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A Missed Tuberculosis Diagnosis Resulting in Hospital Transmission

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Abstract

OBJECTIVE—To find the source of tuberculin skin test conversions among 38 hospital employees on 1 floor during routine testing January–February 2010.

METHODS—Record review of patients at a private hospital during September–December 2009 and interviews with hospital employees. Names of patients from the state tuberculosis (TB) registry were cross-referenced with hospital records for admissions. *Mycobacterium tuberculosis* genotype results in the county and adjacent counties were examined, and contacts were evaluated for TB infection and disease.

RESULTS—One of the 38 employees, a nurse, was diagnosed with pulmonary TB with a matching *M. tuberculosis* genotype and drug resistance pattern (isoniazid monoresistant) to those of a county jail inmate also recently diagnosed with pulmonary TB. The nurse had no known contact with that inmate; however, another inmate in his 20's from the same jail had been hospitalized under that nurse's care in October 2009. That young man died, and a postmortem examination result subsequently confirmed TB, which had not been suspected. Exposure to this man with undiagnosed TB could explain the transmission: 87 (27%) of the 318 hospital-based contacts without previous positive tuberculin skin test results were infected, and 9 contacts had active TB.

CONCLUSIONS—This investigation demonstrated *M. tuberculosis* transmission in a hospital due to a missed diagnosis and nonadherence to national TB infection control guidelines. Routine TB screening of employees allowed early detection of this missed TB diagnosis, facilitating prompt evaluation of contacts. Healthcare providers should suspect TB in symptomatic persons and adhere to TB control policies.

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During January–February 2010, a hospital found 38 employees with tuberculin skin test (TST) conversions within 6 months of having a negative TST result. Most of the 38 employees worked on the same medical-surgical floor. TST conversion is a sign of recent infection with *Mycobacterium tuberculosis*, which is associated with an increased risk for progression to tuberculosis (TB) disease.[1] No employee at this hospital had been found to have a TST conversion during the preceding 2 years.

Such a large number of recently positive TST results within 2 months, with no known explanation, was cause for alarm. This report describes a missed diagnosis of TB that resulted in transmission of *M. tuberculosis* in a hospital.

METHODS

Setting

The private hospital, with approximately 1,000 employees, provides emergency and intensive care to a mostly Hispanic population.[2] In 2008 and 2009, TB rates in this geographic area were 10–12 cases per 100,000 population;[3] the corresponding overall state and national rates were approximately 6 and 4 cases, respectively, per 100,000.[4]

Infection Control Policies at the Hospital

National guidelines recommend at least annual TB screening for healthcare workers who may encounter TB patients.[1] In this hospital, employees who have direct contact with patients receive TB screening upon hire and then every 6 months. TB screening consists of an evaluation for signs and symptoms of TB disease and a TST. Employees with a documented positive TST result receive a TB symptom screen and, if symptoms are present, a chest radiograph and sputum examination.[1]

To prevent transmission of airborne infectious agents such as *M. tuberculosis* at this hospital, patients are screened upon admission, using a respiratory risk assessment tool. Questions include history of TB disease or infection, treatment, symptoms, and medical history. Persons with potentially infectious TB are placed in 1 of the hospital's 8 airborne infection isolation rooms.[1] When all isolation rooms are occupied, such patients are placed in a private room with a portable high-efficiency particulate air filtration unit.

Initial Investigation Focus

To validate the TST conversions and other newly positive TST results among hospital staff, the investigation in February 2010 assessed for changes in staff or techniques for TST placement and reading or changes in procedures for storing and handling the tuberculin antigen. Postexposure screening included use of different tests: TSTs and interferon-γ release assay (IGRA) blood tests. The ventilation systems of the airborne infection isolation rooms on the medical-surgical floor (floor X) were evaluated for potential malfunction.

The remaining purified protein derivative tuberculin (Tubersol, manufactured by Sanofi Pasteur) from the hospital was sent to the state public health laboratory to be analyzed for bacterial contamination. A nearby hospital using the same Tubersol lot numbers was asked whether TST results in their setting were unusual in any respect. In collaboration with a

university research laboratory, health department staff offered the first 30 hospital employees who had TST conversions or newly positive TST results a second test for *M. tuberculosis* infection, an IGRA.[5]

Expanded Investigation

Because most of the hospital staff with newly positive TST results had a documented negative result in August–September 2009 followed by a positive result in January–February 2010, the March 2010 investigation focused on searching for exposure to infectious TB on floor X during September–December 2009.

Medical records were reviewed for evidence of undiagnosed TB for patients on floor X who had respiratory illnesses or TB risk factors, including incarcerated persons, those with human immunodeficiency virus (HIV) infection or other immunocompromising conditions, illicit drug users, and persons who were hospitalized for more than 2 weeks. Names of TB patients from local public health records were cross-referenced with the hospital's patient database for any possible hospitalizations during their estimated infectious periods. Employees on floor X were asked if they could recall any coworkers who had symptoms or signs of TB at work (eg, severe coughing, weight loss).

