

## Lung Transplantation: Bronchogenic Carcinoma in the Native Lung

Juan Carlos Peñalver Cuesta, Carlos Jordá Aragón, Juan Escrivá Peiró, José Cerón Navarro, Víctor Calvo Medina, and José Padilla Alarcón

Servicio de Cirugía Torácica, Hospital Universitario La Fe, Valencia, Spain.

**In lung transplantation, the presence of bronchogenic carcinoma in the native organ is uncommon, but doubtless affects patient survival, independently of the transplantation process itself.**

**We describe 2 cases in which a primary tumor was found in the explanted lung—1 case of adenocarcinoma in a patient with pulmonary emphysema and 1 case of bronchioloalveolar carcinoma in a patient with idiopathic pulmonary fibrosis. Both patients died due to the recurrence of the neoplastic disease. Distant metastasis was the initial manifestation of the recurrence.**

**Key words:** Lung transplantation. Bronchogenic carcinoma. Survival.

Trasplante pulmonar. Carcinoma broncogénico en pulmón nativo

**En el trasplante pulmonar, la presencia de un carcinoma broncogénico en el órgano nativo es una situación muy poco frecuente, pero que, sin duda, condiciona la supervivencia de los pacientes, independientemente del propio proceso del trasplante en sí.**

**Se describen 2 casos donde se hallaron sendos tumores primarios pulmonares en el órgano extraído, un adenocarcinoma en el contexto de un enfisema pulmonar, y un carcinoma bronquioloalveolar en un paciente con fibrosis pulmonar idiopática. Ambos pacientes fallecieron por la recidiva de la enfermedad neoplásica, cuya manifestación inicial fue la presencia de enfermedad metastásica a distancia.**

**Palabras clave:** Trasplante pulmonar. Carcinoma broncogénico. Supervivencia.

### Introduction

Lung transplantation can be the treatment for specific end-stage pulmonary processes,<sup>1,2</sup> conditions whose pathogenesis is affected by factors as varied as smoking, repeated infection, autoimmune processes, and genetic alterations. These factors may also be implicated in neoplastic processes that, with very few exceptions, would contraindicate transplantation. Patient selection must be carried out on an increasingly strict basis, given the steady increase in the number of lung transplant candidates and the stabilization of the number of donors in Spain. Therefore, an extensive series of analytical, functional, and imaging tests is necessary to choose the best recipient and to rule out those with relative or absolute contraindications to the procedure.<sup>3,4</sup>

Nevertheless, occasionally, it is almost impossible to rule out specific neoplastic processes in their early stages.

Correspondence: Dr. J.C. Peñalver Cuesta.  
Servicio de Cirugía Torácica, Hospital Universitario La Fe.  
Avda. Campanar, 21. 46009 Valencia, España.  
E-mail: jpenalve@ono.com

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We describe 2 cases in which a lung carcinoma was discovered in the histopathology study of the explanted lung.

### Case Description

Between 1990 and 2005, a total of 286 patients underwent lung transplantation at the Hospital Universitario La Fe in Valencia, Spain. A retrospective review of the histopathology reports for the organs explanted from the recipients revealed 2 organs with non-small cell lung cancer.

The first case involved a 57-year-old man, an ex-smoker who had worked with sand molds. He underwent a bilateral sequential lung transplant for end-stage silicosis. Anthracosilicosis was confirmed in the explanted lung and was accompanied by abundant areas of bullous emphysema. The right lung presented a moderately differentiated adenocarcinoma, 1.8 cm in diameter at its widest point, located in the hilum and very close to the main bronchus, with involvement of a neighboring lymph node. The classification was T1 N1 M0 (stage IIa)<sup>5</sup> (Figure 1). Six months after transplantation, multiple bone metastases were detected in the spine and, 3 months later, on the left lobe of the liver. Progression of the patient's adenocarcinoma was assessed and palliative radiotherapy was given for persistent pain. He died 16 months after transplantation due to tumor progression.

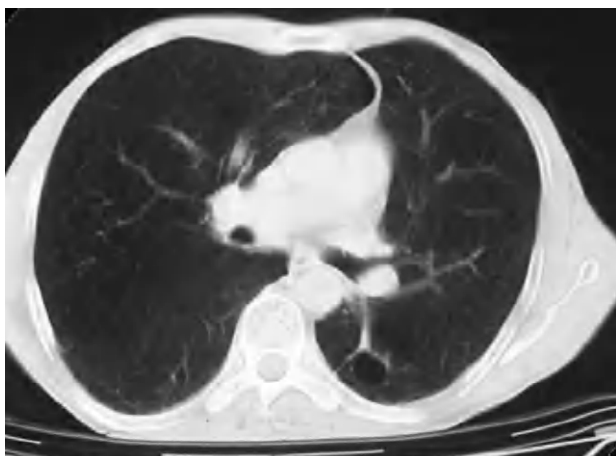


Figure 1. Case 1: bronchogenic adenocarcinoma.

