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Three cases of donor-derived pulmonary tuberculosis in lung transplant recipients and review of 12 previously reported cases: opportunities for early diagnosis and prevention

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Abstract

Introduction.—Solid organ transplant recipients have a higher frequency of tuberculosis (TB) than the general population, with mortality rates of approximately 30%. Although donor-derived TB is reported to account for <5% of TB in solid organ transplants, the source of *Mycobacterium tuberculosis* infection is infrequently determined.

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Methods.—We report 3 new cases of pulmonary TB in lung transplant recipients attributed to donor infection, and review the 12 previously reported cases to assess whether cases could have been prevented and whether any cases that might occur in the future could be detected and investigated more quickly. Specifically, we evaluate whether opportunities existed to determine TB risk on the basis of routine donor history, to expedite diagnosis through routine mycobacterial smears and cultures of respiratory specimens early post transplant, and to utilize molecular tools to investigate infection sources epidemiologically.

Findings.—On review, donor TB risk was present among 7 cases. Routine smears and cultures diagnosed 4 asymptomatic cases. Genotyping was used to support epidemiologic findings in 6 cases.

Conclusion.—Validated screening protocols, including microbiological testing and newer technologies (e.g., interferon-gamma release assays) to identify unrecognized *M. tuberculosis* infection in deceased donors, are warranted.

Keywords

Mycobacterium tuberculosis; lung transplantation; interferon gamma release assay; donor selection

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With an incidence rate 20–74 times that of the nontransplant population (1, 2), the prevalence of tuberculosis (TB) among solid organ transplant recipients ranges from 1.2 – 6.4% in developed countries, and up to 15% in highly endemic areas (1). TB presents differently in transplant recipients, resulting in diagnostic delay (3). Diagnosis delays, combined with underlying immunosuppression, treatment-related toxicities, and drug interactions, complicate management, resulting in mortality rates that may approach 30% (2, 3).

Sources of *Mycobacterium tuberculosis* infection post transplantation include pre-transplant latent infection in the recipient, infection from exposure after transplant, and latent infection or disease acquired from the donor organ. Pre-transplant latent infection in the recipient is most common, whereas recognized donor-derived *M. tuberculosis* infection accounts for <5% of published cases (2). The risk of graft *M. tuberculosis* infection and the incidence of TB are greater for lung transplant patients, compared with other solid organ transplant recipients (1, 3).

Guidelines for evaluating deceased donors recommend that lungs from donors with active TB by clinical history or radiograph not be used for transplantation (4). Conversely, although clear donor chest radiographs are preferred, they do not guarantee an *M. tuberculosis*-free organ. For donor lungs with abnormal chest radiographs, insufficient data are available to provide specific guidelines regarding utilization (5). Because of transplant-related time constraints, the tuberculin skin test (TST) cannot be used, leaving clinicians with limited *M. tuberculosis* screening tools (4).

In the context of 12 previously reported cases, we reviewed 3 new cases of pulmonary TB after lung transplantation attributed to donor infection, to identify opportunities to recognize,

mitigate, and possibly prevent this potentially fatal complication of an otherwise life-saving intervention.

Methods

Three cases of TB in lung transplant recipients attributed to donor transmission were identified from reports of public health authorities to the Centers for Disease Control and Prevention (CDC) in 2008 and 2009. We reviewed the medical and public health records of these cases and their 3 donors, and United Network for Organ Sharing outcome reports for patients who received other organs from these same donors. Specimens collected for acid-fast bacilli (AFB) smear microscopy and culture during routine protocol evaluations for airway ischemia post transplant were reviewed. As part of the case investigation, we also interviewed and tested organ recipient household members and health care worker contacts by TST. All *M. tuberculosis* isolates were genotyped at the California Department of Public Health by spacer oligonucleotide typing (spoligotyping) and by mycobacterial interspersed repetitive unit-variable number of tandem repeats (MIRU-VNTR) analysis (6). Genotyping results were compared with the National Tuberculosis Genotyping Service's database at the Division of Tuberculosis Elimination, CDC. *M. tuberculosis* isolates retrieved from organ recipients were matched to CDC's surveillance data from the Report of Verified Case of TB (RVCT) of known TB patients. For previously reported cases, Medline was searched using Medical Subject Headings terms 'tuberculosis' and 'lung transplantation.' Reports in English of TB appearing after transplantation were retrieved for review. We abstracted information from published case reports in which the authors of those reports classified the case as probable or proven donor-derived infection. All cases were subsequently classified as possible, probable, or proven using recently proposed criteria (7).

