CASE REPORT

Lung transplantation in an intensive care patient with pulmonary alveolar microlithiasis - a case report [v1; ref status: indexed, http://f1000r.es/3c2]

Bülent Güçyetmez[1], Aylin Ogan[1], Aylin Çimet Ayyıldız[1], Berrin Yalçın Güder[1], Walter Klepetko[2]

[1]Intensive Care Unit, International Hospital, Istanbul, 34149, Turkey
[2]Division of Thoracic Surgery, Medical University of Vienna, Vienna, A-1090, Austria

v1 **First published:** 28 May 2014, **3**:118 (doi: 10.12688/f1000research.4035.1)
Latest published: 28 May 2014, **3**:118 (doi: 10.12688/f1000research.4035.1)

Abstract

Introduction: Pulmonary alveolar microlithiasis (PAM) is an autosomal recessive disease characterized by the deposition of phosphate and calcium in the alveoli. The disease progresses asymptomatically until later stages. When it becomes symptomatic, lung transplantations performed before the onset of right heart failure may improve life expectancy and quality. Here we present a case report concerning the very first Turkish PAM patient to have undergone lung transplantation surgery.

Patient information: A 52 year-old female, Caucasian patient, already diagnosed with PAM in infancy, was admitted to the intensive care unit, diagnosed with pneumonia and hospitalized for 20 days. We decided to refer the patient to a specialized center for lung transplantation. Bilateral lung transplantation was performed in Vienna 14 months later and no recurrence was observed during the first postoperative year.

Conclusion: Bilateral lung transplantation may improve both the life expectancy and the quality of life of PAM diagnosed patients with severe respiratory failure who do not suffer from right heart failure. The risk of recurrence should not be considered as a justifying reason to avoid transplantation as a treatment method.

Open Peer Review

Invited Referee Responses

	1	2
version 1 published 28 May 2014	✓ report	✓ report

1 **Michael O'Connor**, University of Chicago USA

2 **Johan Groeneveld**, Erasmus Medical Center Netherlands

Latest Comments

No Comments Yet

Corresponding author: Bülent Güçyetmez (drbulentgucyetmez@yahoo.com)

How to cite this article: Güçyetmez B, Ogan A, Çimet Ayyıldız A *et al.* **Lung transplantation in an intensive care patient with pulmonary alveolar microlithiasis - a case report [v1; ref status: indexed, http://f1000r.es/3c2]** *F1000Research* 2014, **3**:118 (doi: 10.12688/f1000research.4035.1)

Grant information: The author(s) declared that no grants were involved in supporting this work.

Competing interests: The authors declare that they have no competing interest.

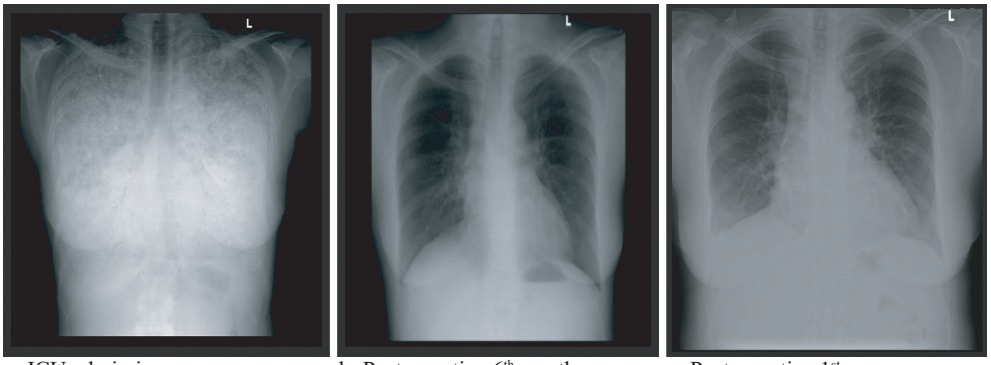
First published: 28 May 2014, **3**:118 (doi: 10.12688/f1000research.4035.1)
First indexed: 24 Jul 2014, **3**:118 (doi: 10.12688/f1000research.4035.1)

