Development of adenocarcinoma of the lung in a transplanted lung of a scleroderma patient

Sirs.

Systemic sclerosis (SSc) is an autoimmune disease characterised by progressive fibrosis of the skin and internal organs. Interstitial lung disease (ILD) is a known complication. Lung transplantation has been shown to improve survival. In this report we present a patient with SSc and ILD who underwent bilateral lung transplantation and developed adenocarcinoma of the lung. In our study we discuss the different challenges in the management of such patients and the one-year outcome in our patient.

We report a 48-year-old woman with systemic sclerosis diagnosed in 2002 with the presence of diffuse cutaneous thickening, Raynaud's phenomenon, bibasilar crackles and gastrointestinal dysmotility. Her baseline Modified Rodnan Skin Score (MRSS) was 17. Her antibody profile was positive for anti-nuclear antibody and negative anti-centromere and anti-Topoisomerase-1 antibodies.

Her disease was complicated by pulmonary hypertension and interstitial lung disease. She was treated with oral cyclophosphamide but despite this her disease progressed with a forced vital capacity of 0.9 liters (30% of predicted) and a right ventricular systolic pressure (RVSP) of 74 mmHg. She eventually underwent bilateral lung transplantation in 2006 and was maintained on standard immunosuppressive therapy. Following transplantation her FVC stabilised at 44% predicted, RVSP normalised, and skin score decreased to 3.

In July 2010 she was investigated for a 3-month history of increasing shortness of breath and fatigue and found to have a solitary right lung nodule measuring 1x1 cm which was biopsied and proved to be localised adenocarcinoma of the lung (T1 N0 M0).

Due to poor lung function (PFTs), she was not a candidate for lobectomy and underwent stereotactic body radiation therapy (SBRT) with 4800 centi-Gray units (cGy) in 4 fractions.

The patient tolerated the procedure well with no local complication or reactivation of her skin disease. Although the lung nodule stabilised she developed progressive dyspnea and died in September 2011.

Pulmonary involvement in SSc is a common finding, at least one-third will develop clinically significant fibrosis and up to 70% will have PFT abnormalities (1). Symptoms are usually subtle in early disease and discovered late because patients are often sedentary and do not note mild reductions in exercise tolerance (2). Mortality due to ILD has increased from 6% to 33% over a 25-year period making it the leading cause in SSc patients (3). Treatment with oral cyclophosphamide for a year had a significant but modest beneficial effect on lung function, dyspnea, skin thickening, and health-related quality of life (4). Other drugs such as mycophenolate mofetil, iminatib mesylate and bosentan have been tried in limited studies and require larger controlled clinical trials to determine their efficacy.

Lung transplant has been shown to improve survival in advanced cases and can be a lifesaving procedure (5). Survival from lung transplants in SSc was found similar to survival from lung transplants carried out for other diseases and the cause of mortality in SSc patients who underwent lung transplant was similar to patients with idiopathic pulmonary fibrosis (IPF) and idiopathic pulmonary hypertension (IPAH) at 24 months (6). The incidence of lung malignancy in the SSc population was found to be increased compared to the normal population in several cohorts including ours (7). ILD was noted to be an independent risk factor for the development of lung cancer (7) and smoking further increased the risk seven times compared to the general population (8). No specific antibody that increases the risk of lung cancer has been identified. The most common lung cancers identified were small cell, squamous cell and adenocarcinomas (8). Schachna *et al*. described the outcome of 29 SSc patients who underwent lung transplantation. Two died after developing cholangiocarcinoma and glioblastoma multiforme but none developed lung cancer (6).

In lung transplant patients, lung cancer has been described in the native lung of single lung recipients, in the recipient's explanted lung and rarely in the donor lung (9). The possible etiology could be related to viral infections, scarring and immunosuppressive agents (9).