Results

Case 1

During November 2008, a white woman in her 60s who was born in the United States underwent left lung transplantation in California. The organ recipient's TST was negative before transplant; however, she had been taking prednisone for treatment of idiopathic pulmonary fibrosis. Her post-transplant course was complicated by rejection and she was treated with corticosteroids. During month 3 post transplant, AFB smear microscopy and cultures of bronchoscopic specimens collected during a scheduled surveillance examination were negative, and without growth respectively. Three weeks later, AFB smear microscopy and cultures of bronchoscopic specimens collected during evaluation for amiodarone lung toxicity and a new right upper lobe native lung infiltrate were again negative, and without growth respectively.

During month 5 post transplant, after 2 weeks of malaise, she was hospitalized for acute onset of shortness of breath. Her chest radiograph revealed bilateral pulmonary infiltrates, numerous small nodules, and a patchy consolidation of the left lung allograft. A bronchoscopic alveolar lavage (BAL) specimen was 4+ AFB smear-positive; culture with drug susceptibility testing revealed an *M. tuberculosis* isolate that was sensitive to all first line anti-tuberculous agents. The patient's caretaker was initially TST negative with a

normal chest radiograph, but subsequently had TST conversion, suggesting recently acquired *M. tuberculosis* infection. Additional close contacts were TST negative with normal chest radiographs. Other than being a lung-transplant recipient, the patient had no known TB risk factors identified before or after transplantation.

The lung donor was a homeless Hispanic man in his 20s, born in Mexico, with a history of substance abuse and multiple incarcerations, who died of traumatic brain injury. His admission chest radiograph was within normal limits, whereas an abdominal computed tomography scan revealed a moderate infiltrate or contusion involving the right lower lobe of the lung, with a smaller infiltrate in the left lower lobe. Because of these findings, the right lung was not recovered. Respiratory specimens were not obtained for AFB smear microscopy or culture before transplantation. Autopsy performed by the coroner included examination of the right lung; tissue pathology was consistent with pneumonia and showed no granuloma formation and AFB smears were negative; autopsy specimens were not sent for mycobacterial culture. Subsequent genotyping analysis of the recipient's *M. tuberculosis* strain revealed that the isolate matched a larger U.S. *M. tuberculosis* genotype cluster of 91 patients, 70% of whom were Hispanic and 50% of whom were born in Mexico (8).

The organ recipient was treated for 3 months with rifampin, isoniazid, pyrazinamide, and ethambutol, followed by rifabutin and isoniazid, but died of sepsis unrelated to *M. tuberculosis* 10 months after transplantation. At the time of the patient's TB diagnosis, other same-donor recipients, including the heart, pancreas, left kidney, right kidney, and liver recipients, remained without signs or symptoms of TB.

Case 2

During November 2008, a white man in his 50s who was born in the United States underwent bilateral lung transplantation in Florida. The organ recipient was TST negative before transplant; AFB smear microscopy and culture of BAL specimens were negative for AFB on 3 separate days during the first month post transplant. During the second month post transplant, and in the absence of constitutional or respiratory complaints, the BAL specimen collected at a scheduled bronchoscopic reevaluation was 4+ AFB smear-positive. Nucleic acid amplification testing of the BAL specimen identified *M. tuberculosis* complex; culture and drug susceptibility testing revealed an isolate that was fully drug susceptible. Re-review of a posterior-anterior and lateral chest radiograph taken immediately before the BAL revealed the presence of a small nodule and area of atelectasis in the upper-right lung field, which had not been present 1 week before. The organ recipient was without identifiable TB risk. Household contacts were TST negative, with negative chest radiographs at the time the organ recipient was diagnosed with TB. Forty-four of 46 previously TST-negative health care worker contacts were also TST negative; 2 health care worker contacts were lost to follow-up. Previously TST-positive health care worker contacts were, and remained, without signs or symptoms of TB.