The second case involved a 46-year-old man with no medical history of interest. The underlying condition was idiopathic pulmonary fibrosis, for which he underwent a bilateral sequential lung transplant. The histopathology of the explanted lungs revealed alterations indicating end-stage idiopathic pulmonary fibrosis, and multiple bronchioloalveolar formations with cellular atypia, corresponding to well differentiated foci of diffuse bronchioloalveolar carcinoma (Figure 2). Three months later, the patient was diagnosed with multiple bone metastases in the iliac plate, femur, cranium, and at different levels of the spine. The patient received palliative radiotherapy and died 5 months after transplantation.

In both cases, metastasis was confirmed by puncture of the most accessible bone lesions: the spine in the first case, and the ilium in the second.

## Discussion

Many studies have analyzed the appearance of malignant tumors after a lung transplant.<sup>6-9</sup> However, as occurred in our study, there are few published cases that analyze the presence of tumors in the explanted organs of recipients.

Of the 183 lungs analyzed by Stewart et al,<sup>10</sup> adenocarcinoma was observed in only 1 case. Svendsen et al<sup>11</sup> also reported 2 cases of adenocarcinoma. Lastly, Abrahams et al,<sup>12</sup> in a series of 214 transplants, detected 4 cases of occult carcinoma in the explanted lung (3 adenocarcinomas and 1 squamous cell carcinoma). The last study, which was the only one to analyze both the incidence of this phenomenon in a large series and its impact on survival, reported 1 postoperative death and long-term survival ranging from 2 to 6 years.

The presence of these occult tumors can, to a large extent, determine long-term survival in a procedure that is already difficult at each of its different stages. Therefore, and given the paucity of donors, it is necessary to screen likely transplant candidates, ruling out those who cannot fully benefit from receiving such a "costly" item because of their theoretically poor prognosis.

In the exhaustive study of patients to determine whether they can benefit from lung transplantation<sup>13</sup> there are many analytical and imaging tests whose objectives include the detection of an occult tumor that might contraindicate the

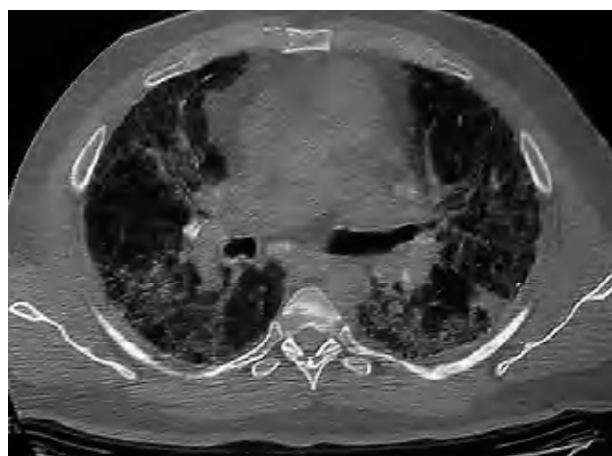


Figure 2. Case 2: multiple bronchiolar formations with cellular atypia corresponding to foci of bronchioloalveolar carcinoma.

procedure.<sup>14</sup> Notwithstanding the important information provided by computed tomography (CT),<sup>15</sup> some tumors go unnoticed because of their small size or the varied appearance of the underlying pulmonary lesions. Similarly, neither laboratory analyses nor tumor markers can predict the presence of malignant pulmonary tumors. According to Hadjiliadis et al,<sup>16</sup> who studied 200 heart-lung and lung transplants, the level of carcinoembryonic antigen, which was proposed as a marker of occult tumors, is elevated in end-stage pulmonary conditions, especially in idiopathic pulmonary fibrosis. The authors also state that patients who developed tumors after transplantation had not presented elevated levels of this antigen in the pretransplant study.

Abrahams et al<sup>12</sup> advised performing a high-resolution CT scan before transplantation (under 24 hours) as a means of detecting these cases. The organization of lung transplantation in Spain makes this proposal very difficult to carry out because of time limitations in maintaining the potential donor, coordinating the arrival of the organ at the recipient's hospital, and the performance of the surgical procedure itself.

