1249

A Tuberculosis Outbreak in a Renal Transplant Program

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OF THE opportunistic infections reported in renal transplant patients, tuberculosis has been infrequently encountered, although its incidence is higher in this group than in the general population.[1–3] In our own program, sporadic cases have occurred at the rate of one or two per year. Beginning in October 1990, however, an epidemic of seven cases of tuberculosis was seen with one additional sporadic case. We studied its etiology and epidemiology, and implemented a program of isoniazid prophylaxis to stop the outbreak.

THE CASES

A summary of the cases is given in Table 1. The index case (patient 1) in this series was infected while visiting his mother in an outlying hospital, where another patient with tuberculosis was hospitalized. The diagnosis in this other patient was not established until autopsy; 19 of 29 nurses caring for this patient became PPD positive. The index case was admitted at the end of September 1990 to our hospital, with chest pain and a normal chest x-ray. It was 2 weeks before radiographic abnormalities developed, and a diagnosis was made on bronchoalveolar lavage. As is the usual protocol, this case was reported to the hospital Infection Control Committee and the County Health Department.

The next 4 cases all presented in December 1990, in rapid succession. One patient was diagnosed and treated in an outlying hospital; the others were treated in our hospital. They presented with fevers, night sweats, and pulmonary infiltrates, and were diagnosed either by sputum stains for acid-fast organisms or by bronchoalveoalar lavage. The two additional cases were diagnosed in January and March of 1991.

In January 1991, all renal transplant patients who might have been exposed were started on prophylactic isoniazid (INH) 300 mg/d, and pyridoxine 50 mg/d. Thereafter, the only new case that developed, ie, the one in March 1991, was in a patient who had been noncompliant with her INH prophylaxis.

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Table 1. Cases of Tuberculosis in Renal Transplant Recipients

Patient No.	Age/ Sex/Race	TB Time After Tx (Months)	CXR	Presenting Symptoms	Pos. Culture Sites	Other Infections	Rejection Treatments Prior to TB	Outcome
1	33/M/C	5	RUL	Chest pain	BAL, BM	Staph epid. bacteremia	1 g SM	Recovered with preserved renal function
2	41/M/B	1.5	LUL	Fever	BAL	CMV pneumonia	0	Recovered with graft loss due to rejection
3	36/F/C	6.5	RUL	Fever	BAL	—	0	Recovered with preserved renal function
4	20/F/C	1.5	RML	Fever, cough	BAL	CMV pneumonia	3 g SM, 50 mg OKT3	Died from infection
5	65/F/C	5	Lin LLL	Dehydration, lethargia	BAL	CMV pneumonia	1.5 g SM	Died from infection
6	59/F/C	4.5	RUL	Fever	BAL	Klebsiella pyelonephritis, CMV pneumonia	1 g SM	Died from infection
7	43/F/C	9	Interstitial infiltrate	Fever	BAL	CMV pnuemonia	4 g SM	Graft loss due to rejection prior to tb diagnosis. Recovered from infection, Died from seizures on dialysis
8	28/F/C	6.5	LUL	Tonsillitis	Tonsil, cervical lymph node, sputum	—	1 g SM	Recovered with preserved renal function

Abbreviations: M: male, F: female, B: black, C: caucasian, TB: tuberculosis, RUL: right upper lobe infiltrate, LUL: left upper lobe infiltrate. LLL: left lower lobe infiltrate, Lin: lingula infiltrate, BAL: bronchoalveolar lavage, BM: bone marrow, SM: solumedrol.

Upon further investigation, we discovered that all seven patients had been on the same hallway of the same floor at some time in October 1990, before the diagnosis was established in the index case. DNA analysis of the organism[4] revealed that all cases had the same strain of *Mycobacterium tuberculosis*, which was sensitive to all antituberculous agents. Ventilatory studies of the floor revealed a relatively stagnant airflow, with two rooms actually having a positive pressure airflow from the room to the hallway. The sporadic case presented with a tonsillar abscess and scrofula; she was diagnosed by a lymph node aspiration and examination of the tonsillectomy specimen. She had been away from Pittsburgh throughout this time, and was thought not to be part of the epidemic.

After the diagnosis of tuberculosis was made, antituberculous therapy with three to five agents was started. The immunosuppression was either stopped or markedly reduced.

Three patients died as a result of infection, all of whom also had infection with organisms other than *M. tuberculosis*. Another patient, who had lost her allograft to rejection prior to the diagnosis of tuberculosis, died from a dialysis complication. One patient survived with the loss of the allograft to rejection, whereas three patients, including the index case, survived with a functioning allograft.

All eight patients had received FK 506 for immunosuppression after renal transplantation. Of the 42 renal transplant patients who were at highest risk, ie, who had been on the same floor with the index case in October 1990, only one had been on cyclosporine (CyA) instead of FK 506.

DISCUSSION

Over 140 cases of tuberculosis in renal transplant recipients have been reported. Most published series are small, and the reported success of treatment is variable, with the reported mortality rate ranging from 0% to 100%.[1-7] However, a recent review of all the cases in the literature, found that the mortality from tuberculosis infection was 20%; another 10% of these cases died from other complications.[1] These represent the first cases of mycobacterial infections in patients treated with FK 506. The mortality from tuberculosis in this series, 37.5%, appears to be comparable to the experience in the literature with conventional immunosuppression.

Simultaneous infections with cytomegalovirus and/or various bacterial pathogens occurred in six of our eight cases; these simultaneous opportunistic infections probably contributed to the morbidity and mortality in this material. The combination of cytomegalovirus and tuberculosis was especially lethal—four of the five patients requiring antituberculous therapy and gancyclovir ultimately died.

Ordinarily, nosocomial transmission of opportunistic infections in immunosuppressed patients is uncommon, and this epidemic was unprecedented in our experience. We think that it is unlikely that the mere fact of FK 506 immunosuppression played a role here. Our speculation is that the unusual infectivity of this organism (as seen in the high conversion rate among the nurses in the outlying hospital) combined with the ventilatory airflow pattern on the floor to cause this outbreak. At present, all transplant patients admitted to the hospital with a question of a pulmonary problem are placed on respiratory isolation until three sputa are found to be AFB negative.

Prophylaxis with isoniazid has been shown to prevent the reactivation of tuberculosis in immunosuppressed patients,[1] and it has been used previously in our PPD-positive recipients. In this situation, widespread use of prophylactic isoniazid was effective in terminating the epidemic. Hepatotoxicity was monitored with routine liver function screening, and no cases of serious hepatotoxicity developed.

This report serves to underscore the seriousness of tuberculosis in renal transplant patients, during a time when the overall incidence of tuberculosis is increasing,[8] as well as the need to diagnose, isolate, and treat this disease as soon as it is suspected. In addition, widespread prophylaxis with isoniazid may be necessary to prevent nosocomial spread.

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