

In conclusion, we have demonstrated that Tc-99m-DTPA allograft scintigraphy is a useful tool in the diagnosis of the etiology of renal graft dysfunction in CsA-treated allograft recipients. When used in conjunction with clinical assessment and CsA blood levels, it forms a pivotal component in a non-invasive diagnostic algorithm that is highly sensitive and specific for the differentiation of acute cellular rejection and CsNT.

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FK506 AND PREGNANCY IN LIVER TRANSPLANT PATIENTS

1439

There have been several reports of successful pregnancy in organ transplant patients treated with AZA, steroids, or CsA (1, 2). However, the use of these immunosuppressive drugs in renal transplant patients is often associated with preeclampsia, preterm births, and severe intrauterine growth retardation (1). Earlier, we have reported pregnancy in liver transplant patients treated with AZA or CsA at the University of Pittsburgh Medical Center (3). In the present communication, we summarize our recent experience with pregnancy in liver transplant patients treated with FK506 as the primary immunosuppressive drug.

At the present time, there are 876 males and 627 female liver transplant patients on FK506 immunosuppression at the Uni-

versity of Pittsburgh Medical Center. Nine pregnancies have been recorded in 9 of these patients on FK506 therapy. These patients received liver transplantation for Caroli's disease (1), primary biliary cirrhosis (1), alcoholic cirrhosis (2), cryptogenic cirrhosis (2), fulminant hepatic failure (1), autoimmune hepatitis (1), or non-A non-B hepatitis (1). The age of the mothers ranged from 18 to 35 years. Four of them were primary FK506 patients and 5 of them were switched to FK506 therapy after chronic rejection while on CsA. All of the patients received FK506 with (n=5) or without steroid (n=4) therapy during the entire period of pregnancy. The FK506 doses ranged from 2 mg qd to 32 mg bid. Two patients had mild hypertension and 1 had proteinuria during pregnancy. Six of the 9 patients had

TABLE 1. Clinical Data in Pregnancies Occurring in Liver Transplant Recipients Treated with FK506

Case	Time post-OLT ^X to delivery (years)	Duration of FK506 therapy (months)	FK506 dosing in pregnancy (mg)			Gestation period (weeks)	Infant birth weight
			Before	During	After		
1	2.3	8.3	6 bid	10 qd	10 qd	36	4 lb 15 oz
2	1.3	16.5	10 qd	10 qd	10 qd	35	4 lb 13 oz
3	2.8	21	8 bid	8 bid	7 bid	34	4 lb 1 oz
4	5.75	19	3 bid	3-4 bid	3 bid	34	3 lb 12.5 oz
5	1.8	22	2 bid	2-3 bid	3 bid	40	8 lb 10 oz
6	1.6	19.5	24 bid	32 bid	32 bid	37.5	5 lb 8.5 oz
7	0.56	6.75	6 bid	6-7-5 bid	2 qd	22	Unknown
8	3.6	24	4 bid	5 bid	5 bid	36	5 lb 8 oz
9	1.5	18	5 bid	5 bid	5 bid	37	5 lb 6 oz

OLT^X, orthotopic liver transplantation.

normal vaginal delivery; 3 patients required cesarean section for previous classical cesarean section, placenta abruptio, or antepartum hemorrhage. All the patients had normal liver function before pregnancy, and 2 patients who experienced an episode of rejection during pregnancy were treated successfully with high-dose steroids. Table 1 lists the clinical data on the patients and the infants born. None of the babies was considered small for gestational age, based on the Colorado intrauterine Growth Charts (4).

Five of the 7 babies for whom potassium levels were available had hyperkalemia (range 6.1–10.9 mEq/L) at the time of birth that resolved spontaneously within 24–48 hr without any treatment. One baby who was delivered by a patient known to be a cocaine addict was hypoxic, tested positive for cocaine, remained in the incubator for 2 weeks, but recovered after that time period. One baby who was born to a mother with renal impairment during pregnancy was anuric for 36 hr, secondary to high FK506 concentrations in the cord, but regained normal renal function in 1 week. The only baby that died 2 hr after birth was born prematurely (22 weeks) to a 20-year-old patient who conceived within a month after transplantation. This patient had evidence of CMV in the blood and gastrointestinal tract and was treated with ganciclovir. Eight of the 9 babies are currently alive and are developing normally. In conclusion, liver transplant patients on FK506 appear to have a normal course of pregnancy and, in the majority of cases, give birth to normal and healthy babies.

