

Tuberculosis in Patients with End-Stage Renal Disease¹

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Purpose: The purpose of our study was to describe the clinical and radiological manifestations of tuberculosis in patients with end-stage renal disease.

Materials and Methods: The medical records, chest radiographs, and CT scans of 42 patients with tuberculosis among 871 consecutive patients with end-stage renal disease were reviewed. Patterns of initial chest radiographs were categorized as primary, postprimary, miliary, or atypical, according to the predominant radiologic findings.

Results: Chest radiographs and CT scans revealed pulmonary tuberculosis in 28 patients and extrapulmonary tuberculosis in 15. The pattern of chest radiographs indicative of pulmonary tuberculosis was primary in 12 cases, postprimary in 11, miliary in one, demonstrated atypical infiltrates in three, and was normal in one. Tuberculosis involved the extrathoracic lymph nodes in six cases, the peritoneum in four, the spine in three, and the bone marrow in two. The primary pattern, seen in 12 patients, manifested as pleural effusion or segmental consolidation, and in ten of the twelve the former was dominant.

Conclusion: The radiological pattern of pulmonary tuberculosis in end-stage renal disease is often primary, and extrapulmonary involvement is frequent.

Index words : Tuberculosis
Kidney, failure
Radiograph
Computed Tomography (CT)

The worldwide incidence of pulmonary tuberculosis has been increasing in recent years, a fact which is largely attributable to human immunodeficiency virus (HIV) infection (1, 2). It has been suggested that pulmonary tuberculosis in immunocompromised patients often has

an atypical pattern and distribution, and this has been well documented particularly in patients with acquired immunodeficiency syndrome (AIDS) (1, 2).

End-stage renal disease (ESRD) is synonymous with the late stages of chronic renal failure, eventually requiring maintenance dialysis or kidney transplantation (3). Patients with ESRD belong to the moderately immunocompromised sector of the population and are thus susceptible to tuberculous infections (4 - 6). The purpose of our study was to describe the clinical and radiological manifestations of tuberculosis in patients with ESRD.

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Materials and Methods

Retrospective analysis of the medical records at our institution relating to the period January 1995 to December 1999 revealed 871 cases in which maintenance dialysis had been required. Patients who had received kidney transplantation or had renal tuberculosis were excluded from the analysis. In 42 (4.8%) of the 871 patients [26 men and 16 women, aged 21 - 74 (mean, 53.2) years] active tuberculosis was diagnosed. The medical records of all patients were reviewed to identify those for whom the cause of renal failure, as well as clinical signs and symptoms, was stated. All patients were HIV-seronegative, as indicated by the negative results of enzyme-linked immunosorbent assay tests.

In 33 patients, the diagnosis of tuberculosis was confirmed bacteriologically and/or histopathologically (Table 1). Clinical and radiological diagnosis (n=9) was based on relevant radiographic findings, which showed radiological and clinical improvement with antituberculous chemotherapy. In all patients, culture demonstrated that no other organisms existed concurrently with tuberculosis.

Patients fulfilling at least one of the following criteria were considered to have extrapulmonary infection: (1) biopsy specimen revealing caseating granuloma with acid-fast bacilli (n=12); (2) decreased size of lesion(s) at an extrapulmonary site following antituberculous chemotherapy (n=3).

In 12 patients chest CT images were obtained with continuous 7 to 10-mm collimation and intravenous injection of contrast material, and in two, thin-section CT images (with 1-mm collimation at 10-mm intervals and a high spatial frequency reconstruction algorithm, but without injection of contrast material) were obtained. One patient underwent both thick- and thin-section chest CT scanning. Abdominal CT scans and neck CT scans were obtained in two and three patients, respectively.

Chest radiographs and CT scans were retrospectively reviewed by two experienced observers; conclusions were reached by consensus, with radiographs always interpreted before scans. Both sets of images were used to determine the presence and location of lymphadenopathy, consolidation, nodules, cavitation, and pleural effusion.