The donor was a white man in his 20s born in the United States, who lived alone in Florida and died of injuries sustained in an accident. He had been incarcerated for 1 year, approximately 6 years before donation. His chest radiograph was without infiltrates. Routine bronchoscopic evaluation was without evidence of lower respiratory tract infection;

specimens were not provided for AFB smear microscopy and culture. Genotyping of the recipient's *M. tuberculosis* isolate revealed an identical spoligotype and a nearly identical MIRU-VNTR (i.e., 1 variation in the number of tandem repeats in 1 of 12 loci), to an outbreak strain in an urban residential center 5 miles from the donor's home. After diagnosis of *M. tuberculosis* disease in the recipient, further investigation of the donor uncovered another 6-month period of incarceration, having concluded approximately 1 year before donation. The jail was located <5 miles from the urban residential center. Circulation of the outbreak strain at the jail has been suspected.

A repeat chest radiograph of the organ recipient 3 months post transplant and 1 month after initiation of rifampin, isoniazid, pyrazinamide, and ethambutol revealed a cavitating right upper lobe infiltrate that subsequently resolved. Among 4 other same-donor organ recipients, 1 died without evidence of *M. tuberculosis* infection 90 days after transplant. One recipient was administered isoniazid for possible latent TB. Two were observed without treatment. All 3 remained without evidence of TB 1 year after transplantation.

Case 3

During January 2009, a white man in his 50s born in the United States underwent bilateral lung transplant in Florida. Before transplantation, the organ recipient was TST negative. His post-transplant course was complicated by ischemic airway stenosis that required multiple bronchoscopic dilatations and stenting, primary cytomegalovirus infection, and 2 episodes of rejection treated with pulse corticosteroids. AFB smear microscopy and culture of BAL specimens were negative during the first, second, and third months post transplant. A chest radiograph taken at 3 months post transplant revealed no infiltrates, and the patient was without new constitutional or respiratory complaints. AFB smear microscopy of a BAL specimen was also negative at that time. The patient remained asymptomatic when AFB smear microscopy of a BAL specimen was 4+ AFB smear-positive at 4 months post transplant, the same day the BAL culture obtained at 3 months post transplant was reported to have yielded *M. tuberculosis* (subsequently determined to be fully drug susceptible). Four days later, a new peripheral right upper lobe nodular opacity was evident. The organ recipient had no known TB exposure, and on the day he was diagnosed with TB, his only household contact was TST negative. All previously TST-negative health care worker contacts remained TST negative, while previously TST-positive health care worker contacts remained without signs or symptoms of TB.

The donor was a white man in his 20s born in the United States who died as a result of injuries sustained in an accident. His chest radiograph was without infiltrates. Bronchoscopic evaluation was without evidence of lower respiratory tract infection; BAL specimens were without mycobacterial growth in culture. He had spent a year in the Philippines immediately before his death, but was otherwise without known TB exposure. Genotyping of the recipient's isolate identified a spoligotype associated with the Manila family, a strain circulating predominantly, although not exclusively, in the Philippines (9). The organ recipient had never traveled outside the United States.

The organ recipient's TB was treated with 2 months of rifampin, isoniazid, pyrazinamide, and ethambutol, followed by 7 months of rifampin and isoniazid. Among the 4 other same-

donor organ recipients, 1 was administered isoniazid for treatment of possible latent TB, while the other 3 were observed. All 4 remained without evidence of TB.

Literature review

Twelve other cases of donor-derived pulmonary TB after lung transplantation have been reported in the literature. Characteristics of all 15 recipients, including the 3 new cases from the present report, are summarized in Table 1 (10-19). Reported cases date to 1990. Median age was 49 (range: 18–68) years. Seven (47%) were men. Seven (47%) received anti-lymphocyte antibody induction. Eleven (73%) were bilateral lung transplant recipients. Two (13%) received single lungs from the same donor. Two (13%) received single lungs from donors whose contralateral lungs were not transplanted.

Nine (60%) were treated with pulse corticosteroids for acute rejection before TB diagnosis. Median time to TB diagnosis was 88.5 (range: 21–153) days post transplant. Five of 15 (33%) patients had no symptoms; pulmonary TB was recognized by protocol AFB smear microscopy or culture of respiratory specimens in 4 cases, with median diagnosis at 68.5 days post transplant. A fifth asymptomatic illness was diagnosed at 42 days post transplant, when the same-donor contralateral lung recipient developed pulmonary TB. A TB diagnosis was made at 87, 90, and 147 days post transplant in 3 fatal cases, respectively, where the cause of death was attributed to *M. tuberculosis*.

