APGAR scores were 7 and 10, respectively. A total of 1500 mL solution, composed of 1000 ml ringer lactate and 500 mL colloid, was administered during operation. There

**TABLE 1:** Laboratory findings of the patient in the perioperative and postoperative periods.

	Hb (g/dL)	INR (0.8-1.2)	TB (0.2-1.2 mg/dL)	AST (5-34 U/dL)	ALT (5-34 U/dL)	BUN (8-21 mg/dL)	Creatinine (0.6-1.1 mg/dL)	Glucose (70-105 mg/dL)
Preoperative period	8.9	1	2.13	149	219	14	0.6	78
Postoperative period								
First day	8.3	1	2.75	138	203	17	0.7	70
Second day	7.2	-	1.21	138	172	23	1	99
Third day	7.4	-	0.98	90	120	31	1	68

Hb: Hemoglobin, INR: International normalized ratio; TB: Total bilirubin; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BUN: Blood urea nitrogen.

were no development of hypotension and no need of ephedrine during the operation. Routine control was performed postoperatively. An improvement on liver function tests was observed at the second day (Table 1). Baby was taken to intensive care unit due to postnatal superficial respiration and was given oxygen therapy. On the second day, oxygen therapy was reduced, stepwise, upon normalization of the symptoms. The patient was discharged at third day of post-operation with recommendations of continuation to tacrolimus treatment (2x2 mg) and not to breast-feed the baby.

## DISCUSSION

The number of liver transplantations as well as the related survival chance is increasing in our country compatible with the worldwide in liver transplantation. It is reported that over 80% of women have a normal menstrual cycle within 8 months of transplantation and restoration of menstrual bleeding may occur as early as 2 months post transplant.<sup>2</sup> This indicates the increased probability of pregnancy and anesthesia practice for non-transplant surgical interventions among premenopausal female liver recipients.

There are no certain limits concerning timing of pregnancy following transplantation. However, expert opinion is in favor of at least one year of interval provided together with good general health status of recipients, stable graft functions and control of co-morbid disorders such as hypertension and diabetes mellitus.<sup>3,4</sup>

In a study including 71 pregnancies by Christopher et al, increased incidence of premature birth and acute rejection were reported in patients who conceived within one year of transplantation.<sup>2</sup> In another retrospective study including 38 pregnancies, abortus 86% of pregnancies developed within 1 year of transplantation were documented to be associated with abortus in the first trimester.<sup>5</sup> In this regard, patients planning to become pregnant must be informed about the appropriate timing and associated risks.

Our patient, having no problems related to graft function, immunosuppressive agents and general health status during postoperative follow up period, became pregnant in the 9<sup>th</sup> postoperative month. Upon her wish of continuation of pregnancy, she was taken into close follow up under tacrolimus therapy.

The main problems likely to occur during pregnancy following transplantation were documented to be prematurity and low birth weight for the fetus while hypertension, pre-eclampsia and increase incidence of renal dysfunction for the mother.<sup>1</sup> These risks while indicated to be lower than kidney recipients, have been suggested to be higher in liver recipients compared with the normal population. Besides, hypertension and pre-eclampsia were associated with immunosuppressive drugs with the highest risk indicated for cyclosporine followed by tacrolimus and corticosteroids, respectively.<sup>4</sup> In our case with administration of tacrolimus throughout

the pregnancy, the dose of tacrolimus was increased due to identification of elevated liver enzymes two weeks before the delivery. There were no obstetric pathology such as pre-eclampsia or hypertension and no malformation developed in the fetus.

Tacrolimus is known to be a more potent calcineurin inhibitor than cyclosporine with FDA pregnancy category of C.<sup>4</sup> In a past prospective study concerning evaluation of 49 babies from 37 mothers using tacrolimus, the incidence of pre-eclampsia associated with tacrolimus was determined to be lower than that of cyclosporine. Furthermore, rare fetal malformations were reported to be evident none of which having a direct relation to tacrolimus.<sup>6</sup> No difference between normal population and tacrolimus usage was evident in terms of fetal malformation ratio. Tacrolimus passes into breast milk and there is not enough data available about the safety of breastfeeding for mothers receiving tacrolimus treatment.<sup>4</sup> Accordingly, breastfeeding was not allowed in our case.

While vaginal delivery has been indicated to be possible in these cases, consideration of cesarean section has been recommended in case of development of obstetric complications like pre-eclampsia and preterm labor.<sup>4</sup>

One of the important points to consider during preoperative evaluation is the graft function and the presence of rejection. Additionally, side effects including renal dysfunction related to immunosuppressive agents as well as thrombocytopenia must be considered and carefully evaluated. Increase in morbidity was demonstrated in surgical

operations in the presence of rejection. However, the maintenance of hepatic perfusion by appropriate anesthesia method was documented to prevent postoperative graft dysfunction.<sup>7</sup> In line with the emphasis of coagulation parameters and thrombocyte count to be normal in case of selection of epidural or spinal methods of anesthesia.<sup>8</sup> Spinal anesthesia was performed in our patient due to appropriate hemodynamic parameters and normal value of hemostasis panel. Based on suitable hydration and adequate level of spinal anesthesia, there was no hypotension development and no need to vasoconstrictor agent during operation.

Acute rejection, acid-base imbalance and serious infection were indicated to be possible problems that may be encountered postoperatively and the frequency is higher in the early post-transplantation period particularly.<sup>8</sup>

Timing of pregnancy, the obstetric problems during pregnancy, perioperative maternal and fetal safety in cases with cesarean delivery and the principles of the postoperative follow up are basic components of clinical practice concerning management of pregnancy after transplantation. These patients must be closely followed up with a multidisciplinary approach and interventions must be performed by clinicians experienced in the high risk pregnancies.

In conclusion, spinal anesthesia is a preferable method in the cesarean delivery of post-transplantation pregnancies among recipients with good graft function, normal hemodynamic parameters as well as normal coagulation profile.

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