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SUCCESSFUL PREGNANCY IN A PATIENT AFTER LIVER TRANSPLANTATION MAINTAINED ON FK 506

FK 506 is a novel macrolide immunosuppressant that is currently under clinical investigation in patients after solid organ transplantation. We here report on a successful pregnancy in a patient treated with FK 506. To our knowledge, this is the first report of a patient under FK 506 immunosuppression who gave birth to a healthy child.

Case report. A 28-year-old woman was liver grafted for post-hepatic cirrhosis. After the loss of the first graft due to intractable chronic rejection, the second graft again showed signs of chronic rejection (Fig. 1). Therefore, FK 506 treatment (0.10 mg/kg body wt/day; target plasma level < 1.0 ng/ml [1]) was initiated, leading to a complete normalization of the patient's liver function.

On week 61, the patient presented in our outpatient clinic after having conceived 6 weeks before. After extensive discussions as to whether an abruptio should be performed, it was decided not to interrupt the pregnancy. This decision was made primarily based on the extensive will of the patient, who was fully aware of the risks of this pregnancy. The subsequent course of the pregnancy was uneventful; regular sonograms showed normal fetal growth. However, on week 28 of pregnancy, the patient was readmitted to the hospital with acute graft rejection (FK 506 plasma level < 0.05 ng/ml), which was successfully treated with bolus steroids and an increase in FK 506 dosage from 0.10 mg/kg body wt/day to 0.15 mg/kg body wt/day. On week 36, after a cesarean section, a healthy male newborn of 2860 g was delivered. Apgar scores were normal; no congenital abnormalities or birth defects were observed. The FK 506 plasma concentration in the placental vein was 0.24 ng/ml compared with 0.49 ng/ml in the plasma of the mother,

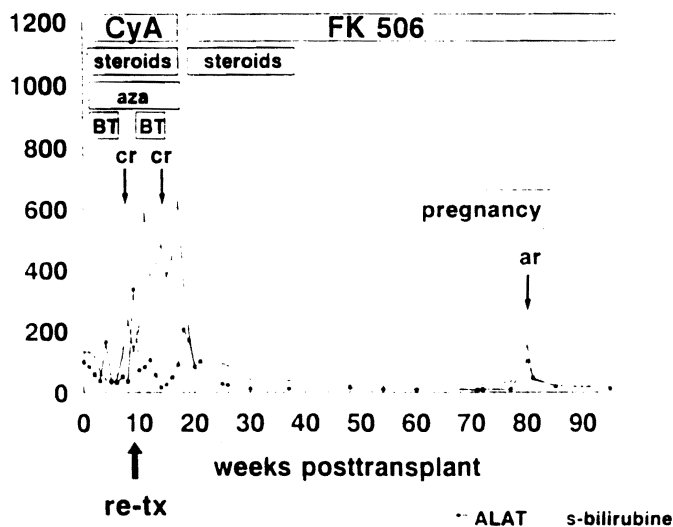


FIGURE 1. Clinical course of the patient. Bilirubin as well as alanine transferase levels shown. Abbreviations: BT, BT563 (anti-T cell IL-2R MAb); ar, acute rejection; cr, chronic rejection.

indicating a transplacental transfer of the drug. Three days after delivery, the FK 506 plasma concentration in the fetal blood was 0.09 ng/ml, and after 1 week, no detectable FK 506 was present in the blood of the newborn. The mother and the healthy newborn were discharged from hospital 12 days after delivery. The child is now 12 months old, and in normal condition.

Numerous reports on pregnancies in patients after organ transplantation under cyclosporine have been published (re-