Treatment of malignancy in this situation is complicated by the fact that these patients have poor respiratory reserve making surgery difficult, chemotherapy interfering with the immunosuppressive regimen and in SSc patients, radiation can reactivate the primary disease locally (10, 11). The observed time of scleroderma reactivation after conventional radiation therapy is in

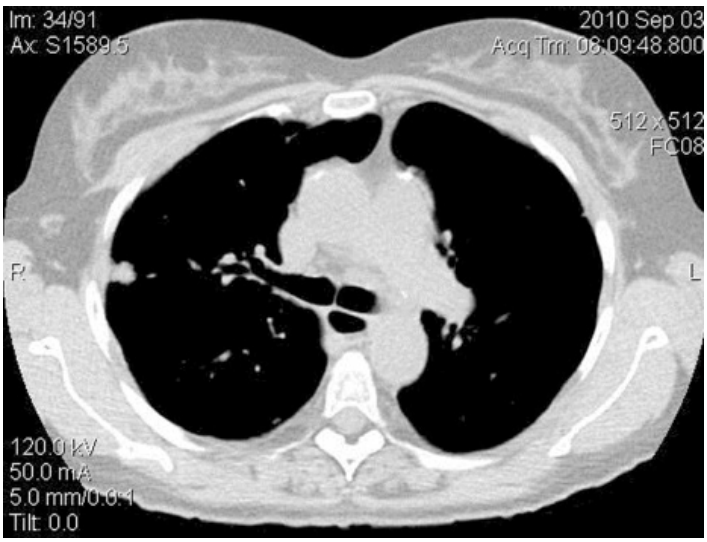

Fig. 1. CT scan of the chest showing a right pleural based nodule (arrow).

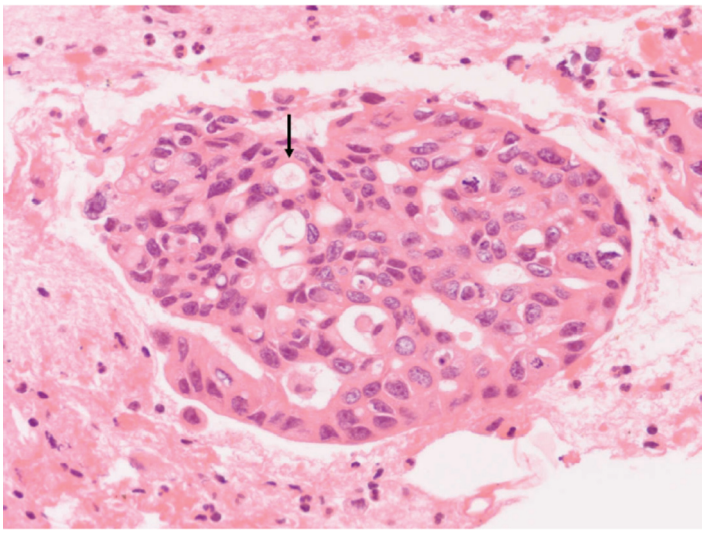

Fig. 2. Tumour obtained by transthoracic fine needle aspiration biopsy consists of a network of morphologically malignant glandular cells forming acini (arrow) containing mucin. Haematoxylin and Eosin, cell block section, 40x objective.

the first 4 months (11). SBRT involves the delivery of a small number of ultra-high doses of radiation to a target volume using very advanced technology and has emerged as a novel treatment modality for cancer. The role of SBRT is most important at two cancer stages in early primary cancer and in oligometastatic disease. This modality has been used in the treatment of many types of tumour including lung cancer. The risk of pneumonitis is reduced with such a modality, and when protracted regimens such as the one used in our patient are applied the risk is even lower (12).

To our knowledge, this is the first patient with SSc who developed localised adenocarcinoma of the lung after transplantation and successfully managed with SBRT without complication or disease reactivation with a 12-month survival period.

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Acknowledgment: The authors would like to thank Dr William Geddie for providing the fine needle aspiration figure.

Competing interests: none declared.

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