Introduction

Pulmonary alveolar microlithiasis (PAM) was first described by Harbitz in 1918[1]. This rare disease which progresses with calcium and phosphate deposition in the alveolar space is an autosomal recessive disorder caused by the *SLC34A2* gene mutation[2,3]. Radiological images reveal typically bilateral, diffuse and symmetrical sandstorm-like widespread radiopaque micronodules[4]. Turkey is the country with the highest PAM prevalence (16.3%), followed by Italy and USA[5,6]. The only known treatment is lung transplantation performed before the onset of right heart failure. No recurrence has been reported after transplantation[7,8]. Here we present the case report of the first Turkish patient followed-up in the intensive care unit (ICU) with the diagnosis of PAM, who needed ventilator support at the time of discharge from the ICU and received lung transplantation in Austria.

Patient information

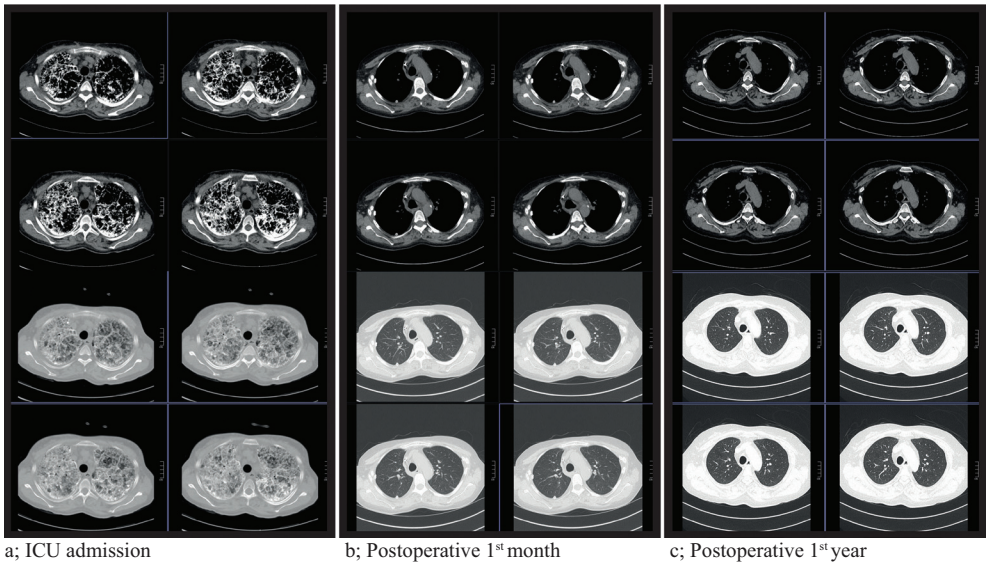
A 52 year-old female patient, with a family history of PAM, was diagnosed with the same disease when she was 10 years old and received no treatment or intervention until 2012. The patient affected by PAM presented with tachypnea, exertional dyspnea and fatigue to the Emergency Department and she was admitted to the ICU in 2012 with suspicion of pneumonia. At the time of ICU admission, she was conscious, cooperative and the initial vital signs were SpO_2: 57% (spontaneous respiration under 5lt/min mask O_2 support), pulse rate: 127/mn: blood pressure: 126/65mmHg, body temperature: 37°C, C-reactive protein (CRP): 10.83 and leucocyte: 9600/mm^3. The arterial blood gas values (10lt/min mask O_2) were detected as pH:7.45 PaO_2: 53.5mmHg $PaCO_2$: 34mmHg SaO_2: 86.5% HCO_3: 24.9 mmol/L base excess: 0.3 mmol/L Na: 133 mmol/L K: 4.8 mmol/L Cl: 106 mmol/L Ca: 1.09 mmol/L lactate: 1.3 mmol/L. The patient was given non-invasive mechanical ventilation (NIMV) support with positive end-expiratory pressure (PEEP): 10cmH_2O and inspiratory pressure (IP): 22cmH_2O FiO_2: 60%. The chest X-ray and thoracic computed tomography (CT) taken at the ICU admission revealed bilateral, diffuse involvement (sandstorm) and decreased aeration areas of both lungs (Figure 1, Figure 2). The infection markers (body temperature, leucocyte, CRP) of the patient receiving NIMV support



