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CASE REPORT

Twin pregnancy after kidney transplant – the insight of the prenatal and postnatal problems based on a case report

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ABSTRACT

Twin pregnancy after a kidney transplant is rare and is known to be a high-risk pregnancy. Chances of getting pregnant after a kidney transplant are higher than for patients with renal chronic disease. The most common problems which can occur are: severe hypertension, preeclampsia, abruption of the placenta and fetal growth restriction. We present a case of twin pregnancy after a kidney transplant, on three immunosuppressant medications, complicated by arrhythmia treated by cardioversion, severe fetal growth restriction in twin 2, and preeclampsia. The pregnancy was ended at nearly 28 weeks of gestation due to abruption of the placenta in the normally growing twin. The birth weight was as follows: in twin 1-1200 g and in twin 2-620 g. We present problems during the postnatal period and outcomes at 12 months of life.

KEY WORDS:

twin pregnancy, kidney transplant, immunosuppressant therapy.

INTRODUCTION

Data has shown that the pregnancy rate is higher after a kidney transplant (KT) and the miscarriage rate is lower than in the general population. However, the risk of adverse pregnancy outcomes such as preeclampsia, cesarean section and preterm delivery are much higher in the KT group than in the general population [1, 2]. The most important determinant of adverse pregnancy outcomes is kidney function impairment not the fact of having KT [3]. The rate of multiple pregnancies in patients with chronic kidney disease is around 6%. However, these pregnancies were associated with higher risk of adverse outcomes. Apart from preterm delivery, higher frequencies of small for gestational age (SGA), perinatal and neonatal mortality were also observed [4].

CASE REPORT

A 35-year-old patient three years after a kidney transplant due to glomerulonephritis on immunosuppressant therapy, conceived spontaneously a dichorionic diamniotic twin pregnancy (DCDA). A previous pregnancy (2012) was complicated by chronic kidney disease (glomerulonephritis) and ended by c-section in 27 weeks of pregnancy because of HELLP syndrome. The neonate died a few days after delivery. In the current pregnancy, the patient was admitted to the hospital (Tertiary Center) due to acute atrial fibrillation episode in 21 weeks of

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TABLE 1. Summary of postnatal period in both twins

Parameter	Twin 1 (normal growth)	Twin 2 (intrauterine growth restricted)
Birth weight	1200 g	620 g
Apgar score	6-9-9-9	4-6-7-7
NICU	Yes	Yes
Surfactant	Yes	Yes
SIMV	From 2nd day of life	From 1st day of life
Oscillatory ventilation	No	From 10th day
NAVA mode	No	Till 49th day of life
Non-invasive ventilatory support	From 7th day of life till 25th day	From 77th day of life till 92nd day
PPHN	No	Yes
Nitric oxide treatment	No	Yes (from 34th till 49th day of life)
Catecholamine supply	No	Yes
Passive oxygen therapy	From 25th day of life till 43rd day	From 92nd day of life till 133rd day
Blood transfusion	Yes	Yes
Parenteral nutrition	Till 16th day of life	Till 19th day of life
BPD	Yes, mild	Yes, severe
Retinopathy	Stage 1	Stage 1/2
Enteral feeding via the teat	From 53rd day of life	From 132rd day of life
IVH	Stage 1	None
Stay in hospital	65 days	141 days
Weight on discharge	2920 g	4880 g

NICU – neonatal intensive care unit; SIMV – synchronized intermittent mandatory ventilation; NAVA – neurally adjusted ventilatory assist; PPHN – persistent pulmonary hypertension of the newborn; BPD – bronchopulmonary dysplasia; IVH – intraventricular hemorrhage

gestation. On admission, she had low blood pressure and complete arrhythmia. Blood results were within the normal range. She needed an electrical cardioversion and was put on heparin. On the ultrasound, DCDA twin pregnancy was confirmed, additionally, severe fetal growth restriction (FGR) with oligohydramnios of twin two was diagnosed. Furthermore, the pregnancy was complicated by hypertension and a change in hypertensive medication was needed due to poor control, her blood pressure was nicely controlled by labetalol. As an immunosuppressant therapy, she was receiving azathioprine, tacrolimus, and prednisone. In the subsequent ultrasounds during hospitalization deterioration of the condition of the growth restricted twin was observed. Due to poor medical and obstetrical history, the multidisciplinary team with the patient made the decision not to end the pregnancy due to the growth restricted fetus indication until 28 weeks, to improve chances of having at least one child. Further close monitoring of the mother and twin's condition during a stay in hospital was performed. At 27 weeks and 5 days, bleeding from the vagina was noted, on the ultrasound abruption of the placenta of the twin, which was growing normally, was confirmed and an emergency c-section was performed. The steroids for lung maturation and neuroprotection were given one day before the c-section. The weight of twin one was 1200 g, with an Apgar score of 6-9-9-9 points and twin two (intrauterine growth restricted) 620 g, Apgar score 4-6-7-7 points. Both twins were admitted to the Neonatal Intensive Care Unit. A summary of the postnatal period in both twins is provided in Table 1. A 12-month follow up revealed normal psychomotor development in twin one (normally growing twin) with weight and height on the 50th centile. He caught up with his peers who were born appropriate for gestational age. In twin two (born below 3rd centile) developmental delay was observed. His weight and height were below the 10th centile. The developmental milestones of twin 2 are presented in Table 2.

