

CASE REPORT

Primary lung adenocarcinoma in transplanted lung in post bilateral lung transplantation

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Key Clinical Message:

Primary lung cancer was reported by a bilateral lung transplant patient without any risk factors. Single lung transplantation should be contemplated instead of double lung transplantation as it has been shown to increase the risk of lung cancers.

Abstract:

This is a case report of a 37-year-old woman, with no history of smoking, who developed adenocarcinoma in her transplanted lung 17 years post transplantation. The development of lung cancer 17 years after transplantation is considered as a rare finding in this case report. According to the Annual Report on Cardiothoracic Organ Transplantation 2019–2020, the NHS Blood and Transplant Data, approximately 156 lung transplants were performed in the UK during 2019–2020. The third most common primary disease group recipient was cystic fibrosis and bronchiectasis. There are several medical complications described in the recipients' post-lung transplantation, and the increased risk of lung malignancy due to immunosuppression is well-established in comparison to the general population. Most cancers, however, develop in the native lung following a single lung transplant. Several cases of lymphoproliferative malignancies in the transplanted lung have been reported following bilateral lung transplantation. This is a case report of a 37-year-old woman with no history of smoking who developed adenocarcinoma in her transplanted lung 17 years later. This patient underwent lobectomy via thoracotomy and was discharged home in good condition. Only a few cases of patients developing primary lung cancer in the transplanted lung with no recipient risk factor have been reported in the literature to date. The development of lung cancer 17 years after transplantation was a rare finding in this case report.

KEYWORDS

adenocarcinoma of the lungs, Bi lateral lung transplant, cardiothoracic surgery, lung transplant, malignancy in transplanted lungs

JEL CLASSIFICATION

Cardiothoracic surgery, Transplantation, Acute medicine, Neurosurgery

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1 | CASE REPORT

This young lady had bilateral lung transplantation for cystic fibrosis in 2005 and has been monitored by a transplant team and a cystic fibrosis specialist ever since. Tacrolimus, prednisolone and azathioprine were among her immunosuppressive medications. During her 2021 follow-up, she reported recent anemia and weight loss, prompting a Computed Tomographic (CT) scan to rule out post-transplant lymphoproliferative disease. The CT scan revealed the right upper lobe posterior segmental ground glass nodules (Figure 1), so she was referred for a multidisciplinary team (MDT) discussion. Based on the MDT discussion, she was referred to the Sheffield thoracic unit.

According to the radiologists, this ground glass nodule lacked the classic characteristics of the post-transplant lymphoproliferative disorder, which is common in immunocompromised patients. Because of the nature of the lung lesion, surgery with diagnostic, staging, and curative intent was considered. Her FEV1 was 89% predicted, her FVC was 102% predicted, and her transfer factor was 65% predicted. She denied any smoking history and performed well on the pre-operative assessment. However, she has a strong family history of cancer. In groups of patients undergoing lung resection after lung transplantation, mortality and morbidity are reported to be higher. This was explained to the patient, and she agreed to the surgery after being informed of the potential surgical risks and complications.

In March 2022, she underwent a segmentectomy of the right upper lobe posterior and lymph node sampling. Intraoperatively, extensive pleural adhesions, bleeding and anthracotic lymph nodes with fibrosis made single-port VATS access difficult; hence, right open thoracotomy was performed. The postoperative course was uneventful, and she recovered well from surgery. Her immunosuppressive

agents were started on Day 1 postoperative. In her postoperative period, she received analgesics, antibiotics for a post-operative chest infection and chest physiotherapy. In the immediate postoperative period, a prolonged air leak was observed, prompting her discharge home on an atrium bottle on the eighth postoperative day. Her chest drain was successfully taken out 2 weeks later in an advanced thoracic nurse-led clinic. A follow-up in the post-operative thoracic clinic was done on her by the operating consultant, and as there were no concerns, she was discharged back to the care of her primary treating physician. The histopathology report was communicated to the patient during the clinic appointment, which showed features of moderately differentiated adenocarcinoma (Figures 2–4). She was assured that there would be a need for further treatment of this primary lung malignancy as it was R0 resection, as confirmed by histology. She would be followed up with an interval surveillance CT scan in a year's time.

The nature of the histopathology as primary lung cancer developing in the transplanted lung seemed to be a rare finding during the literature review.