a; ICU admission b; Postoperative 6th month c; Postoperative 1st year

L; left side

Figure 1. Chest X-rays of the PAM diagnosed patient. a; ICU admission (typical chest image of PAM) **b**; 6th month after transplantation **c**; 1st year after transplantation.



a; ICU admission b; Postoperative 1st month c; Postoperative 1st year

Figure 2. Thoracic CT scans of the PAM diagnosed patient. a; ICU admission (bilateral sandstorm image) **b**; 1st month after transplantation **c**; 1st year after transplantation.

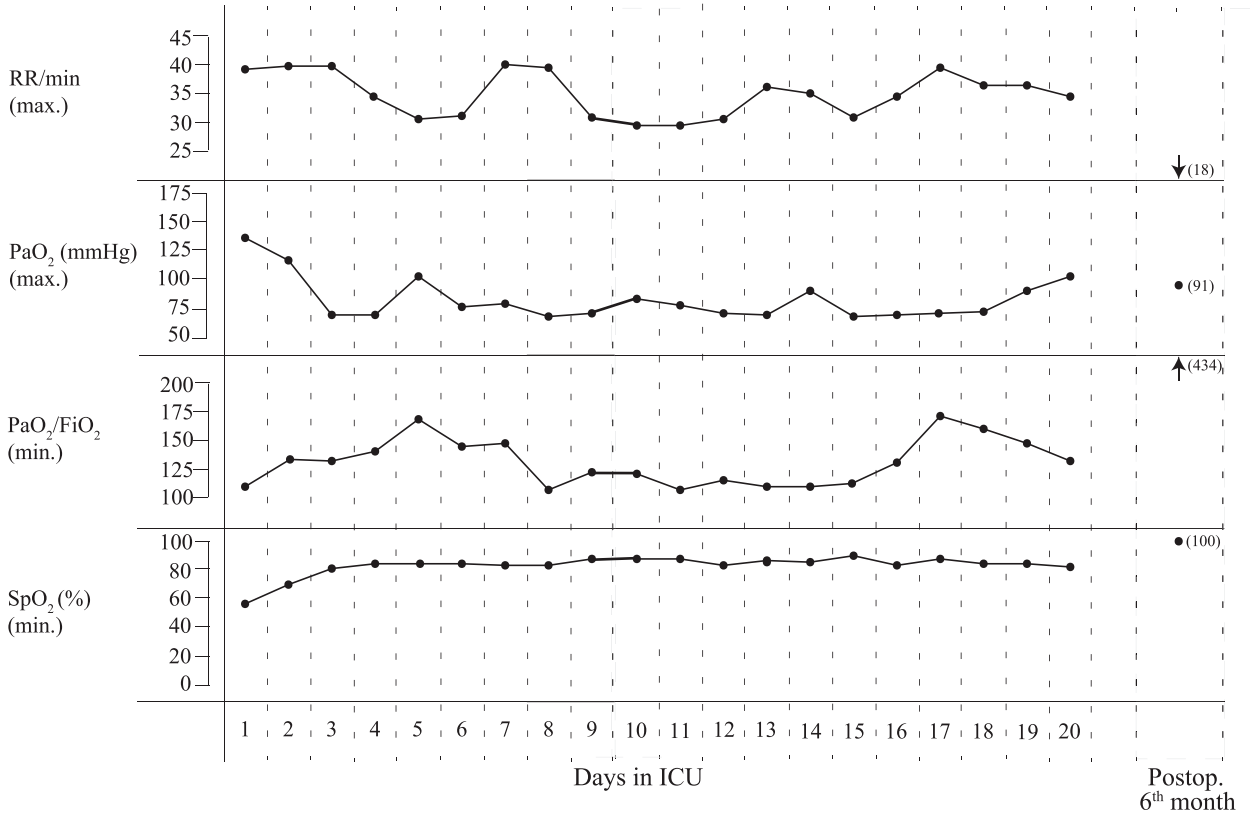
during the 20 days of ICU hospitalization improved after the 15th day. The daily respiratory parameters (respiratory rate, PaO_2, PaO_2:FiO_2 ratio, SpO_2), infection markers and the administered medications are shown in Figure 3 and Figure 4. Since the patient still had the consistent need of NIMV support despite the improvement of the laboratory values, and no changes were detected in the radiological images, she was evaluated together with Pulmonary Diseases and Cardiology departments. Following thoracic CT, echocardiography (mild pulmonary hypertension, EF 60%) and respiratory function tests (Forced Expiratory Volume in 1 second, FEV_1:0.51L Forced Vital Capacity, FVC:0.54L FEV_1/FVC:0.94), the patient was discharged from the ICU on the 20th day and referred to a specialized lung transplantation center. No extrapulmonary involvement was observed by Positron Emission Tomography (PET). The patient underwent bilateral lung transplantation in Vienna 14 months after initial admission (she was under oxygen and NIMV support during these 14 months). She was followed-up during the first seven postoperative days in the ICU and discharged on the 21st day from the hospital. On the postoperative 6th month, the values of the patient, having no need for oxygen or NIMV support, were FEV_1:2.21 FVC:2.26 FEV_1/FVC:98%. The results of chest X-rays taken on the postoperative 1st month and 1st year, the thoracic CT scans taken on the postoperative 6th month and 1st year and the arterial blood gas under room air on the postoperative 6th month of the patient administered mycophenolic acid 760mg/day, tacrolimus 0.5mg/day, and prednisolone 5mg/day medication are demonstrated in Figure 1, Figure 2 and Figure 3 respectively.

