CASE STUDY

Successful combined lung and kidney transplantation for pulmonary lymphangioleiomyomatosis and renal angioliipomas

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Successful combined lung and kidney transplantation for pulmonary lymphangioleiomyomatosis and renal angioliipomas. M. de Perrot, M. Licker, J. Robert, L. Nicod, A. Spiliopoulos. ©ERS Journals Ltd 1998.

ABSTRACT: Pulmonary lymphangioleiomyomatosis (LAM) and renal angioliipomas are rare but distinct clinical entities that share similar morphological features. Lung transplantation is considered as a valuable therapeutic modality in patients with end-stage pulmonary LAM. However, in some patients, renal complications due to bleeding angiomyoliipomas and cyclosporin-induced nephropathy have become newly identified problems.

This study reports the first case of combined lung and kidney transplantation for pulmonary lymphangioleiomyomatosis and renal angioliipomas. Two years after transplantation, renal and pulmonary function have remained stable and the patient has resumed a normal daily life, including a full-time professional activity.

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Combined transplantations, although performed infrequently, have become accepted therapeutic procedures in selected patients with end-stage dual-organ failures, such as kidney and heart, kidney and pancreas, or liver and kidney insufficiencies [1]. Pulmonary lymphangioleiomyomatosis (LAM) and renal angiomyoliipomas are rare diseases that could be related to a single disease process, such as tuberous sclerosis [2]. This study reports the first case of combined lung and kidney transplantation in a patient with pulmonary LAM and bilateral renal angiomyoliipomas with allografts harvested from the same donor.

Case report

In June 1995, a 41-yr-old female with a 9-yr history of pulmonary LAM was referred to our hospital for evaluation as a candidate for lung transplantation. An open lung biopsy had established the diagnosis of LAM and, despite a therapeutic trial with progesterone, her dyspnoea had progressively worsened over the last 3 yrs and she required continuous administration of nasal O₂ (fig. 1). On admission, pulmonary function tests and blood gas analyses demonstrated a severe obstructive defect (forced expiratory volume in one second (FEV₁), 19% predicted; forced vital capacity (FVC), 49% pred) and hypoxaemia with hypercarbia at rest (arterial oxygen tension (P_aO₂), 8.2 kPa; arterial carbon dioxide tension (P_aCO₂), 7.2 kPa; arterial oxygen saturation (S_aO₂), 90% with 2 L·min⁻¹ O₂). Her quality of life was dramatically impaired and her six-minute walking distance was limited to 222 m. No neurological or dermatological signs of tuberous sclerosis were detected.

Besides the history of pulmonary LAM, a diagnosis of renal angiomyoliipoma had been made in 1978 after a right nephrectomy had been performed to rule out a renal cell

Fig. 1. – Preoperative chest radiograph showing a bilateral interstitial pattern more prominent in the right lower lung field and a small residual pneumothorax of the right upper lung field.

carcinoma in a large, irregular, solid renal mass. In 1985, a small asymptomatic angiomyoliipoma was incidentally detected by computed tomography (CT) scan in her remaining left kidney. Several years later (November 1995), the patient complained of flank pain and an abdominal CT scan revealed a giant pseudoaneurysm (10 cm) of the left kidney with an important perirenal haematoma and multiple angioliipomas (fig. 2). Selective embolization of one of

Fig. 2. — Axial computed tomography scan showing the important perirenal haematoma and a reduction of renal volume to <15%.

the renal lobar arteries was successfully performed under radiological guidance and, at that time, creatinine clearance remained within a normal range (105 mL·min⁻¹ in December 1995 and 120 mL·min⁻¹ in March 1996), despite reduction of the renal volume to <15% of a normal-sized kidney.

After a multidisciplinary consultation, we elected to perform a combined lung and kidney transplantation in this female presenting with an end-stage lung disease and marked reduction of renal functional units due to large and multiple angioliopomas. The patient accepted the procedure and, in June 1996, she underwent a combined lung and kidney transplantation from the same donor, a 55-year-old male, who shared the same ABO blood group as well as one-antigen human leukocyte antigen (HLA)-A and two-antigen HLA-DR.

Bilateral sequential lung transplantation was performed using standard techniques without cardiopulmonary bypass. For the right and left lung, the cold ischaemia time was 240 and 360 min, respectively. After reperfusion and reventilation, adequate lung oxygen exchange and stable haemodynamic conditions were easily achieved (P_{a,O_2} of 15 kPa with an inspired O_2 fraction of 0.5). The renal graft was transplanted in the patient's right iliac fossa and the kidney cold ischaemia time was 540 min.

