Nosocomial Transmission of Congenital Tuberculosis in a Neonatal Intensive Care Unit

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Congenital tuberculosis is uncommon, and nosocomial transmission from a congenitally infected infant to another infant has not been reported in the English literature. We report an investigation of 2 infants with tuberculosis who were cared for in the same neonatal intensive care unit. Isolates from both infants were genetically indistinguishable. Transmission between the 2 infants was likely due to contaminated respiratory equipment.

Congenital tuberculosis is rare, with ~340 cases described in the literature [1–20]. We describe the outbreak investigation associated with a case of nosocomial transmission of tuberculosis from a congenitally infected infant to another infant.

Patient 1. Patient 1 was born 15 December 2001 by spontaneous vaginal delivery at 25 weeks’ gestation to a healthy 42-year-old woman (gravidia 5, para 3, spontaneous abortion) and weighed 800 g. The infant was transferred to the neonatal intensive care unit (ICU) on 19 December amid development of numerous complications and remained until death on 4 February 2002. Histopathologic examination of autopsy tissue specimens revealed disseminated tuberculosis with necrotizing pneumonitis, lymphadenitis, and hepatosplenic abscesses. Tissue specimens grew Mycobacterium tuberculosis (figure 1).

Methods. The diagnosis of tuberculosis for both infants was made within a 24-h period: for patient 1, by final autopsy results that were reported 14 April, and, for patient 2, by results of nucleic acid amplification assay of BAL fluid samples on 13 April. A multidisciplinary outbreak investigation team was urgently assembled to investigate and manage a suspected outbreak and prevent further transmission.

The mother of patient 1 had emigrated from Southeast Asia 20 years earlier, after living in refugee camps for 2 years. Although asymptomatic during her child’s hospitalization in the neonatal ICU, the mother developed a cough and sterile pyuria several weeks later. A tuberculin skin test (TST) and chest radiography were performed, and she was referred for further investigation. Three adult siblings of patient 1 were also evaluated by TST, but the father was estranged and not assessed. The parents of patient 2 were asymptomatic for tuberculosis. They were evaluated by TST and chest radiography in April 2002 and again 3 months later.

Health care workers, family members, and visitors of neonatal ICU infants were evaluated as possible sources of transmission and as contacts of the infected neonates. Those who had spent at least 8 cumulative hours in the neonatal ICU were assessed by TST and chest radiography in April 2002 to complete 12 months of therapy.

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Figure 1. Micrograph of a Zeehl-Neelson stain of acid-fast bacilli in a lung specimen obtained at the autopsy of patient 1 during hospitalization of patient 1 were assessed by either the Occupational Health Department of the Hospital for Sick Children or their local public health units [21]. Hospital engineers reviewed the neonatal ICU’s ventilation system. Reprocessing procedures for all equipment that was possibly used while caring for the 2 infants were reviewed.

The first priority of this investigation was to identify other potentially infected newborns. Because the 2 patients had been located in different rooms in the ICU, all infants who had been in the neonatal ICU during their hospitalizations required evaluation (n = 132). Ten of these infants were deceased, and these deaths were reviewed. Of the remaining 122 infants, 15 were hospitalized or living in other provinces, and 107 were at home. Special assessment clinics were convened at the Hospital for Sick Children. Families unable to attend were sent letters for their physicians that outlined testing and treatment recommendations and requested results to be forwarded to the Hospital for Sick Children. Others were referred to their local health unit for follow-up examination.

Most infants (79 of 107) were evaluated at the Hospital for Sick Children with physical examination, TST, liver function testing, and chest radiography, and medical histories were obtained. Infants were treated with isoniazid at a dosage of 15 mg/kg per day and pyridoxine at a dosage of 2 mg per day. One infant could not tolerate isoniazid and was given rifampin at a dosage of 10 mg/kg per day. Infants with abnormalities on chest radiographs were admitted for performance of 3 rounds of gastric aspiration and thoracic CT scanning. Infants were evaluated 1 month later (i.e., ~3 months after exposure) and again at 3 months after their expected date of delivery (i.e., at a corrected age of 3 months). Treatment was continued until the final evaluation and stopped if TST results were negative for M. tuberculosis at that time.

All microbiological testing was done at the Ontario Provincial Health Laboratory, according to standard procedures [22]. M. tuberculosis was identified by the Accuprobe test (Gen-Probe; California). Amplification detection of rRNA from M. tuberculosis was performed directly on specimens using a nucleic acid amplification assay. Restriction fragment–length polymorphism (RFLP) typing analysis was performed using the international reference method [23]. Spoligotyping analysis was based on the detection and analysis of the spacer elements in the M. tuberculosis genome’s direct repeat region [24].