Initial chest radiographs were categorized on the basis of the predominance of findings (2, 7). Hilar or mediasti-

nal lymphadenopathy, pleural effusion, air-space consolidation without cavitation, or any combination of the above were considered typical findings of the primary pattern of tuberculosis. Our operational definition of features that suggested a postprimary infection was focal consolidation and/or cavitary lesions in the apical and posterior segments of the upper lobe and superior segment of the lower lobe with occasional evidence of endobronchial spread to other segments of the lungs. Bilateral, symmetric and diffuse micronodules of 1 to 3 mm were considered typical of the miliary pattern of pulmonary tuberculosis. Radiographic findings that were abnormal but did not fit either of the above categories were arbitrarily classified as atypical.

Results

Twenty-seven of the 42 patients had pulmonary tuberculosis only, 14 had extrapulmonary tuberculosis only, and in one there was both pulmonary and extrapulmonary involvement (Fig. 1) (Table 2). The clinical findings are summarized in Table 3. Seven patients had a history of previous pulmonary tuberculosis and one had previously suffered tuberculous spondylitis. In 26 patients tuberculosis was diagnosed 1 to 108 months after the initiation of maintenance dialysis, and in the remaining 16, diagnosis was 1 to 24 months before the initiation of dialysis. Pleural tapping was performed in eight patients, and in all cases laboratory testing demonstrated that the exudate contained mainly lymphocytes.

The radiographic characteristics of the 28 patients with pulmonary involvement are summarized in Table

Table 1. Basis for Diagnosis of Tuberculosis in Patients with End-Stage Renal Disease

Method		Number of patients
Bacteriology		
Culture positive	Sputum	6
	Bronchial washing	1
	Spine	1
AFB positive	Sputum	10
	Pleural effusion	2
	Ascites	2
Histology		
	Lymph node biopsy	6
	Spine surgery	3
	Pleural biopsy	2
	Bone marrow biopsy	2
	Peritoneum biopsy	1
Therapeutic trial		
	Response to antituberculous drugs	9

AFB: acid-fast bacilli

4. In twelve of these (43%), a primary pattern of pulmonary tuberculosis was observed (Fig. 2), and within this subgroup, ten patients demonstrated pleural effusion (bilateral 5, right-sided 3, left-sided 2), five had middle or lower lung zone consolidation, and one manifested intrathoracic lymphadenopathy. Five of the 28 had a cavitary lung lesion.

Chest CT scanning was performed in 13 patients whose chest radiographs showed a primary (n = 9), post-primary (n = 1), or atypical (n = 3) pattern (Fig. 3). The results demonstrated mediastinal lymphadenopathy in

Table 2. Involved Sites of Tuberculosis in 42 Patients with End-Stage Renal Disease

	Number of patients (n = 42)
Pulmonary tuberculosis	28 (67)
Extrapulmonary tuberculosis	15 (36)
Extrathoracic lymphadenopathy	6 (14)
Cervical lymphadenopathy	4
Axillary lymphadenopathy	1
Abdominal lymphadenopathy	1
Peritoneum	4 (10)
Spine	3 (7)
Bone marrow	2 (5)

Note. one patient had both pulmonary and extrapulmonary involvement. Numbers in parentheses are percentages.



Fig. 1. 55-year-old woman with who presented with malaise. CT scan shows portocaval and retroperitoneal lymphadenopathy with central low-density areas and an enhancing wall (arrows). CT guided biopsy revealed granulomatous inflammation with caseation necrosis. She underwent hemodialysis one month after the initiation of antituberculous medication.

