Miliary Pulmonary Infection Caused by Mycobacterium terrae in an Autologous Bone Marrow Transplant Patient

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A 64-year-old woman with ovarian carcinoma that had been treated with high-dose chemotherapy and autologous bone marrow transplantation presented with a maculopapular rash on the extremities and miliary infiltrates evident on chest roentgenogram. Transbronchial biopsy specimens revealed caseating granulomas, and cultures grew Mycobacterium terrae. Six weeks after therapy with isoniazid, rifampin, and pyrazinamide was begun, her rash and pulmonary infiltrates had cleared, despite the in vitro resistance to these drugs and continued spread of her carcinoma. This case suggests that spontaneous resolution may be part of the natural history of M terrae infections.

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Mycobacterium terrae complex, first described by Richmond and Cummings in 1950, is usually considered to be a nonpathogenic saprophyte. The complex, which consists of three closely related species, M terrae, M nonchromogenicum, and M triviale, has produced only 14 documented infections in humans. We describe a case of disseminated M terrae infection that occurred after high-dose chemotherapy and autologous bone marrow transplantation in a woman with metastatic ovarian carcinoma. The patient presented with a maculopapular rash and miliary infiltrates evident on chest roentgenogram. Both resolved despite in vitro resistance to her antituberculosis therapy and progression of her malignancy.

CASE REPORT

In September 1988, a 64-year-old white woman, during a routine follow-up visit for ovarian carcinoma, complained of a two-week history of a maculopapular rash on her extremities. A chest roentgenogram taken at that time showed miliary infiltrates (Fig 1). Her only symptoms were occasional night sweats for one month and mild dyspnea. She was a housewife with no known exposure to tuberculosis and recalled having a negative PPD test in the past. She was a nonsmoker, never drank alcohol, and had no history of recent foreign travel. She was taking only tamoxifen and had not received any other chemotherapy in four months. Metastatic ovarian carcinoma had been diagnosed seven months earlier, for which she received two courses of chemotherapy. These were followed by an additional two courses of high-dose chemotherapy, with an autologous bone marrow transplantation after each course. These therapies produced a brief remission, but her carcinoma soon recurred and hormonal therapy was begun. On physical examination, she was afebrile and did not appear chronically ill. There were four or five erythematous lesions of 1 cm or less scattered on her wrists and legs. Results from the remainder of her examination were unremarkable.

Laboratory evaluation revealed a normal white blood cell count and differential count. Results of liver function studies were normal. Findings of two sputum examinations were negative for acid-fast bacilli, fungi, and malignant cells. Results of deep fungal serologic studies were also negative. A skin test battery, which included tuberculin, showed results consistent with anergy. Transbronchial biopsy specimens, taken in early October 1988, revealed numerous caseating granulomas, but auramine-O stains for acid-fast bacilli were negative. A skin biopsy specimen revealed noncaseating granulomas, but no acid-fast bacilli were identified. A bone marrow biopsy specimen showed no granulomas or evidence of malignancy.

Two weeks after the transbronchial biopsies were performed, she had more than 100 papulonodular skin lesions, mostly confined to her extremities (Fig 2). A repeat chest roentgenogram demonstrated increasing infiltrates. Therapy was begun with rifampin (600 mg), isoniazid (300 mg), and pyrazinamide (2 g) daily for presumed tuberculosis. Four weeks after her bronchoscopy, mycobacterial cultures from the transbronchial biopsy specimens were noted to be positive, but the skin biopsy specimens showed no growth. Six weeks after starting antituberculosis therapy, the patient felt well.

FIGURE 1. Close-up view of the chest roentgenogram showing the miliary infiltrates.
and the skin lesions and pulmonary infiltrates had cleared.

In February 1989, 12 months after the original ovarian carcinoma diagnosis was made, the tumor was noted to have spread further, and therapy with alpha-interferon and interleukin 2 was begun. Antituberculosis therapy was interrupted during immunotherapy. Based on initial in vitro resistance to isoniazid, rifampin, and streptomycin, her antituberculosis therapy, when restarted, was changed to ethambutol (1,400 mg), streptomycin (1 g), and pyrazinamide (2 g) daily.

Her ovarian carcinoma progressed, and the patient and her attending physician opted to continue only supportive care. Her antituberculosis therapy was discontinued after she had completed seven months of therapy. Her last chest roentgenogram, obtained nine months after the diagnosis of tuberculosis was made and one month before her death, remained clear. The patient died in August 1990 from widespread carcinomatosis with no evidence of tuberculosis, but no autopsy was performed to rule out occult tuberculosis infection.

Using high-pressure liquid chromatography, the Centers for Disease Control identified the organism as M. terrae complex, which was resistant in their laboratory to isoniazid, rifampin, pyrazinamide, capreomycin, streptomycin, ciprofloxacin, kanamycin, and cycloserine.

**DISCUSSION**

The response to therapy for atypical tuberculous infections is usually difficult to predict and commonly requires multiple antituberculosis drugs. Our patient had an excellent clinical response to antituberculosis therapy despite her continued immunosuppression from chemotherapy and the in vitro resistance pattern of M. terrae. Of the 14 published cases of M. terrae infections, seven were pulmonary infections and the other seven cases involved joint or synovial spaces. Although pulmonary infections often involve preexisting tuberculous cavities, primary infections occur as well. However, a disseminated M. terrae infection, as seen in this case, is distinctly uncommon. Only one similar case of M. terrae infection has been reported and it resolved without any antituberculosis therapy. While some joint infections with M. terrae are difficult to eradicate, this case and four of five other primary pulmonary cases resolved either spontaneously or with suboptimal therapy, suggesting that spontaneous resolution may be a part of the natural history of M. terrae infections. Although our patient did receive immunotherapy with alpha-interferon and interleukin 2, which could potentially have improved her T-cell function, this treatment was begun two months after her pulmonary infiltrates and skin lesions had cleared, making it unlikely that these agents influenced her recovery. However, we cannot rule out that the improvement occurred because of in vitro susceptibility of the organism to the antituberculosis therapy.

With the epidemic of acquired immunodeficiency syndrome and the routine use of more intense chemotherapy and bone marrow transplantation, it may be important to consider previously nonpathogenic organisms as potential etiologies of pulmonary infections. Since our patient had no known prior risk factors for tuberculosis, the repeated courses of very intense chemotherapy and autologous bone marrow transplantation must have predisposed her to this infection.

**REFERENCES**


Figure 2. Papulonodular rash on the patient's leg prior to starting antituberculosis therapy.

1450

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