After diagnosis of pulmonary TB among lung transplant recipients, epidemiologic investigation identified TB risk factors in 7 (47%) donors. Donor risk factors included incarceration (in 1); travel to a high TB burden country (in 1); high TB burden in country of origin (in 3); household exposure to a TB illness (in 1); and both incarceration history and country of origin (in 1). In 2 donors, abnormalities consistent with prior TB infection were also identified retrospectively by review of chest radiographs.

Genotype analysis supported attribution of infection to the donor in 6 of 15 (40%) cases, and in all cases in which this analysis was performed. Two recipients were reported to have an identical *M. tuberculosis* genotype result after undergoing single lung transplantations from the same donor at the same facility; no pre-transplant *M. tuberculosis* risk or epidemiologic link was identified in these recipients. In the remaining 4 cases, the donors were known to have epidemiologic risk factors for TB. Furthermore, genotyping combined with epidemiologic data specifically linked the recipients' isolates to TB risks identified in their donors. In 2 instances, genotyping linked the recipient's isolate to the donor's country of origin, both of which had high rates of TB. Genotyping linked 1 recipient's isolate to a known TB outbreak that occurred in close proximity to the donor's residence and a jail where he was incarcerated. Genotyping linked 1 recipient's isolate to a TB endemic country where the donor had traveled and resided for an extended period. In none of the 6 cases did the recipient share the epidemiologic risk of the donor for TB. These genotyping results, in conjunction with the epidemiologic data, provide strong circumstantial evidence that TB in the recipients originated from their donors.

All 3 of the cases reported here and 11 of 12 previously reviewed cases met recently recommended criteria for probable donor-derived transmission (7). One of the 12 previously reported cases (Case 7) would be classified as possible by these criteria.

Discussion

We report 3 cases of lung transplant-associated TB where transmission was probably acquired from a donor-derived latent infection, based on specific TB risks identified retrospectively in the donor, and lack of evidence of recipient infection pre-transplant or primary infection post transplant. Genotyping of *M. tuberculosis* isolates corroborated the evidence.

Genotyping is a useful epidemiologic tool for investigating the origin of the *M. tuberculosis* strain, as demonstrated by Cases 1–3, 9, 12, and 13. As genotype testing methods with greater discriminatory power improve, and strain typing archives are increased, the value and role of genotyping in epidemiologic investigations of TB among transplant recipients will expand and should increase, thereby, our understanding of *M. tuberculosis* infection after solid organ transplantation.

M. tuberculosis genotyping does have certain limitations when used to attribute the source of *M. tuberculosis* infection among transplant recipients. Results for the 3 cases reported here can only be considered supportive of donor-derived *M. tuberculosis*, because *M. tuberculosis* was not recovered from any of the 3 donor specimens before organ recovery, and direct comparisons of recipient and donor genotypes was not possible. Also, Mexican and Philippine *M. tuberculosis* strains with spoligotypes identical to the isolates recovered from Case 1 and 3, respectively, are found in limited numbers within the United States and, therefore, acquisition of these strains through airborne transmission within the United States cannot be ruled out. Finally, the MIRU-VNTR for Case 2 was very similar but not identical to the epidemiologically linked outbreak strain.

The majority of the 15 recipients with donor-derived TB following lung transplantation reviewed in this report were diagnosed ≥90 days post transplant, after they had already made repeated visits to both inpatient and outpatient transplant centers frequented by other immunocompromised patients. In addition to expediting life-saving antimicrobial treatment, early recognition of pulmonary TB would allow implementation of prompt infection control precautions, thus preventing the spread of TB to other highly susceptible patients, health care providers, and the general public.

Pulmonary TB was recognized, in the absence of symptoms and chest radiograph abnormalities, by routine AFB smear and culture of lower respiratory specimens in only 4 of 15 cases before day 90 after transplantation. The proportion of all reported cases that could have been identified in this manner is unknown. In Case 1, mycobacterial stains and cultures of bronchoscopic specimens were negative, and without growth, respectively, through day 84 post transplant; AFB stains and cultures of respiratory specimens were not performed again until symptomatic pulmonary TB was present on day 153. The benefits of regular assessment of lower respiratory specimens for *M. tuberculosis* during the initial 6 months

after lung transplantation, typically the period of maximal immunosuppression, should be systematically evaluated for utility in detection of unrecognized donor-derived transmission.