Results. The mother of patient 1 had positive TST results (induration 16 mm in diameter). Sputum and uterine biopsy specimens were positive for M. tuberculosis by nucleic acid amplification assay and culture. The isolates of M. tuberculosis from patient 1, his mother, and patient 2 were very closely related.
by RFLP (91% genotypic identity by dendrogram analysis) and identical by spoligotyping (figure 2), confirming nosocomial transmission. All 3 siblings had negative TST results.

The parents of patient 2 had negative baseline TST results for *M. tuberculosis* and normal chest radiograph findings; however, both had positive TST results 3 months later (indurations of 16 and 22 mm). Treatment with isoniazid was initiated.

Nine of the 328 health care workers identified as contacts of patient 1 had worked in the infant’s room. Two (0.6%) of the health care workers were noncompliant with follow-up examination. Three (0.9%) had newly positive TST results (2 nurses who provided direct care for patient 1 and a unit clerk) and normal chest radiograph findings. They were referred for treatment for latent tuberculosis infection. No family members or visitors were found to have active tuberculosis.

The 2 patients were located in nonadjacent multi-bed rooms along the same corridor in the neonatal ICU. The ventilation system has a dedicated supply and exhaust with 6–9 air exchanges per hour. The filtration system is 95% effective in removing particles that are at least 1 micron in size. No shutdowns occurred on the days 19–26 January. The engineering review indicated that the transmission of *M. tuberculosis* particles by back-flow of the air exhaust was very unlikely.

Chart review revealed that both infants were in incubators, intubated, and ventilated. Patient 1 required frequent ventilatory manipulations toward the end of life. Reprocessing of respiratory equipment was done manually in the neonatal ICU by patient service aides. Instructions for cleaning and disinfection were scant, and used equipment was not consistently segregated, leading to the possibility of reusing a contaminated device. Therefore, inadequate disinfection of respiratory equipment was likely responsible for *M. tuberculosis* transmission from patient 1 to patient 2. No other infant had evidence of latent or active tuberculosis, and no neonatal ICU death was attributed to tuberculosis.

**Discussion.** Inadequately disinfected respiratory equipment was likely responsible for nosocomial transmission of tuberculosis from a congenitally infected infant to another infant in our neonatal ICU. This conclusion is supported by the presence of a normally functioning ventilation system, absence of other infected neonates, and absence of adults (apart from the mother of patient 1) with active infection. Inadequately

![Figure 2](https://example.com/figure2.png)

**Figure 2.** Restriction fragment-length polymorphism analysis (RFLP) (A) and spoligotyping analysis of isolates from patient 1, his mother, and patient 2, and reference (control) strains. BCG, bacille Calmette-Guerin; *M. bovis*, *Mycobacterium bovis*; *M. tuberculosis*, *Mycobacterium tuberculosis*. 
reprocessed bronchoscopy and anesthesia equipment has been described as sources of tuberculosis transmission, as has the reuse of improperly disinfected feeding tubes [25–29].

Medical equipment that has been in contact with mucous membranes requires thorough cleaning followed by high-level disinfection [30–31]. In the cases we describe, a review of the disinfection procedures revealed a number of deficiencies, identifying several pieces of equipment which might have been shared between the infants. Modifications to reprocessing procedures resulting from this investigation included centralization of the hospital’s reprocessing system, checks to ensure there were protocols for reprocessing all reusable equipment, and development of tracking systems for clinical equipment.

There is no standard approach for dealing with hospitalized infants who are potentially exposed to an infant with congenital tuberculosis [8–10, 19–20, 32–34]. We based our approach on a consensus opinion held by several experts on pediatric infectious diseases and tuberculosis, treating all potentially exposed infants until they had negative TST results at a corrected age of 3 months and had no signs, symptoms, or chest-radiograph evidence of tuberculosis. Although the age at which a TST becomes an accurate screen for tuberculosis infection in infants is unknown, we chose to stop prophylaxis at a corrected age of 3 months (minimum 3 months after exposure), which is consistent with current recommendations [35].

Transmission of tuberculosis from infants to health care workers has been reported and is likely related to aerosolization of bacilli during respiratory manipulations [8–10, 19–20, 36–37]. Patient 1 required frequent manipulations and high frequency–oscillation ventilation, a recognized risk factor [10]. Current recommendations state that most children with tuberculosis disease are not contagious and require only standard isolation precautions [35]. Airborne precautions are recommended for children with cavitary pulmonary tuberculosis, sputum smears positive for acid-fast bacilli, laryngeal involvement, or extensive pulmonary infection. Infants suspected of having congenital tuberculosis have recently been added to this list.

This case of indirect infant-to-infant transmission of tuberculosis underscores the need for appropriate infection control precautions if the diagnosis of congenital tuberculosis is suspected. Given the increasing number of immigrants to North America from countries where tuberculosis is endemic and imposes a high burden [38], a high index of suspicion for congenital tuberculosis must be maintained for ill neonates born to women at risk for tuberculosis.

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