Discussion

The etiology, epidemiology, clinical findings and typical radiological images related to PAM disease have been almost completely documented. The aim here is to discuss the advantages of lung transplantation as a treatment option for PAM.

It has been described that PAM is an autosomal recessively inherited disorder related to genetic factors[2,3]. Although PAM is rarely observed in infants[9], the clinical findings and the radiological changes advance progressively over-time; micronodular structure (sandstorm) develops due to the deposition of calcium and phosphate, aeration areas decrease, fibrosis increases and hypoxemia occurs. Patients presenting to the hospital with these clinical findings are generally over the age of 40 and no administered treatments result in full recovery. Systemic corticosteroids, calcium-chelating agents and bronchoalveoler lavage (BAL) are palliative solutions[10]. Ozçelik *et al.* have described the positive effects of the long term use of sodium etidronate which is effective by inhibiting the hydroxyapatite microcrystal formation in pediatric patients[11]. However, there are also some studies showing that the sodium etidronate treatment is ineffective[7].

The priority for these patients admitted to the ICU should be to seek solutions for recovering hypoxemia. It is observed that patients presenting highly decreased aeration areas have already undergone many treatment methods[11]. In Figure 4 we show that the patient was administered sodium etidronate, methylprednisolone and sildenafil in the ICU.



RR; respiratory rate

Figure 3. Daily respiratory parameters in ICU.