As TB prevention is the ultimate goal, the best approach would be to screen donors before transplantation, rather than investigating infection after *M. tuberculosis* has been transmitted. This benefits the potential organ recipient and also the general public. Three case donors described in this report and 4 donors of 12 previously reported cases had well-defined risk for TB infection. For these 7 cases (47%), recognition of donor TB risk at the time of transplantation would not only have triggered more complete donor TB evaluations, but also might have improved recipient surveillance through regular AFB smear and culture of lower respiratory secretions. The need to collect detailed donor history of TB risk factors is a critically important and strongly endorsed component of organ donor evaluation (7).

TB screening of deceased donors without recognized increased risk for TB infection is not standardized among organ procurement agencies in the United States. Although chest radiographs can identify deceased potential donors with findings indicative of active or latent TB infection, their utility is limited in the presence of other common lung abnormalities among deceased donors (e.g., pulmonary contusions or pneumonia). Although more sensitive and specific than chest radiographs, computed tomography scans could indicate, but might not confirm, the diagnosis of active or latent *M. tuberculosis* infection, and could result in the exclusion of suitable organs. Routine microbiologic screening of donor tracheal aspirate or BAL specimens for AFB smear microscopy and mycobacterial culture is potentially appealing, and has recently been recommended for lung donors by several large professional transplantation societies (7). Although some positive AFB smears might be the result of non-tuberculous mycobacteria, the concomitant use of nucleic acid amplification testing and other rapid diagnostic tools could reduce the likelihood of donor lungs being removed from the organ pool unnecessarily. Among AFB smear-negative specimens, growth of *M. tuberculosis* could lead to more rapid diagnosis and treatment of lung recipients. However, the utility and cost effectiveness of these screening methods have not been critically evaluated.

TB screening of living donors of transplant organs is routinely performed by TST (3), but is not timely enough for use among deceased donors. Given the increased risk of lung allograft *M. tuberculosis* infection compared with other solid organ allografts and the TB-associated morbidity and mortality in these patients (1), newer and more rapid methods for detecting *M. tuberculosis* infection in donors, including interferon-gamma release assays (IGRA), should be evaluated. IGRA have limitations similar to TST, including an inability to differentiate latent from active *M. tuberculosis* infection and lack of sensitivity (20). In addition, corticosteroids initiated during donor screening might interfere with IGRA performance, and the interpretation of results might be further complicated by donor stress responses. However, the benefits to individual organ recipients and the general public warrant evaluation of lung donor screening with IGRA.

As the population of potential organ donors in the United States becomes increasingly diverse, the need for improved donor screening for TB must be emphasized. For example, the percentage of Hispanic lung donors has increased from 8.5% during 1999 to 15.9%

during 2008, a population with a higher TB incidence than their non-Hispanic counterparts (21, 22). During 2010, the CDC revised case-report form, RVCT, now collects information identifying TB cases in the United States occurring after organ transplantation (23).

In conclusion, 3 probable cases of donor-derived pulmonary TB after lung transplantation are reported. Review of these cases, and of 11 probable and 1 possible previously reported cases, has identified opportunities to improve recognition of donor TB risk by a more thorough review of incarceration, travel, and immigration history. IGRA testing, routine AFB smear microscopy, smear and culture of respiratory specimens, and other screening methods of lung donors with increased risk of TB should be evaluated. As part of routine surveillance, diagnostic BAL fluid and other respiratory specimens can be tested at regular intervals by AFB smear microscopy and culture during the initial 6 months post transplant to expedite diagnosis. *M. tuberculosis* genotyping of all lung and non-lung post-transplant TB cases could improve the understanding of the epidemiology of this potentially fatal communicable disease.