The contribution to pretransplantation studies of new diagnostic imaging techniques such as positron emission tomography remains to be seen. The literature contains many references to this technique in the study of bronchogenic carcinoma,<sup>17-19</sup> but we have been unable to find publications analyzing its inclusion in lung transplant screening. Furthermore, the small number of cases of localized occult lung cancer and the probability of false positives in inflammatory and infectious processes mean that the systematic application of this test is neither clinically nor financially viable at present. It may be useful, however, for patients whose history, clinical condition, or CT scan suggests the presence of a malignant pulmonary lesion.

Finally, once a native lung tumor has been detected, there are no guidelines as to which approach should be adopted for this currently uncommon event. The description of new cases and the knowledge gained from seeing the clinical development of this condition will probably help us to decide the best treatment approach to take.

REFERENCES

1. Varela A, Álvarez Kindelan A, Román A, Ussetti P, Zurbano F. Grupo de trabajo de la SEPAR. Normativa SEPAR. Trasplante pulmonar. Arch Bronconeumol. 2001;37:307-15.
2. Pacheco Galván A. Expectativas en el paciente respiratorio terminal. Arch Bronconeumol. 2004;40:51-3.
3. Borro JM. Actualización del trasplante pulmonar en España. Arch Bronconeumol. 2005;41:457-67.
4. Salvatierra Velázquez A. Trasplante pulmonar en España. Arch Bronconeumol. 2004;40 Supl 6:41-8.
5. Grupo de Trabajo de la SEPAR. Normativa actualizada (1998) sobre diagnóstico y estadificación del carcinoma broncogénico. Arch Bronconeumol. 1998;34:437-52.
6. Penn I. Incidence and treatment of neoplasia after transplantation. J Heart Lung Transplant. 1993;12(6 Pt 2):S328-S36.
7. Choi YH, Leung AN, Miró S, Poirier C, Hunt S, Theodore J. Primary bronchogenic carcinoma after heart or lung transplantation: radiologic and clinical findings. J Thorac Imaging. 2000;15:36-40.
8. Anyanwu AC, Townsend ER, Banner NR, Burke M, Khaghani A, Yacoub MH. Primary lung carcinoma after heart or lung transplantation: management and outcome. J Thorac Cardiovasc Surg. 2002;124:1190-7.
9. Shin MS, Ho KJ. Recurrent bronchioloalveolar carcinoma after lung transplantation: radiographic and histologic features of the primary and recurrent tumors. J Thorac Imaging. 2004;19:79-81.
10. Stewart S, McNeil K, Nashef SA, Wells FC, Higenbottam TW, Wallwork J. Audit of referral and explant diagnoses in lung transplantation: a pathologic study of lungs removed for parenchymal disease. J Heart Lung Transplant. 1995;14(6 Pt 1):1173-86.
11. Svendsen CA, Bengtson RB, Park SJ, Shumway SJ. Stage I adenocarcinoma presenting in the pneumonectomy specimen at the time of single lung transplantation. Transplantation. 1998;66:1108-9.
12. Abrahams NA, Meziane M, Ramalingam P, Mehta A, deCamp M, Farver CF. Incidence of primary neoplasms in explanted lungs: long-term follow-up from 214 lung transplant patients. Transplant Proc. 2004;36:2808-11.
13. Glanville AR, Estenne M. Indications, patient selection and timing of referral for lung transplantation. Eur Respir J. 2003;22: 845-52.
14. Maurer JR, Frost AE, Estenne M, Higenbottam T, Glanville AR. International guidelines for the selection of lung transplant candidates. The International Society for Heart and Lung Transplantation, the American Thoracic Society, the American Society of Transplant Physicians, the European Respiratory Society. J Heart Lung Transplant. 1998;17:703-9.
15. Kazerooni EA, Chow LC, Whyte RI, Martínez FJ, Lynch JP. Preoperative examination of lung transplant candidates: value of chest CT compared with chest radiography. AJR Am J Roentgenol. 1995;165:1343-8.
16. Hadjiliadis D, Tapson VF, Davis RD, Palmer SM. Prognostic value of serum carcinoembryonic antigen levels in patients who undergo lung transplantation. J Heart Lung Transplant. 2001;20: 1305-9.
17. Resino MC, Maldonado A, García L. Utilidad de la tomografía de emisión de positrones en el carcinoma de pulmón no microcítico. Arch Bronconeumol. 2004;40:103-5.
18. Deterbeck FC, Falen S, Rivera MP, Halle JS, Socinski MA. Seeking a home for a PET, part I: defining the appropriate place for positron emission tomography imaging in the diagnosis of pulmonary nodules or masses. Chest. 2004;125:2294-9.
19. Pieterman RM, Van Putten JW, Meuzelaar JJ, Mooyaart EL, Vaalburg W, Koeter GH, et al. Preoperative staging of non-small-cell lung cancer with positron-emission tomography. N Engl J Med. 2000;343:254-61.