i.) Title:
Bilateral Lung Transplantation in Antisynthetase Syndrome

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- vii.) Abstract:

Improved survival rates following bilateral lung transplantation has led to emerging interest in the role of lung transplantation (LTx) in the management of refractory interstitial lung disease (ILD) secondary to connective tissue diseases (CTD). This case highlights the potential success of LTx in such patients.

Key words:

Rheumatic Diseases

Lung Transplantation

Myositis

Lung Diseases, Interstitial

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i.) Text:

There has been emerging interest in the role of lung transplantation (LTx) in the management of refractory interstitial lung disease (ILD) secondary to connective tissue diseases (CTD). This may reflect the improved long-term survival rates following bilateral LTx in Australia, being 90%, 74% and 65% at 1, 3 and 5 years respectively, and exceeding international standardsⁱ. Despite this, Australian data reveal low rates of LTx for autoimmune conditionsⁱⁱ. Consensus documents for selection of candidates note the highly variable manifestations of CTD requiring individual patient considerationⁱⁱⁱ. Data regarding predictors of prognosis are limited and insufficient to support specific guidelines in this setting. However, for refractory lung disease it is reasonable to extrapolate from guidelines proposed for idiopathic ILD, and evidence of quiescent systemic disease is recommended.

In August 2002, a 43 year old male farmer presented with profound muscle weakness (hip flexors 2/5), Gottron's papules, recent-onset Raynaud's phenomenon, elevated serum creatinine kinase (CK) and the presence of antibodies to Ro52 and Jo-1. Muscle biopsy showed dermatomyositis. Respiratory function tests (RFT) demonstrated forced vital capacity (FVC) 3.69L and corrected diffusion capacity for carbon monoxide (DLCOc) 66%. High resolution computed tomography chest revealed bilateral lower lobe alveolar opacities indicating ILD. A diagnosis of antisynthetase syndrome (ASS) was made and he was prescribed methotrexate and oral prednisolone 1mg/kg daily.

By February 2003, prednisolone had been reduced to 7.5mg daily. Power had normalised though he had persistent dyspnoea. In June 2004, he presented with increased exertional dyspnoea and radiographic progression of bilateral lower zone alveolitis. There was 16% reduction in FVC to 3.09L and drop in DLCOc to 42%. Prednisolone was increased to

50mg daily and he received six cycles of intravenous cyclophosphamide followed by oral prednisolone and azathioprine.

This led to a prolonged period of stability until 2013 with good exercise capacity and DLCOc of greater than 50%.

In 2013 he had respiratory deterioration, required continuous supplemental oxygen and commenced mycophenolate mofetil 1g twice daily (BD). Power remained normal and ILD was the dominant and refractory manifestation of ASS (DLCOc 32% and FVC 42% by January 2015). The patient underwent extensive transplant work-up, including testing to ensure the non-pulmonary manifestations of disease were quiescent. In September 2015, at age 56 with a body mass index (BMI) of 27.5 and total lung capacity (TLC) of 3.3L (predicted 7.1L), he underwent bilateral sequential LTx. The donor was a 70 year old female non-smoker with brain death and BMI 24.8 with TLC of 5.22L. The CXR dimensions in the donor were right (R) 21.5cm, left (L) 22.3cm whilst in the recipient were considerably smaller (R 15cm, L 19cm). The explant showed usual interstitial pneumonia. There were no post-operative complications and the patient was maintained on prednisolone 7.5mg daily, mycophenolate mofetil 1.5g BD and tacrolimus 3mg daily.

Transplantation led to prompt resolution of dyspnoea; DLCOc improved to 51% within 6 months post-transplant. At three years post-transplant, he takes prednisolone 5mg daily, mycophenolate 1.5g BD and tacrolimus 0.5mg BD. He walks 6 km per day without dyspnoea, and has FVC of 61%. Muscle power and serum CK levels remain normal, with magnetic resonance imaging (MRI) of the lower limb musculature confirming absence of

inflammation, though antibodies to Ro52 and Jo-1 persist. His quality of life has improved significantly.

There are sparse reports of LTx in ASS and this may be an under-utilised treatment modality for patients with ILD-dominant ASS^{iv,v}. Our case highlights the potential success of LTx in such patients.

Nationwide there is a mismatch in terms of organ demand and supply, and difficulties in obtaining a size matched donor, especially in advanced cases of ILD. Current consensus guidelines from the American Thoracic Society and International Society for Heart and Lung Transplantation (ISHLT) recommend transplant discussion at the time of diagnosis and early referral for transplant to facilitate listing.ⁱⁱⁱ

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