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LETTER TO THE EDITORS

Successful pregnancy outcome in a patient following heart, lung and renal transplant

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Pregnancy following solid organ transplant is no longer unusual. The National Transplantation Pregnancy Registry (NTPR) database demonstrates that a growing number of heart and/or lung transplant recipients are in their reproductive years [1]. We report the first case worldwide of pregnancy in a heart, lung and kidney transplant recipient.

A 33-year-old Caucasian patient presented at 11 weeks in her first pregnancy in 2010. She had been diagnosed with cystic fibrosis aged 2 years. She underwent a heart lung transplant when she was 19 years (HLA match grade 2,2,1). Ten years post-transplant she developed cyclosporine-induced renal failure and received a cadaveric renal transplant (HLA match grade 1,1,1) in July 2009. She had previously discussed the possibility of a pregnancy with her transplant physicians. She was advised to wait 1 year post-transplantation.

One year following renal transplant, the patient had stable creatinine levels (100–115 mmol/l). Tacrolimus levels remained therapeutic (6–8 ng/ml) on 1.5–2 mg twice daily (bd). Her pulmonary status remained stable with a forced expiratory volume in one-second (FEV1) of 2.8 l. An angiogram performed prior to her renal transplant showed normal coronary arteries, right heart pressures and an ejection fraction of 65%. Medications included prednisolone, trimethoprim-sulphamethoxazole, colistin sulphomethate sodium, azithromycin, simvastatin, ursodeoxycholic acid, calcium carbonate, darbopoetin alpha, allopurinol, lansoprazole and pancrelipase capsules.

She became pregnant in July 2010, 1 year after her renal transplant. The patient self discontinued prednisolone and was commenced on folinic acid. She was referred to a high-risk obstetric clinic. Monthly multidisciplinary meetings were held to discuss her case. A detailed anatomical scan at 20 weeks gestation revealed a normal anatomical survey.

Her transplant physicians saw her every 2 weeks during her pregnancy. Her FEV1 decreased incrementally from 2.8 l prepregnancy to 1.63 l at 32 weeks (Fig. 1). Creatinine levels rose from 30 weeks gestation, from 116 mmol/l to a peak of 165 mmol/l at 33 weeks. A renal ultrasound revealed a mild hydonephrosis likely to be secondary to a mechanical obstruction by the foetal head. Her required Tacrolimus dose increased from 1.5 mg bd pre pregnancy to 6.5 mg bd just prior to delivery.

At 34 weeks 4 days gestation, patient complained of palpitations. Atrial fibrillation was noted on echocardiogram. Her obstetrician and transplant physician decided, in view of the uncertainty surrounding her cardiac status, to deliver by Caesarean section. She was delivered the next day via Caesarean section, under regional anaesthesia, of a healthy female infant weighing 2450 g at birth. The delivery occurred in the hospital where she receives her post-transplant care. The patient received 100 mg hydrocortisone intraoperatively, to surmount the stress of labour and attenuate possible graft rejection, and was returned to the High Dependency Unit. She was restarted on a maintenance dose of 10 mg Prednisolone and discharged home with her baby on day 6 postoperatively. Pulmonary function tests done 1 week postdischarge showed that her FEV1 had been restored to 2.31 l. Her creatinine had returned to 125 mmol/l. Two months postpartum her required tacrolimus dose fell from 6.5 to 2.5 mg bd. At postnatal review she remains well.

Risks associated with pregnancy, post-transplant, can pose a threat to the mother, foetus and graft. These risks may be managed in the correct setting. The primary issue, with our patient, was the observed deterioration in lung function as her pregnancy progressed. This displayed a dramatic decline in FEV1 of over 41%, over the course of her pregnancy. The dilemma, in such a case, is distinguishing whether this deterioration is secondary to rejection or whether it is simply a mechanical disturbance of pulmonary function. Unfortunately, there is little data currently published which outlines observed changes in the transplanted lung during pregnancy and so it is difficult to ascertain what is an acceptable range for FEV1 decline, if one such exists. It is known, however, that on average, at term, there is a 4 cm rise in the diaphragm and a decrease in functional residual capacity of 10–20% [2]. Compromise of the main expiratory muscles (anterior abdominal wall and intercostal muscles) contributes to FEV1 decline [3]. Physiological fluid retention of

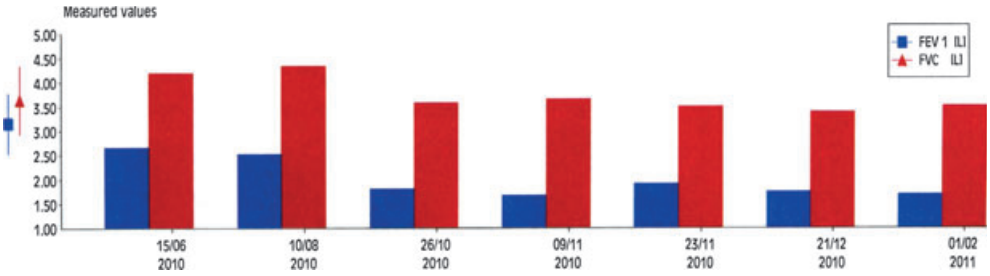

Figure 1 Trend of FEV1 and FVC during pregnancy. Patient became pregnant in July 2010 and delivered baby in February 2011.

pregnancy provides a predisposition to pulmonary oedema. This is exaggerated, in the lung transplant population, secondary to postoperative disruption of the lymphatics [4]. These changes make it difficult to interpret spirometry results and thus identify rejection episodes. In the lung transplant pregnancy cohort, the NTPR reports that 27% of woman experience a rejection episode with 21% experiencing graft loss at 2 years. This makes them high risk when compared with other transplant recipients [1]. If there is ambiguity, over the aetiology of the decline in spirometric values, the patient should undergo biopsy and be treated accordingly. Although our patient's FEV1 was shown to drop significantly, this deterioration was shown to have reversed 1 week postpartum suggesting that the perceived deterioration in lung function was not immunological but most likely anatomical deterioration.

The second dilemma we encountered was the progressive need to increase her tacrolimus dose. Several factors may have contributed to subtherapeutic levels including renal hyperfiltration of pregnancy [5], physiological plasma expansion of pregnancy [6] and pregnancy associated vomiting. Although nausea was not a prominent feature of our patient's pregnancy, it should be noted that if nausea/vomiting is an issue, close care should be paid to any alterations in the timing/nature of drug administration. The patient may have modified drug administration to accommodate her nausea e.g. delaying until nausea has subsided or ingestion of immunosuppressants with food, which will decrease absorption [7]. Patients should be advised of the importance of tight immunosuppressive control and any nausea should be managed aggressively with antiemetics if needed.

In conclusion, the management of pregnancy in a multiple transplant patient is complex and associated with a substantial risk of graft loss at 2 years but good outcomes are achievable with close multidisciplinary control. In the lung transplant population, perceived lung function decline is difficult to interpret in the pregnant patient, however, there should be a high index of suspicion for a rejection episode, which should be investigated appropriately.

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