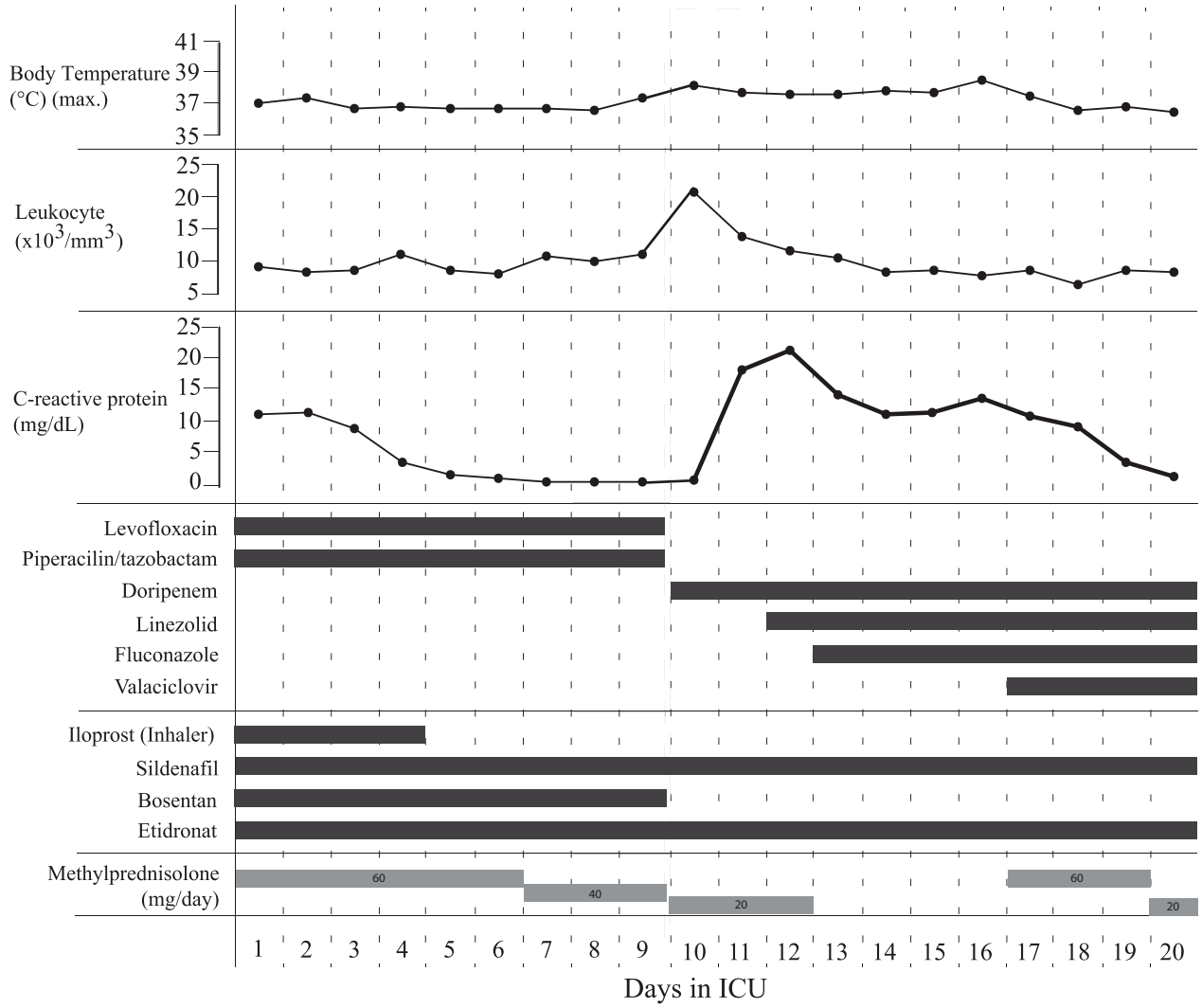


Figure 4. Daily infection markers and therapies in ICU.

Besides, no improvement was observed in the radiological images or respiratory parameters despite the oxygen and NIMV support and the regress in the infection markers. Even at the time of discharge from the ICU, the patient was under NIMV support, and was oxygen dependent with a peripheral saturation of 90%, PaO_2 90–95mmHg and with PaO_2/FiO_2 ratio under 150. The patient clinically worsened with infection; after the regression of the infection, she could only return to her previous hypoxemic condition despite NIMV support.

The issue that intensivists should discuss is whether a patient with a hypoxemic condition should be discharged with the recommendation of oxygen and NIMV support or whether the transplant choice should be brought forward.

