NDT Plus (2008) 2: 124–125
doi: 10.1093/ndtplus/sfm023
Advance Access publication 19 December 2007

NDT PLUS
Nephrology Dialysis Transplantation

Images in Nephrology
(Section Editor: G. H. Neild)

Sirolimus-induced interstitial pneumonitis in a renal transplant recipient

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Keywords: interstitial pneumonitis; sirolimus; transplantation

A 64 year-old man, who received a renal transplant in 1988 for end-stage renal disease due to chronic pyelonephritis, developed persistent dry cough, progressive dyspnoea, fatigue and fever, 2 weeks after he was shifted from cyclosporine to sirolimus for recurrent squamous cell carcinomas. Physical examination was unremarkable except for mild fever. Moderate acute phase reaction (CRP: 5.2 mg/dl) was present and sirolimus trough level was 6 ng/ml. A left lower infiltrate was noted on chest radiograph. He was treated with a course of moxifloxacin without improvement. High-resolution CT scan of the lungs revealed bilateral heterogeneous ground-glass opacities predominant in the lower lung zones (Figure 1A), associated with mild interlobular septal thickening. Bronchoalveolar lavage (BAL) disclosed 63% macrophages, 11% lymphocytes and 26% neutrophils. Specific stainings and culture of BAL fluid samples were negative for bacteria, mycobacteria, viruses, fungi and parasites. Serological tests for *Chlamydia pneumoniae, C. psittaci, Mycoplasma pneumoniae, Coxiella burnetti* and *Legionella pneumoniae* as well as cytomegalovirus antigenemia remained negative. Sirolimus was discontinued and the patient improved gradually, with complete disappearance of the symptoms and normalization of CRP level within 2 weeks. High-resolution thoracic CT scan returned to normal 4 months later (Figure 1B).

Sirolimus is a potent immunosuppressive drug, increasingly used in solid-organ transplantation for its nephrotoxic-sparing and antitumour effects. Interstitial pneumonitis following sirolimus prescription has been reported with an estimated frequency of 5–11% [1,2]. It presents clinically one to several months following sirolimus initiation by fever, dyspnoea and cough, mimicking opportunistic infections that must be ruled out by appropriate blood and BAL tests [3]. Chest radiography shows infiltrates but can also be normal. CT scan of the lungs usually reveals ground-glass opacities that can be accompanied with bilateral interstitial infiltrates. High sirolimus blood trough levels may increase the risk, but pneumonitis may also occur with low trough levels as in our patient [2]. Pathogenesis is not yet elucidated but toxicity may be immune-mediated or dose-dependent [3]. Discontinuation of sirolimus is the treatment of choice and is associated with regression of the pneumonitis within 2 weeks [2].

Thus, in transplant patients, sirolimus-induced interstitial pneumonitis can mimic infection and must be rapidly recognized as it is associated with prompt recovery upon withdrawal of sirolimus.

Conflict of interest statement. None declared.

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Received for publication: 7.11.07
Accepted in revised form: 16.11.07

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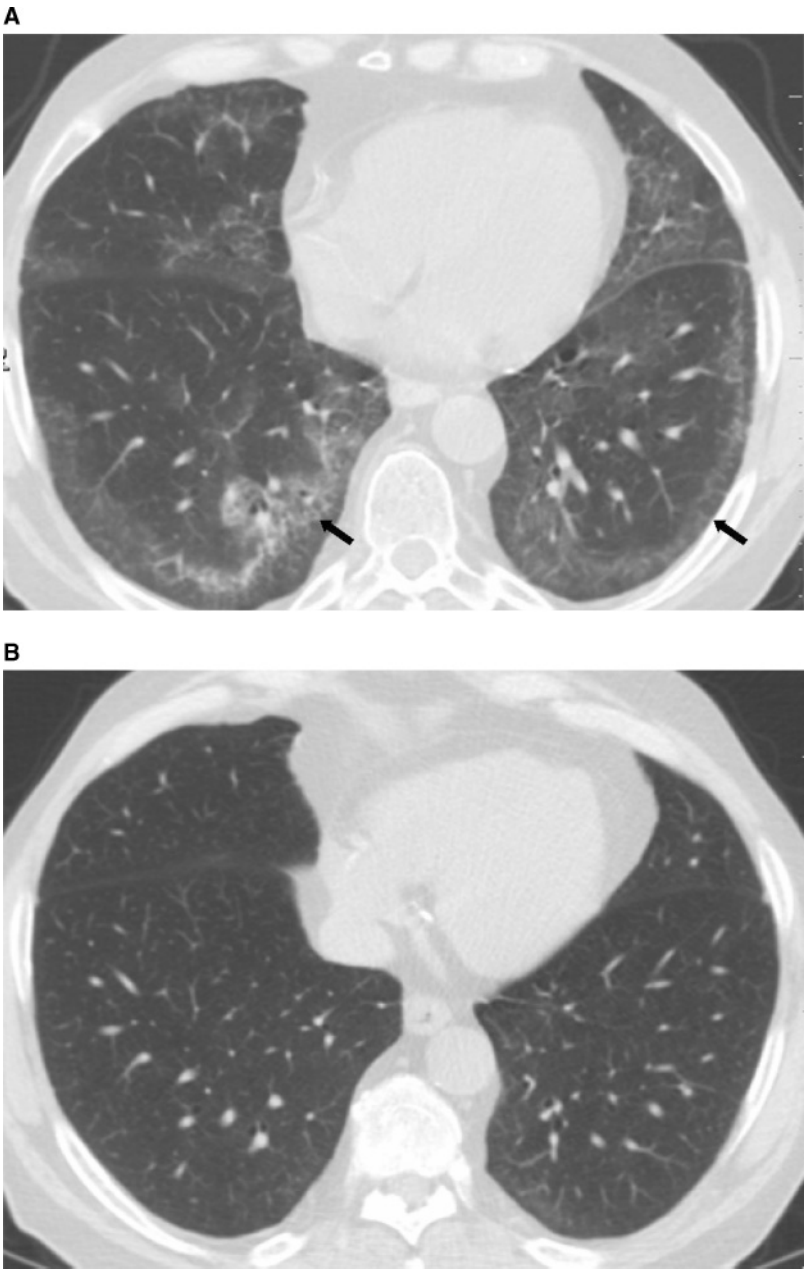

Fig. 1. (A) High-resolution CT through the lung bases demonstrates bilateral areas of ground-glass opacity in a patchy distribution. Also note interlobular septal thickening in subpleural location (arrows). **(B)** Follow-up high-resolution CT at the same level as in (**A**) shows complete resolution of interstitial abnormalities.