In February 2010, a nurse working on floor X had a TST conversion and a chest radiograph, which indicated minimal interstitial infiltrates. Sputum specimens were collected, and smear results were negative for acid-fast bacilli. The nurse denied having symptoms, but several coworkers named the nurse as coughing at work for several months. In March, the sputum culture grew an isoniazid-monoresistant strain of *M. tuberculosis*. The genotype pattern of the nurse's *M. tuberculosis* isolate was compared with genotype results of other persons diagnosed with TB in the county and adjacent counties.

RESULTS

TST application and reading techniques of the employee health nurse who administered the tests in January–February 2010 as well as during the previous 2 years were found to be acceptable, and no changes in the storing or handling of the antigen were discovered. The airborne infection isolation rooms on floor X met required ventilation standards. The public health laboratory found no evidence of bacterial contamination in the tuberculin used in the hospital. The manufacturer had no reports of adverse reactions with the same lot numbers, and no increase in the number of positive TST results were reported by the nearby hospital using the same antigen. Twenty-five staff with positive TST results were additionally tested with an IGRA (either QuantiFERON-TB Gold In-Tube or T-SPOT); 20 (80%) also had a positive IGRA result.

Because the floor X nurse diagnosed with TB disease had a history of consecutive negative TST results—most recently 4 months prior—and reported no symptoms, the nurse was considered an unlikely source for transmission. The nurse's *M. tuberculosis* genotype did not match that of any persons with known TB diagnoses at the hospital in 2009. However, the *M. tuberculosis* strain had been found in 10 previous instances: 5 in this county, 2 in the rest of the state, and 3 others nationally.

All 7 previous known TB disease occurrences in this state with this same *M. tuberculosis* genotype were also isoniazid monoresistant but were seen exclusively in Hispanic persons; the nurse was not Hispanic. The most recent matching *M. tuberculosis* genotype came from a Hispanic person (patient A) with cavitary TB in August 2009 in a nearby county jail. Despite careful reinterviewing to establish a link between the 2, the nurse was not found to have known contact with patient A, suggesting that an intervening transmission event might have linked the person in the jail to the hospital.

Further investigation revealed that in July 2009, patient A was arrested on the same day and time as another inmate (patient B), who was hospitalized and under the nurse's care on floor X in October–November 2009. Jail records indicated that patient A and patient B arrived at the jail within 10 minutes of each other and were also transferred to general population within 10 minutes of each other. Records also indicated the possibility of the men sharing the same holding cell for about 10 hours before moving to general population; however, that could not be confirmed, because rosters of persons in holding cells are not kept at the jail.

In October 2009, patient B, a Spanish-speaking, HIV-infected man in his mid-20s, was admitted to floor X of this hospital from a county jail. He had cough, fever, chills, and weight loss, and his initial chest radiograph result showed bilateral infiltrates. His admitting diagnosis was community-acquired pneumonia. He was placed on antibiotics and 1 week later was discharged back to the jail. Two days after that, he was readmitted to the hospital with cough and fever. A portable air filtration system was ordered for his room initially but was removed after 1 day with the explanation that his pneumonia was not contagious. Patient B died 36 days later.

During his hospitalization, patient B had hemoptysis and a worsening chest radiograph. He had a documented history of drug use and homelessness. In 2007 at the same hospital, patient B had been treated under a different name for drug-susceptible TB and HIV/acquired immunodeficiency syndrome. His 2007 TB strain did not match that of patient A or of the nurse by either drug susceptibility (isoniazid mono-resistant) or *M. tuberculosis* genotype result.

Epidemiologic links between patients A and B and between patient B and the nurse—in addition to the matching *M. tuberculosis* genotypes of patient A and the nurse—led to the hypothesis that a first transmission wave occurred in July 2009 from patient A to patient B in the county jail. Although he had been treated for drug-susceptible TB in 2007, patient B may have been reinfected in 2009 with a different, isoniazid-monoresistant strain of TB. Because he was not under airborne infection isolation precautions on days 2–37 of his 2009 hospitalization, patient B could have been the source of a second wave of transmission, explaining the large number of TST conversions and newly positive TST results among staff assigned to floor X.

On the basis of this new hypothesis, in April 2010, the county health department requested polymerase chain reaction–based nucleic acid amplification testing on a formalin-fixed esophageal tissue specimen collected from patient B during exploratory surgery of a neck abscess 2 days before his death. Testing was conducted at a research laboratory at the

University of Texas Health Science Center Houston, Brownsville campus, as described previously.[6] Nucleic acid amplification test results demonstrated the presence of *M. tuberculosis* in the tissue. Neither culture confirmation nor genotype testing was possible on the nonviable sample.