2 | DISCUSSION

Per the Annual Report on Cardiothoracic Organ Transplantation 2019–2020, the NHS Blood and Transplant Data from NHS Blood and Transplant published in August 2020, there were 156 lung transplants performed in the UK during 2019–2020.¹ This report also suggests that over the last decade, from 1 April 2010 to 31 March 2020, there has been a steady rise in the number of lung transplants until 2014–2015. Following this period, the number dipped slightly and has been steady over the last few years. Of the 156 transplants in 2019–2020, the majority of them, 137 (88%), were bilateral lung

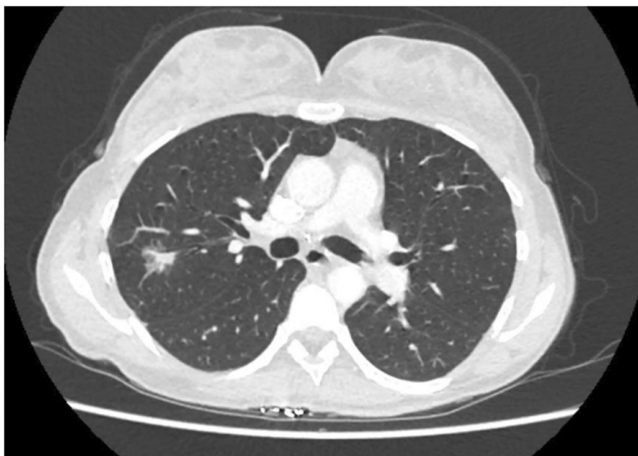


FIGURE 1 CT image demonstrating right upper lobe posterior segmental ground glass nodules.

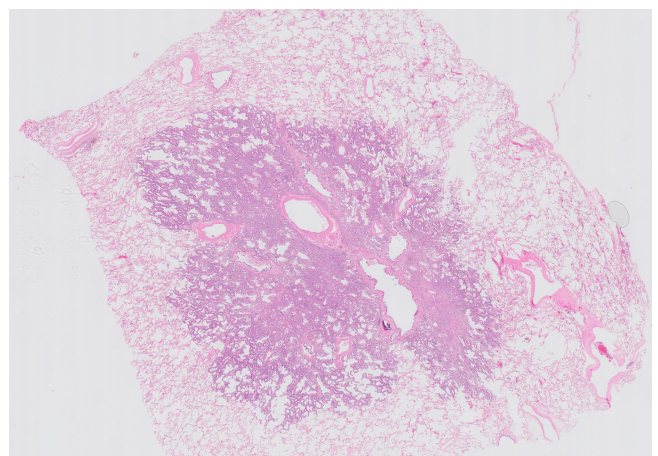


FIGURE 2 Showing histopathological slides, courtesy of the Pathology Department at the Northern General Hospital, Sheffield.

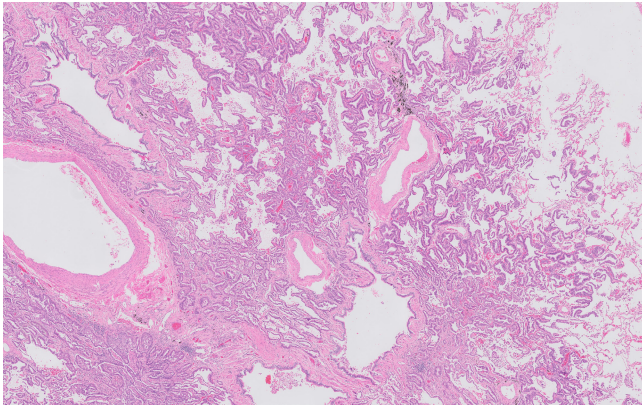


FIGURE 3 Showing histopathological slides, courtesy of the Pathology Department at the Northern General Hospital, Sheffield.