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Disclaimer: The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Abbreviations:

AFB	acid-fast bacilli
BAL	bronchoscopic alveolar lavage
CDC	Centers for Disease Control and Prevention
IGRA	interferon-gamma release assays
MIRU-VNTR	mycobacterial interspersed repetitive unit-variable number of tandem repeats
RVCT	report of verified case of TB
TB	tuberculosis
TST	tuberculin skin test

References

1. Aguado JM, Torre-Cisneros J, Fortun J, et al. Tuberculosis in solid-organ transplant recipients: consensus statement of the group for the study of infection in transplant recipients (GESITRA) of the Spanish Society of Infectious Diseases and Clinical Microbiology. Clin Infect Dis 2009; 48: 1276–1284. [PubMed: 19320593]

2. Singh N, Paterson DL. *Mycobacterium tuberculosis* infection in solid-organ transplant recipients: impact and implications for management. Clin Infect Dis 1998; 27: 1266–1277. [PubMed: 9827281]
3. Subramanian A, Dorman S; AST Infectious Diseases Community of Practice. *Mycobacterium tuberculosis* in solid organ transplant recipients. Am J Transplant 2009; 9 (Suppl 4): S57–S62. [PubMed: 20070696]
4. Fischer SA, Avery RK; AST Infectious Diseases Community of Practice. Screening of donor and recipient prior to solid organ transplantation. Am J Transplant 2009; 9 (Suppl 4): S7–S18. [PubMed: 20070698]
5. Orens JB, Boehler A, de Perrot M, et al. A review of lung transplant donor acceptability criteria. J Heart Lung Transplant 2003; 22: 1183–1200. [PubMed: 14585380]
6. National TB Controllers Association/CDC Advisory Group on Tuberculosis Genotyping. Guide to the Application of Genotyping to Tuberculosis Prevention and Control. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, 2004.
7. Morris MI, Daly JS, Blumberg E, et al. Diagnosis and management of tuberculosis in transplant donors: a donor-derived infections consensus report. Am J Transplant 2012; 12: 2288–2300. [PubMed: 22883346]
8. CDC. Launch of TB Genotyping Information Management System (TB GIMS). MMWR 2010; 59: 300.
9. Douglas JT, Qian L, Montoya JC, et al. Characterization of the Manila family of *Mycobacterium tuberculosis*. J Clin Microbiol 2003; 41: 2723–2726. [PubMed: 12791915]
10. Lee J, Yew WW, Wong CF, Wong PC, Chiu CS. Multi-drug resistant tuberculosis in a lung transplant recipient. J Heart Lung Transplant 2003; 22: 1168–1173. [PubMed: 14550827]
11. Wong CF, Fung SL, Yan SW, Lee J, Cheng LC, Chiu CS. Lung transplantation in Hong Kong: 12 years of experience. Respirology 2008; 13: 903–907. [PubMed: 18811889]
12. Boedefeld RL, Eby J, Boedefeld WM, et al. Fatal *Mycobacterium tuberculosis* infection in a lung transplant recipient. J Heart Lung Transplant 2008; 27: 1176–1178. [PubMed: 18926414]
13. Place S, Knoop C, Remmelink M, et al. Parodoxical worsening of tuberculosis in a heart-lung transplant recipient. Transpl Infect Dis 2007; 9: 219–224. [PubMed: 17692068]
14. Shitrit D, Bendayan D, Saute M, Kramer MR. Multidrug resistant tuberculosis following lung transplantation: treatment with pulmonary resection. Thorax 2004; 59: 79–80. [PubMed: 14694255]
15. Winthrop KL, Kubak BM, Pegues DA, et al. Transmission of *Mycobacterium tuberculosis* via lung transplantation. Am J Transplant 2004; 4: 1529–1533. [PubMed: 15307842]
16. Schulman LL, Scully B, McGregor CC, Austin JH. Pulmonary tuberculosis after lung transplantation. Chest 1997; 111: 1459–1462. [PubMed: 9149616]
17. Ridgeway AL, Warner GS, Phillips P, et al. Transmission of *Mycobacterium tuberculosis* to recipients of single lung transplants from the same donor. Am J Respir Crit Care Med 1996; 153: 1166–1168. [PubMed: 8630561]
18. Miller RA, Lanza LA, Kline JN, Geist LJ. *Mycobacterium tuberculosis* in lung transplant recipients. Am J Respir Crit Care Med 1995; 152: 374–376. [PubMed: 7599848]
19. Carlsen SE, Bergin CJ. Reactivation of tuberculosis in a donor lung after transplantation. AJR Am J Roentgenol 1990; 154: 495–497. [PubMed: 2106211]
20. Herrera V, Perry S, Parsonnet J, Banaei N. Clinical application and limitations of interferon-{gamma} release assays for the diagnosis of latent tuberculosis infection. Clin Infect Dis 2011; 52: 1031–1037. [PubMed: 21460320]
21. US Department of Health and Human Services. 2009 Annual Report of the US Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: Transplant Data 1999–2008. Rockville, MD: US Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation, 2009 Available at: http://www.ustransplant.org/annual_reports/current/default.htm (accessed January 25, 2011).
22. Centers for Disease Control and Prevention. Trends in tuberculosis – United States, 2011. Morb Mortal Wkly Rep 2012; 61: 181–185.