DISCUSSION

The rate of successful pregnancies after kidney transplant is 61%, however, 36% of these are preterm deliveries and 16% are extremely preterm (below 28 weeks) due to severe hypertension, preeclampsia, abruption of the placenta or severe fetal growth restriction. The occurrence of hypertension is around 65% and preeclampsia up to 38% [3, 4]. Severe fetal growth restriction is seen in 50% of cases. In the first year post kidney transplant, pregnancy should be avoided due to the time needed to stabilize the graft function and doses of immunosuppressant medications [5]. Usually after one year post-transplant proph-

TABLE 2. Developmental milestones of twin 2 (intrauterine growth restricted)

Age	Gross Motor	Fine Motor	Language	Social/Cognitive
Newborn	Muscle tone and reflexes appropriate to the fetal age	Grasping reflexes appropriate to the fetal age	No sucking and searching reflex	
2 months of life	On mechanical ventilation with analgosedation – neurological condition cannot be assessed	On mechanical ventilation with analgosedation – neurological condition cannot be assessed	On mechanical ventilation with analgosedation – neurological condition cannot be assessed	
3 months of life	Decreased tension in the axial muscles with excessive tension in peripheral muscles. Decreased tendon reflexes	Limb tremors on touch and dorsal flexion, especially on the left side	Non-invasive ventilation	
4 months of life (corrected age of 1 month)	Low spontaneous motor activity. Decreased tension in the axial muscles. Symmetrical tendon reflexes. Positive Moro reflex and support reflex	Foot clonus present. Grasping reflexes present	Present sucking and seeking reflex. Poor sucking-swallowing-breathing coordination. Starts drinking some portion through the teat	
5 months (corrected age of 2 months)	Low spontaneous motor activity, more marked on the right side. Poor stabilization in the head-torso axis. Raise head when lying on the stomach. No symmetry	Holds the rattle. The tendency to footshake persists, but it is less marked	Proper coordination of sucking-swallowing-breathing	Smiles in response of speech
6 months (corrected age of 3 months)	Raise head and chest when lying on the stomach. Cannot roll over	Clonuses absent. Connects hands in the midline, stretches straight arms towards a toy, reaches out, grabs and holds	Babbles	Calms down at the sound of a voice or when it is taken in arms. Expresses emotions
12 months of life (corrected age of 6 months)	Rolling over. Sits steadily	Grabs with fingers, shifts the rattle from hand to hand, shakes it	Spells and makes sounds to attract attention. Reacts to the word "no"	Demonstrates devotion to the caregiver. Imitates gestures e.g. bye-bye

ylaxis is finished and doses of immunosuppressive drugs are reduced. Azathiopryne is a drug of choice during pregnancy. Prednisone and prednisolone can also be used as are in 90% inactivated by placental enzymes. Cyclosporine and tacrolimus are also allowed to be used. Contraindicated are mycophenolate mofetil and cyclophosphamide [6]. Most of the pregnancies (82%) that were conceived during treatment consist of two medications and only 9% on three medications. However, only 3% according to research, conceived on regime consists of azathiopryne, tacrolimus and prednisone [7]. This immunosuppressant regime was used for our patient when she conceived twins. A further issue which is very important is the influence of immunosuppressant therapy on the fetus and the newborn. Observational studies suggest that azathioprine is safe in pregnant women. However, there are rare reports of congenital malformations such as: hypospadias, polydactyly, atrial or ventricular septal defect. Notwithstanding, there is no clear pattern of congenital malformations [5, 8, 9]. Prednisone in high doses – above 40 mg/d, can cause fetal growth restriction and

FIGURE 1. Twins at 12 months – on the right FGR twin, on the left normally growing twin

neurodevelopmental delay [10]. Some series show increased risk of cleft palate, but most of the data suggests no effects on the fetus [5, 11]. In our case, the patient

received low doses of prednisone, which makes it very unlikely that it was connected with FGR, especially that growth restriction was seen only in one twin. The third drug administered in our case was tacrolimus, which according to data does not cause fetal malformations and most authors reported favourable pregnancy outcomes [5, 6, 12]. However, there are consistent data that tacrolimus therapy can be connected with preterm delivery and low birth weight [13-15]. Furthermore, hypertensive medications such as labetalol (β-blockers) can be a cause of low birth weight, but in the described case, labetalol was added to the therapy when severe FGR in twin 2 was already diagnosed. Furthermore, there are no data about the side effect of the immunosuppressant therapy on the outcome of the babies at 12 or 24 months. At 12 months, according to literature, 93.75% and at 24 months 95.2% of the babies had normal development. The mild neurological deviations (muscle tone disturbances in lower limbs and slightly reduced muscle tone in lower limbs) were noted at one year of age only in babies who were born very prematurely. Notwithstanding, the respective findings had improved at age two [16]. In our case, the FGR twin has some motor development delay, but it seems to be caused by the fact of severe growth restriction and severe prematurity rather than the therapy adopted, as the development of the twin's brother is normal (Fig. 1). Therefore, we can assume that the factor with the most influence on the outcomes is not the fact of having an organ transplant but prematurity and growth restriction, which are caused by the complexity of the medical condition. Additionally, based on this case report, we can identify how important cooperation and multidisciplinary teamwork is, as obstetrics and neonatology are not separate branches of medicine but are a continuity of each other.

DISCLOSURE

The authors declare no conflict of interest.

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