Disseminated Mycobacterial Infection After International Medical Tourism

Brian A. Kendall,[1,2] Adam P. Barker,[2] Jason C. Hadley,[4] Scott R. Florell,[3] and Kevin L. Winthrop[5,6]

Departments of [1]Medicine, [2]Pathology, [3]Dermatology, University of Utah, Salt Lake City, and [4]Department of Dermatology, Intermountain Healthcare, Ogden, Utah; Departments of [5]Medicine; and [6]Public Health and Preventative Medicine, Oregon Health and Sciences University, Portland

International travel for the purpose of receiving medical care is increasing. We report a case of disseminated mycobacterial infection after fetal stem cell infusion.

Keywords. atypical mycobacteria; medical tourism; nontuberculous mycobacteria.

A 45-year-old woman traveled from the United States to Thailand to undergo stem cell treatment for Charcot-Marie-Tooth disease. While in Thailand, she was transfused twice in consecutive weeks with fetal stem cells. Before each infusion, she received 3 doses of intravenous dexamethasone and 2 doses of chlorpheniramine, dosages unknown. After the infusions, she felt generally ill with fever, malaise, and fatigue for the following 2 weeks before improving and returning to the United States. Within days of her return, she began to note purple-brown nodules on her legs with new lesions erupting every few weeks. These lesions were associated with occasional low-grade fevers and mildly painful cervical lymph nodes. Multiple doxycycline courses had no effect.

Five months after her stem cell infusion, she was referred to dermatology. Histopathology of a punch biopsy revealed mixed lobular and septal panniculitis, and culture grew a rapidly growing mycobacteria identified by polymerase chain reaction as *Mycobacterium abscessus/chelonae* complex. She was referred to our international travel clinic. On exam, she had approximately 10 purple-brown, firm, round, smooth subcutaneous and cutaneous nodules scattered around her lower extremities and distal upper extremities. Laboratory evaluation revealed mildly elevated calcium (10.8 mg/dL [normal range, 8.4–10.5] and aspartate aminotransferase 41 U/L [range, 16–40]). Human immunodeficiency virus enzyme-linked immunosorbent assay was negative as was an interferon-gamma release assay (QuantiFERON-TB Gold In-Tube; Cellestis Inc., Carnegie, Australia) for tuberculosis. To further identify the isolate, we sequenced *16s*, *rpoB*, and *erm* [1–3]. Gene sequences were most consistent with *M abscessus* subspecies *abcessus* but with a single nucleotide polymorphism in *erm* associated with subspecies *bolletii* and conferring macrolide susceptibility. Antibiotic susceptibility was determined by broth microdilution [1]. The isolate was sensitive only to clarithromycin (minimum inhibitory concentration [MIC] = 1 μg/mL) and amikacin (MIC = 16 μg/mL), intermediately susceptible to cefoxitin (MIC = 64 μg/mL), imipenem (MIC = 8 μg/mL), and linezolid (MIC = 16 μg/mL), and resistant to fluoroquinolones (ciprofloxacin MIC ≥ 8 μg/mL, moxifloxacin MIC ≥ 16 μg/mL), tetracyclines (minocycline MIC > 16 μg/mL, doxycycline MIC > 32 μg/mL), and trimethoprim/sulfamethoxazole (MIC ≥ 16/304 μg/mL). Acid-fast bacilli (AFB) blood cultures were negative. Computed tomography scans of the chest, abdomen, and pelvis did not reveal additional sites of disease. She began treatment with azithromycin, amikacin, and imipenem but required multiple changes in therapy due to intolerances including ototoxicity and intractable nausea. At the time of manuscript preparation, she had ceased to develop new lesions and multidrug therapy continued.

With the rise of medical tourism, healthcare-associated infections in returning travelers will become more common [4]. Although reports of such infections have focused on drug-resistant, gram-negative organisms, nontuberculous mycobacterium are also of concern given their environmental ubiquity, intrinsic antibiotic resistance, and increasing incidence [5, 6]. We report a case of disseminated disease after infusion of fetal stem cells.

Disseminated infections due to mycobacteria are extremely rare in immunocompetent patients, thus we suspect a high-inoculum exposure during our patient's stem cell infusions. There were no other medical procedures temporally associated with her infection. The immunosuppressive properties of her preinfusion corticosteroids likely helped the infection become established. She did not receive additional immunosuppression after the infusions, possibly allowing for incomplete immune

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Correspondence: Brian Kendall, MD, Division of Infectious Diseases, University of Utah School of Medicine, 30 N 1900 E, Suite 4B319, Salt Lake City, UT 84108 (brian.kendall@hsc.utah.edu).

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control of infection, intermittent mycobacteremia, and thus a negative AFB blood culture. Although this is the first case related to allogeneic stem cell infusion that we are aware of, Liu et al [7] described 4 cases of severe infection, including death, in patients who received autologous natural killer cell infusions for cosmetic purposes and "health boosting" in Hong Kong. In addition, cases of soft-tissue disease related to medical tourism for cosmetic surgery have been identified [8, 9].

International stem cell therapy clinics offer therapies for numerous indications despite limited scientific basis [10]. Fetal neural stem cell infusion for treatment of neurodegenerative conditions has biological plausibility due to the active neurogenesis of the fetal brain [11]. However, clinical data to support the practice does not yet exist.

Although there is not yet evidence of benefit, the risks of such procedures are apparent. Treatment involves infusion of potentially contaminated biological materials, whereas safety practices and oversight are often unclear. The actual stem cells being infused may be the patient's own or of embryonic or fetal origin, and protocols for the handling of materials are not standardized. The quality of facilities varies, and adequate infection control practices cannot be assumed. In the case of our patient, information regarding source screening for infection was not provided. Clinicians should be aware of the risk of infections related to this emerging practice.

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