23. US Department of Health and Human Services. Report of Verified Case of Tuberculosis. Centers for Disease Control and Prevention 2008 9 15 Available at: http://www.cdc.gov/PHIN/library/documents/pdf/2009_RVCT_Form_with_PHIN_Variable_IDs_10292008.pdf.

Table 1

Summary of 15 probable donor-derived tuberculosis (TB) cases, described by recipient and donor characteristics

Case no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Recipient															
Pre-transplant															
Date of transplant	2008	2008	2009	1999	2002	2008	2006[1]	1999	2002	1997[1]	1997[1]	1993	1993	1993	1990[1]
Age	60s	50s	50s	35	48	68	28	18	49	27	57	41	63	57	23
Gender	Female	Male	Male	Female	Male	Male	Female	Male	Female	Male	Male	Female	Female	Female	Female
ALA induction	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	NA	No	No	No	No	No	Yes
TST result	Negative	Negative	Negative	Negative	Negative	Not performed	NA	Negative	NA	Negative	Negative	NA	NA	Negative	Negative
Identified TB risk/exposure	No	No	No	No	No	No	NA	No	No	No	No	No	No	No	No
Type of lung transplant	Single	Bilateral	Bilateral	Bilateral	Bilateral	Single	Bilateral	Bilateral	Bilateral	Bilateral	Bilateral	Single	Single	Bilateral	Bilateral
Post transplant															
Treated for rejection	Yes	No	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	No	No	Yes	Yes
Approximate day of lab diagnosis[2]	153	53	119	140	<1 year	90	81	75	21	90	90	42	42	87	147
Symptoms	Fever, dyspnea	None	None	Malaise	NA	Sepsis	None	Fever, cough	None	Fever	Pleuritic chest pain	Fever	None	Shoulder pain	Dyspnea
Radiologic findings	Infiltrates	None	None	Infiltrates	NA	Infiltrates	None	None	None	Bronchial narrowing	Nodules, effusion	Opacities	None	Cavitary lesion	Infiltrates
Patient outcome	Died[3]	Cured	Cured	Cured	Cured	Died	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Died	Died
Donor															
TB risk	Yes	Yes	Yes	Yes	NA	Yes	NA	Yes	Yes	No	No	No	No	No	NA
TB risk characterized	Mexican immigrant, incarceration	Proximity to TB outbreak; incarceration	Residence in the Philippines	Chinese immigrant	NA	Peruvian immigrant	NA	Mother with TB	Guatemalan immigrant	No	No	No	No	No	NA
Risk identified at transplant	Yes	No	No	Yes	NA	Yes	NA	No	Yes	No	No	No	No	No	NA
TST performed	No	No	No	NA	NA	Yes[4]	NA	No	No	No	No	No	No	No	NA
Radiology consistent with TB	No	No	No	No	NA	No	NA	No	Yes	No	No	No	No	No	Yes
Donor affiliation by strain analysis	Yes	Yes	Yes	NA	NA	NA	NA	NA	Yes	NA	NA	Yes[5]	Yes[5]	NA	NA
Source (reference)	PR	PR	PR	Lee (10)	Wong (11)	Boedefeld (12)	Place (13)[6]	Shitrit (14)	Winthrop (15)	Schulman (15)	Schulman (15)	Ridgeway (17)	Ridgeway (17)	Miller (18)	Carlsen (19)

[1] Date reported (transplant date NA).

[2] AFB smear with rapid identification test or culture positive.

[3] Death due to sepsis unrelated to *Mycobacterium tuberculosis*.

[4] Positive TST.

[5] Identical strain.

[6] Donor-derived status confirmed by author communication.

ALA, anti-lymphocyte antibody; NA, not available; TST, tuberculin skin test, AFB, acid-fast bacilli; PR, present report.