Although Turkey is the country with the highest PAM prevalence, we have not encountered any published reports on transplanted cases upon the diagnosis of PAM in Turkey. Lung transplantation is a treatment option for PAM patients and is recommended in severe cases of oxygen dependent respiratory failure before the onset of right heart failure[7,8,10]. Bonette *et al.* recommended bilateral lung transplantations instead of unilateral transplants on the grounds of resistant shunt development in a lung transplantation series of 14 cases, one of which was caused by PAM[12]. Besides, no recurrence was detected in the presented cases or series[7,8,10,13,14]. Moon *et al.* reported the case of a patient who survived for 15 postoperative years with no recurrence after the lung transplantation was performed after PAM diagnosis[8]. In their series, Shigemura *et al.* reported no recurrence and only two cases of postoperative major bleeding after bilateral lung transplantation[15]. Furthermore, they reported a significant increase in the FEV_1 and FVC levels of the patients and considered bilateral lung transplantation in PAM cases as a successful and reliable treatment method.

Thus, considering lung transplantation as a treatment method in PAM cases instead of medication or artificial respiratory support treatments, both of which are known to be ineffective, seems rational. In our case, we discussed the lung transplantation indication of this PAM-diagnosed patient to offer her a chance of full recovery. The differences observed between the preoperative and postoperative periods demonstrated the importance of performing bilateral lung

transplantation in such cases regardless of the recurrence risk. Not only did the radiological follow-up for one year show no recurrence; but also the patient receiving immunosuppressive treatment no longer needed oxygen or artificial respiratory support systems.

Conclusion

Bilateral lung transplantation may improve both the life expectancy and quality of PAM-diagnosed patients with severe respiratory failure who do not suffer from right heart failure. The risk of recurrence should not be considered as a valid reason to eliminate transplantation option as a treatment method.

Key messages

- All the other treatment methods in PAM are palliative except for transplantation.
- A PAM-diagnosed patient being followed-up in the ICU due to severe respiratory failure needs oxygen and NIMV support even at the time of discharge.
- Intensivists should discuss the transplantation option in cooperation with the pulmonologists, cardiologists and transplantation team; they should also have an active role in the management of the PAM-diagnosed patients after their discharge.
- The risk of recurrence should not be considered as a justifying reason to avoid the transplantation option.

Consent

Written informed consent for publication of this case report and accompanying figures was obtained from the patient.

Author contributions

BG was involved in the initial writing of the manuscript. AO, AÇA and BYG were primarily involved in the care of our patient. WK provided intellectual contributions to the content of the manuscript as well as editorial assistance. All authors have read and approved the final version of the manuscript.

Competing interests

The authors declare that they have no competing interest.

Grant information

The author(s) declared that no grants were involved in supporting this work.

Acknowledgements

The authors thank Idil Cakir for her editorial contribution.