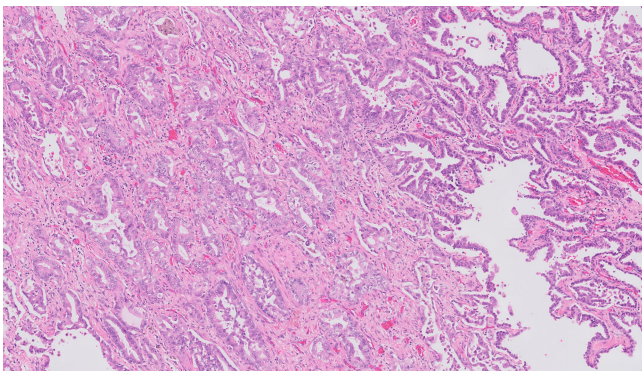


FIGURE 4 Showing histopathological slides, courtesy of the Pathology Department at the Northern General Hospital, Sheffield.

transplants; 14 (9%) were single lung transplants and only a few (3%) were heart-lung transplants. The most common recipient disease was COPD and emphysema (36%), followed by fibrosing lung disease (26%). Cystic fibrosis and bronchiectasis comprised 24% of the recipients' primary disease group.

Post transplantation, the recipients carry an increased risk of developing malignancy in their future life. A registry-linkage study was published in the *American Journal of Transplant* in 2019, which utilized data from the Transplant Cancer Match (TCM) study, to analyze the incidence, risk factors and outcomes of lung malignancy in patients with transplanted lungs.² This research concluded that the risk of developing lung cancer in recipients post-transplant is almost five times compared to the general population.

Furthermore, the probability of malignancy in the native lung after single lung transplant increases by 13-fold. However, the incidence of developing cancer in the transplanted lung is significantly low, and very few cases have been reported in the literature. Grewal et al., for instance, reported an incidence of 1.9% of developing bronchogenic

carcinoma after lung transplant. Of these, only one patient was found to have cancer in the transplanted lung.³ The risk factors for developing lung cancer were found to be age, smoking history and diagnosis of idiopathic pulmonary fibrosis in the recipients. Also, post-transplant lung cancer is associated with long-term immunosuppressive therapy.⁴ The British Thoracic Society suggested eight clinical predictors of malignancy: age, current or ever smokers, time since quitting smoking, pack-years, family history of lung cancer, history of cancer >5 years before nodule detection, any history of previous cancer and hemoptysis.⁵ Though in our case report, this lady clearly had no history of present or past smoking in any form. In a retrospective study that included posts-lung transplant patients in Philadelphia, USA, during a period of 8 years, it was found that the mean time from lung transplant to the diagnosis of lung cancer was 24.2 months.⁶ There is no reported incidence of developing lung cancer after a prolonged period of 17 years, as in our case report. Per the National Health Service guidelines, typically, the recipients are advised to be followed up every 3 months for the rest of their lives. This might differ for different transplant centers. So it renders a good opportunity to pick any new developing lesions in the post-transplant phase. There are treatment issues owing to associated co-morbidities and poor lung function in the post-transplant phase in either of the modalities as surgical, radiotherapy or chemotherapy.⁷ Moreover, reported survival after treatment for lung cancer post-transplant is significantly low. The patient in our study suffered from a chest infection post-operatively and was treated appropriately with inputs from the microbiology and cystic fibrosis specialist team. She had a good recovery and made her way home in healthy condition.

All studies primarily have reported the incidence of developing either primary cancer in the native lung or secondaries in transplanted from an unknown primary in the donor; however, there is only a brief mention of developing primary cancer in the transplanted lung. Another case has been reported of a patient developing metastatic lung disease 13 months after transplant in an ex-smoker with minimal smoking history and had been abstinent for 20 years before transplantation.⁸ There has been no case reported that is similar to our case report of developing adenocarcinoma in a transplanted lung after a delayed period of 17 years.

3 | FUTURE SUGGESTION

Genetic matching, if available, could help in identifying the origin of cancer cells either in donor or recipient origin. If possible, single lung transplantation should be contemplated instead of double lung transplantation as it

has been shown to increase the risk of lung cancer in the native by 6%–9%. In the post-transplant period, regular and close follow-up for a longer duration would help in the early diagnosis as the risk of developing malignancy in the allograft originating from the donor or arising de novo from the recipient exists not only primarily but also in the secondary.

AUTHOR CONTRIBUTIONS

Fathima Shafra Mubarak: Conceptualization; data curation; investigation; methodology; writing – original draft; writing – review and editing. **Sanjay Agrawal:** Resources; writing – original draft. **Jagan Rao:** Resources; supervision.

CONFLICT OF INTEREST STATEMENT

Authors have no conflict of interest to disclose.

FUNDING INFORMATION

None.


CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy. No demographic data of the patient was used in this report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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