



## LETTERS TO THE EDITOR

### Drug related toxicity in lung transplant recipients



During the last two decades, lung transplantation (LTx) has become a life-saving intervention for patients presenting with end-stage respiratory disease.<sup>1</sup>

The lung graft, in contrast to all other transplanted organs, is in permanent contact with the external environment and is thus exposed to various inhaled agents. Moreover, it contains a huge amount of donor antigen-presenting cells constantly processing and presenting HLA alloantigens to recipient lymphocytes that initiate a process of immune recognition.<sup>2</sup> Thus a successful lung transplant relies on an appropriate immunosuppressive strategy and balance.<sup>3</sup> In fact the two main causes of death after LTx are chronic rejection of the allograft and infections.

Although advances have been made and varied immunosuppressive protocols are being used, specific drugs, such as calcineurin inhibitors and proliferation inhibitors (PIs), are very toxic, even at low doses. Nevertheless, they are considered to be indispensable in lung transplantation.<sup>4</sup> Thus, with LTx came along drug toxicity.

We would like to report the results of our own series.

We retrospectively evaluated patients with pulmonary transplantation followed at our Centre since 2005. The lung transplant was performed by two different transplantation Groups – Hospital de Santa Marta (Lisbon) and at Hospital Juan Canalejo (Corunha), according to the Portuguese Health System indications for lung transplant. After the transplant, although patients still maintained follow-up at the transplant centre, they were referred to our Specialized Clinic for Lung Transplanted patients which works very closely with both centres.

Thirty-two patients were included, 19 (59.4%) were male; the mean age at transplant was 44.9 years. The patients have been followed for a mean time of 30.78 months after LTx. The initial immunosuppressive protocol used in all patients was the association of steroids, cyclosporine and azathoprine. Only six patients are still with it, in 20 patients it was changed due to acute rejection and in six patients due to chronic rejection.

In 14 patients the immunosuppressive therapy had to be changed, more than once, due to drug induced toxicity. Two patients had malignancy diagnosis (lymphoma), gastric symptoms were the most frequent complaint, renal malfunction, hirsutism ( $n=1$ ), and gingival hyperplasia

( $n=1$ ) were some of the complications the authors would like to report. No relationship was found between the need to change the therapy and age at transplant or time of follow-up.

Among the diseases that needed to be treated but did not require an immunosuppressive therapy change, diabetes ( $n=10$ , 31.5%), dislipidemia ( $n=12$ , 37.5%) and arterial hypertension ( $n=4$ , 12.5%) were found to be the most prevalent.

Lung transplantation may be a life-saving intervention for end-stage respiratory disease. With the growing number of long-term survivors of lung transplants, chronic rejection and toxicity have emerged as major problems. Drug induced toxicity is prevalent and the clinicians caring for those patients have to be well aware of this so that it can be diagnosed, addressed and treated as early as possible.

### Conflicts of interest

The authors declare no conflicts of interest.

### References

1. Hertz MI, Taylor DO, Trulock EP, Boucek MM, Mohacs PJ, Edwards LB, et al. The registry of the international society for heart and lung transplantation: nineteenth official report-2002. *J Heart Lung Transplant.* 2002;21:950–70.
2. Knoop C, Haverich A, Fischer S. Immunosuppressive therapy after human lung transplantation. *Eur Respir J.* 2004;23:159–71.
3. Patel J, Kobashigawa JA. Minimization of immunosuppression: transplant immunology. *Transpl Immunol.* 2008;20:48–54.
4. Iversen M, Corris PA. Immunosuppression. *Eur Respir Soc Monogr.* 2009;45:177–93.

M. van Zeller<sup>a</sup>, C. Damas<sup>b,\*</sup>

<sup>a</sup> *Serviço de Pneumologia, Centro Hospitalar de São João, Porto, Portugal*

<sup>b</sup> *Consulta Especializada de Transplante Pulmonar, Serviço de Pneumologia, Centro Hospitalar de São João, Porto, Portugal*

\*Corresponding author.

E-mail address: [cdamas@aeiou.pt](mailto:cdamas@aeiou.pt) (C. Damas).

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