References

1. Harbitz F: **Extensive calcification of the lungs as a distinct disease.** *Arch Intern Med.* 1918; **21**(1): 139–146.
Publisher Full Text
2. Dogan OT, Ozsahin SL, Gul E, *et al.*: **A frame-shift mutation in the SLC34A2 gene in three patients with pulmonary alveolar microlithiasis in a inbred family.** *Intern Med.* 2010; **49**(1): 45–9.
PubMed Abstract | Publisher Full Text
3. Ozbudak IH, Bşsorgun CI, Ozbilim G, *et al.*: **Pulmonary alveolar microlithiasis with homozygous c.316G > C (p.G106R) mutation: a case report.** *Turk Patoloji Derg.* 2012; **28**(3): 282–5.
PubMed Abstract | Publisher Full Text
4. Gasparetto EL, Tazoniero P, Escuissato DL, *et al.*: **Pulmonary alveolar microlithiasis presenting with crazy-paving pattern on high resolution CT.** *Br J Radiol.* 2004; **77**(923): 974–6.
PubMed Abstract | Publisher Full Text
5. Mariotta S, Ricci A, Papale M, *et al.*: **Pulmonary alveolar microlithiasis: report on 576 cases published in the literature.** *Sarcoidosis Vasc Diffuse Lung Dis.* 2004; **21**(3): 173–81.
PubMed Abstract
6. Castellana G, Lamorgese V: **Pulmonary alveolar microlithiasis. World cases and review of the literature.** *Respiration.* 2003; **70**(5): 549–55.
PubMed Abstract | Publisher Full Text
7. Jönsson AL, Simonsen U, Hilberg O, *et al.*: **Pulmonary alveolar microlithiasis: two case reports and review of the literature.** *Eur Respir Rev.* 2012; **21**(125): 249–56.
PubMed Abstract | Publisher Full Text
8. Moon E, Tsuang W, Bonnette P, *et al.*: **Lung transplantation outcomes for pulmonary alveolar microlithiasis: a limited case series.** 2009.
Publisher Full Text
9. Yin J, Shen K: **Images in clinical medicine. Pulmonary alveolar microlithiasis in a child.** *N Engl J Med.* 2011; **364**(22): e49.
PubMed Abstract | Publisher Full Text
10. Samano MN, Waisberg DR, Canzian M, *et al.*: **Lung transplantation for pulmonary alveolar microlithiasis: a case report.** *Clinics (Sao Paulo).* 2010; **65**(2): 233–6.
PubMed Abstract | Publisher Full Text | Free Full Text
11. Ozcelik U, Yalcin E, Ariyurek M, *et al.*: **Long-term results of disodium etidronate treatment in pulmonary alveolar microlithiasis.** *Pediatr Pulmonol.* 2010; **45**(5): 514–7.
PubMed Abstract | Publisher Full Text
12. Bonnette P, Bisson A, el Kadi NB, *et al.*: **Bilateral single lung transplantation. Complications and results in 14 patients.** *Eur J Cardiothorac Surg.* 1992; **6**(10): 550–4.
PubMed Abstract | Publisher Full Text
13. Stamatis G, Zerkowski HR, Doetsch N, *et al.*: **Sequential bilateral lung transplantation for pulmonary alveolar microlithiasis.** *Ann Thorac Surg.* 1993; **56**(4): 972–5.
PubMed Abstract | Publisher Full Text
14. Jackson KB, Modry DL, Halenar J, *et al.*: **Single lung transplantation for pulmonary alveolar microlithiasis.** *J Heart Lung Transplant.* 2001; **20**: 226.
PubMed Abstract | Publisher Full Text
15. Shigemura N, Bermudez C, Hattler BG, *et al.*: **Lung transplantation for pulmonary microlithiasis.** *J Thorac Cardiovasc Surg.* 2010; **139**(3): e50–2.
PubMed Abstract | Publisher Full Text

Open Peer Review

Current Referee Status:

Referee Responses for Version 1

Johan Groeneveld
Department of Intensive Care, Erasmus Medical Center, Rotterdam, Netherlands

Approved: 24 July 2014

Referee Report: 24 July 2014
doi:10.5256/f1000research.4322.r5518

Well documented case report. I wonder whether patients with mild cor pulmonale would also qualify for this life saving procedure, since this may ameliorate further remodeling of the heart. Another thing that bothers me is whether this patient was on selective decontamination of the digestive tract during postoperative ICU stay or not? The documentation of pulmonary infections and their (appropriate) antibiotic treatment is somewhat lacking. This is an important issue for lung transplant, immune suppressed patients. Did this patient harbor multi-resistant microorganisms prior to transplant?

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.

Michael O'Connor
Department of Anesthesia and Critical Care, University of Chicago, Chicago, IL, USA

Approved: 07 July 2014

Referee Report: 07 July 2014
doi:10.5256/f1000research.4322.r5369

This case report represents the state of the art in the care of these patients very well. This patient was admitted to the hospital with life threatening respiratory failure. The underlying cause was diagnosed and treated. An excellent discharge plan was created and implemented. The patient was referred for lung transplantation, and underwent the procedure with an apparently good functional result. The duration of follow up is relatively short.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.