Postoperatively, quadruple immunosuppressive therapy was initiated (horse antithymocyte globulin during the first 10 days; azathioprine 2 mg·kg⁻¹; methylprednisolone 0.5 mg·kg⁻¹·day⁻¹, tapered to 0.2 mg·kg⁻¹·day⁻¹ after 6 months; cyclosporin to achieve a serum level of 200–300 µg·L⁻¹). Early in the intensive care unit, high urinary flow resumed and plasma creatinine returned to normal values 48 h after surgery. Weaning of mechanical ventilation was only successful 14 days after transplantation as a result of lung reperfusion oedema followed by an episode of acute lung allograft rejection.

The patient was discharged from the hospital 34 days after surgery. Five months later, the FEV₁ and FVC reached 80% and 72% pred, respectively. Renal function was moderately impaired (creatinine clearance of 30 mL·min⁻¹) and a kidney graft biopsy showed mild to moderate interstitial fibrosis that was attributed to chronic allograft rejection and grade II vascular lesions. The latter was tenta-

tively attributed to cyclosporin nephrotoxicity, as no interstitial inflammation was present. Creatinine clearance improved up to 61 mL·min⁻¹ when cyclosporin was replaced with tacrolimus (blood level of 5–8 µg·mL⁻¹) and low-dose mycophenolic acid (1,500 mg·day⁻¹ in three daily doses).

Two years after combined lung–kidney transplantation, both the renal and pulmonary function have remained stable and the patient has resumed a normal daily life, including a full-time professional activity. The native kidney was left in place and so far has not been the cause of further bleeding.

Discussion

Despite the absence of neurological and dermatological signs, the diagnosis of tuberous sclerosis complex (TSC) can be considered in this female on the basis of the association of LAM and bilateral renal angioliopomas. Indeed, TSC is an autosomal dominant hereditary disorder with a high variability in clinical expression and in about 80% of new mutations [3]. A small percentage of patients with TSC (1%) show pulmonary involvement with similar histopathological lesions found in the lung of LAM. Interestingly, using a specific antibody against melanoma cells (HMB-45), it has been demonstrated that lung and kidney hamartomas have common phenotypic expressions, which supports the theory that LAM and TSC represent the continuous spectrum of the same disease process [4].

Although organ transplantation in patients with multisystem disease has been somewhat controversial, according to a recent survey, 46 patients with LAM have undergone lung transplantation with survival rates of 73% and 65% at 1 yr and 2 yrs, respectively. These figures are very similar to those reported in lung transplantation performed for chronic obstructive pulmonary disease [5, 6]. However, two major concerns require close observation. Firstly, recurrence of LAM in the lung allograft is possible and has been reported in four cases [7–9]. Secondly, renal angioliopomas are being increasingly reported (in up to 57% of the patients) with LAM [10, 11]. Attention has been focused recently on the high prevalence of this association, which is probably attributable to the increasing use of diagnostic imaging techniques and to prolonged survival after lung transplantation, with increasing time for the development of other clinical manifestations [10, 11].

Although sporadic renal angiomyolipomas are most often asymptomatic, those associated with TSC carry a poor prognosis since they are more likely to develop severe complications, such as progressive enlargement with disruption of the functional nephrons or life-threatening haemorrhage [3, 12]. Therefore, the current treatment consists of partial/total nephrectomy, embolization of large (>4 cm) and symptomatic tumours, or ultimately a kidney transplantation [13].

In the present case, pulmonary LAM had evolved into an end-stage obstructive disease with chronic hypoxaemia, whereas the remaining kidney carried the risk of both recurrent haemorrhagic complications and early functional insufficiency due to glomerulosclerosis after extensive renal ablation [14]. Furthermore, if an isolated lung transplantation had been performed, cyclosporin therapy would have probably injured the remaining functional nephrons and precipitated the onset of renal failure. Therefore, al-

though a kidney transplantation in a patient with normal kidney function is debatable, a combined lung–kidney transplantation was considered to be the best medical option in this particular case. Keeping in mind the shortage of donor organs and the remaining renal function, lung transplantation associated with close follow-up of the renal function and repeated abdominal CT scans could also have been considered as an acceptable alternative.

In conclusion, pulmonary lymphangioleiomyomatosis and angiomyolipomas are frequently associated. Recently, with the longer follow-up of patients undergoing lung transplantation for end-stage lymphangioleiomyomatosis disease, renal complications due to bleeding angiomyolipomas and cyclosporin-induced nephropathy have become newly identified problems [6]. A combined lung and kidney transplant may prove fruitful in such cases, as typified in the present case.

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