Exposure to *M. tuberculosis* on Floor X

Interviews with hospital staff and visitors provided further insight into how *M. tuberculosis* transmission potentially occurred on floor X. Employees reported that during patient B's hospitalization, he often walked the halls of floor X accompanied by correctional staff, allowing exposure to many persons, including other patients and visitors. Among hospital-based contacts who were evaluated for TB infection, 23 (77%) of 30 floor X staff and 13 (87%) of 15 correctional staff assigned to patient B had a positive result to either TST or IGRA following a negative TST result (Table 1).

In all, 416 (87%) of 477 hospital-based contacts were screened for *M. tuberculosis* infection; 87 (27%) of the 318 contacts who did not have previous positive TST results were infected. Hospital employees with newly positive TB test results had 14 times the odds of working on floor X as compared with staff working in other areas of the hospital (odds ratio, 14.1 [95% confidence interval, 5.6–35.1]). Because of infection with *M. tuberculosis* that was presumably isoniazid monoresistant, persons with a positive TST or IGRA result were offered the 4-month regimen of rifampin after TB disease was excluded and if no contraindication to the medication was present.[7]

During March 2010 and March 2012, 9 persons who spent time on floor X were diagnosed with TB disease: 3 hospital employees (2 nurses and 1 social worker), 3 correctional officers, 2 visitors, and 1 patient. Seven had culture-positive pulmonary TB, and 2 had culture-negative clinically diagnosed pleural TB. Their ages ranged from 21 to 66 years old, with a mean age of 41 years. The average time from exposure to development of TB was 14 months, with a range of 4–48 months.

The 7 persons with culture-positive TB all had *M. tuberculosis* genotyping results that matched patient A's genotype and had isoniazid-monoresistant TB. Five had pulmonary TB only, and 2 had both pulmonary and extrapulmonary TB. All 9 were treated with a regimen for isoniazid-monoresistant TB and were clinically managed by staff at the local and regional health departments.

DISCUSSION

This investigation demonstrated *M. tuberculosis* transmission that began in a county jail and spread to a private hospital, where 1 missed TB diagnosis appeared responsible for infections in dozens of contacts and at least 9 new occurrences of TB disease. These findings are consistent with other studies reporting high TST conversion rates in institutions caring for many TB patients.[8,9] A delay in the diagnosis of TB is a factor that has been associated with an increased risk of hospital-related transmission.[10]

Because the hospital's infection control program included routine TB screening of employees[1] and baseline TST results were documented for the corrections staff,[11] those who were recently infected were diagnosed within months of their exposure, allowing prompt notification and evaluation of other potentially exposed contacts.

Laboratory findings were essential to this investigation. *M. tuberculosis* genotyping and drug susceptibility results prompted the exploration of a link between the nurse and patient A. Although the 2 had no known direct contact with each other, they were connected indirectly by patient B, which ultimately led to the conclusion that patient B was the likely source for the *M. tuberculosis* transmission in the hospital. Drug susceptibility results were crucial for knowing how to treat the infected contacts.

The following limitations to these results should be recognized. The focus of this investigation was hospital transmission, so the true magnitude of this outbreak might be underestimated. For example, during the weeks leading up to his October 2009 hospitalization, patient B might have exposed others to *M. tuberculosis* at the jail, where he had remained in general population for 3 months. The assumption that patient B was infected by patient A while in jail was based on the positive nucleic acid amplification test result and the epidemiological investigation. Prospective monitoring of *M. tuberculosis* drug susceptibility and genotype results will help elucidate whether transmission also occurred in the jail or community.

Collaborations such as the ones in this investigation between the hospital, local and state health departments, a university, and the correctional facility are essential to find and cure TB, which are the first priorities of TB control.[1] To prevent future incidents, hospital and corrections staff should be mindful of suspecting TB in symptomatic persons, especially in those with risk factors for TB, such as HIV infection, a history of incarceration, homelessness, illicit drug use, or foreign-born background. Because the risk of progression of TB infection to TB disease is particularly high in recently infected persons,[1,12] finding and promptly treating infected contacts is essential to preventing further transmission.

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TABLE 1

Hospital-Based Tuberculosis (TB) Contact Investigation Results

Contacts exposed to patient B	No. of Contacts	Contacts evaluated	Previous positive TST result[a]	Positive TB test result[b]	Contacts completing treatment for TB infection[c]	Active TB diagnosis
Hospital staff excluding floor X	313	279 (89)	73 (26)	39 (19)	31/33 (94)	1
Hospital staff on floor X	47	47 (100)	17 (36)	23 (77)	15/20 (75)	2
Patients and visitors on floor X	99	72 (73)	5 (7)	12 (18)	2/6 (33)	3
Correctional staff on floor X	18	18 (100)	3 (17)	13 (87)	1/6 (17)	3
All	477	416 (87)	98 (24)	87 (27)	49/65 (75)	9

NOTE. Data are no. (%), unless otherwise indicated. TST, tuberculin skin test.

[a] Of contacts evaluated.

[b] Positive TST or interferon-γ release assay result. All hospital and correctional staff had previously documented negative TST results; not all patients or visitors had known previous TST results.

[c] Of contacts who started treatment for TB infection.

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