Table 3. Clinical Findings of Patients with End-Stage Renal Disease

	Number of patients	
Causes of ESRD	Diabetes Mellitus	22
	Glomerulonephritis	3
	Systemic lupus nephritis	2
	Recurrent urinary infection	1
	Unknown etiology	14
Symptoms and Signs	Dyspnea	11
	Cough	9
	Fever	8
	Abdominal pain	6
	Malaise	5
	Chest pain	4
	Low back pain	3
	Palpable mass	3
Clinical outcome	Cure	30
	Aggravation	3
	Expire because of other causes	3
	Follow-up loss	6

ESRD: end-stage renal disease

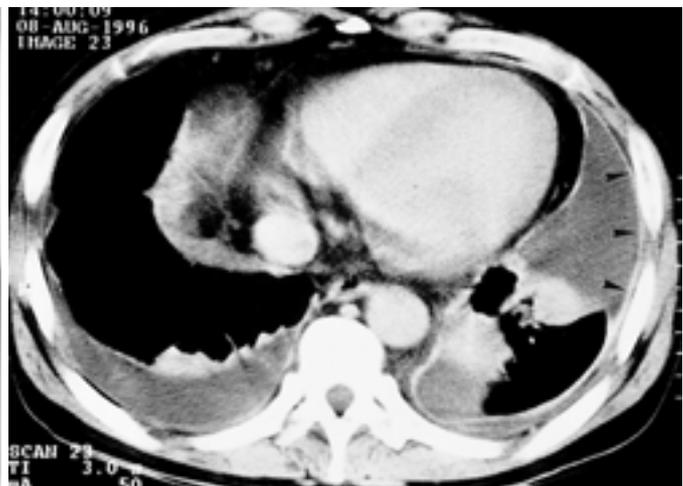
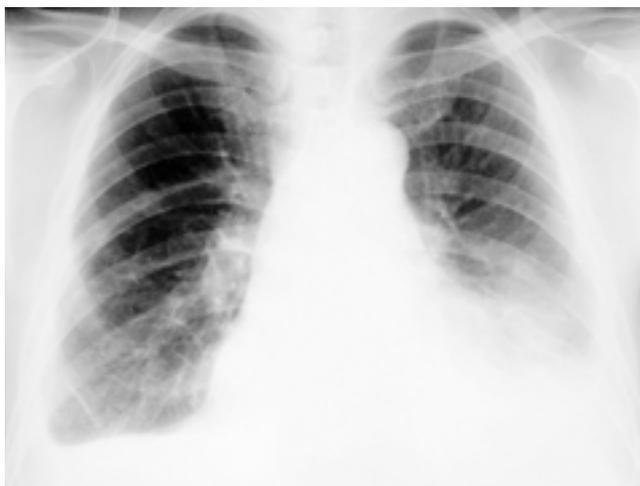


Fig. 2. 58-year-old man undergoing hemodialysis during 14 months who presented with dyspnea.
A. Chest radiograph shows bilateral pleural effusions, which was considered a primary pattern.
B. CT scan shows bilateral pleural effusions with thickening and enhancement of the parietal pleura (arrowheads).

three (23%) of these 13 patients. Enlargement of the mediastinal lymph nodes involved the right paratracheal region in one case and the subcarinal lymph nodes in two. Parenchymal consolidation was observed in six pa-

tients (46%), and nodular opacity with centrilobular distribution in seven (54%). Pleural effusion, identified in nine patients (69%), was left-sided in three cases and bilateral in six.

Table 4. Radiographic Characteristics of Pulmonary Tuberculosis in Patients with End-Stage Renal Disease

Radiographic Finding	Number of patients (n = 28)
Postprimary pattern	11 (39)
Primary pattern	12 (43)
Pleural effusion	10 (36)
Consolidation	5 (18)
Thoracic lymphadenopathy	1 (4)
Atypical opacification	3 (11)
Miliary pattern	1 (4)
Normal radiographs	1 (4)

Note. Numbers in parentheses are percentages.

Discussion

The major host defense against the tubercle bacillus is cell-mediated immunity, effected primarily through macrophages and T-lymphocytes (8). A wide range of immunological derangements in ESRD have been postulated as the cause of the increased susceptibility of dialysis patients to tuberculosis. Tuberculosis has been reported to be more common in the dialysis population than in the general population (5, 6), and in our series, the prevalence of tuberculosis associated with ESRD

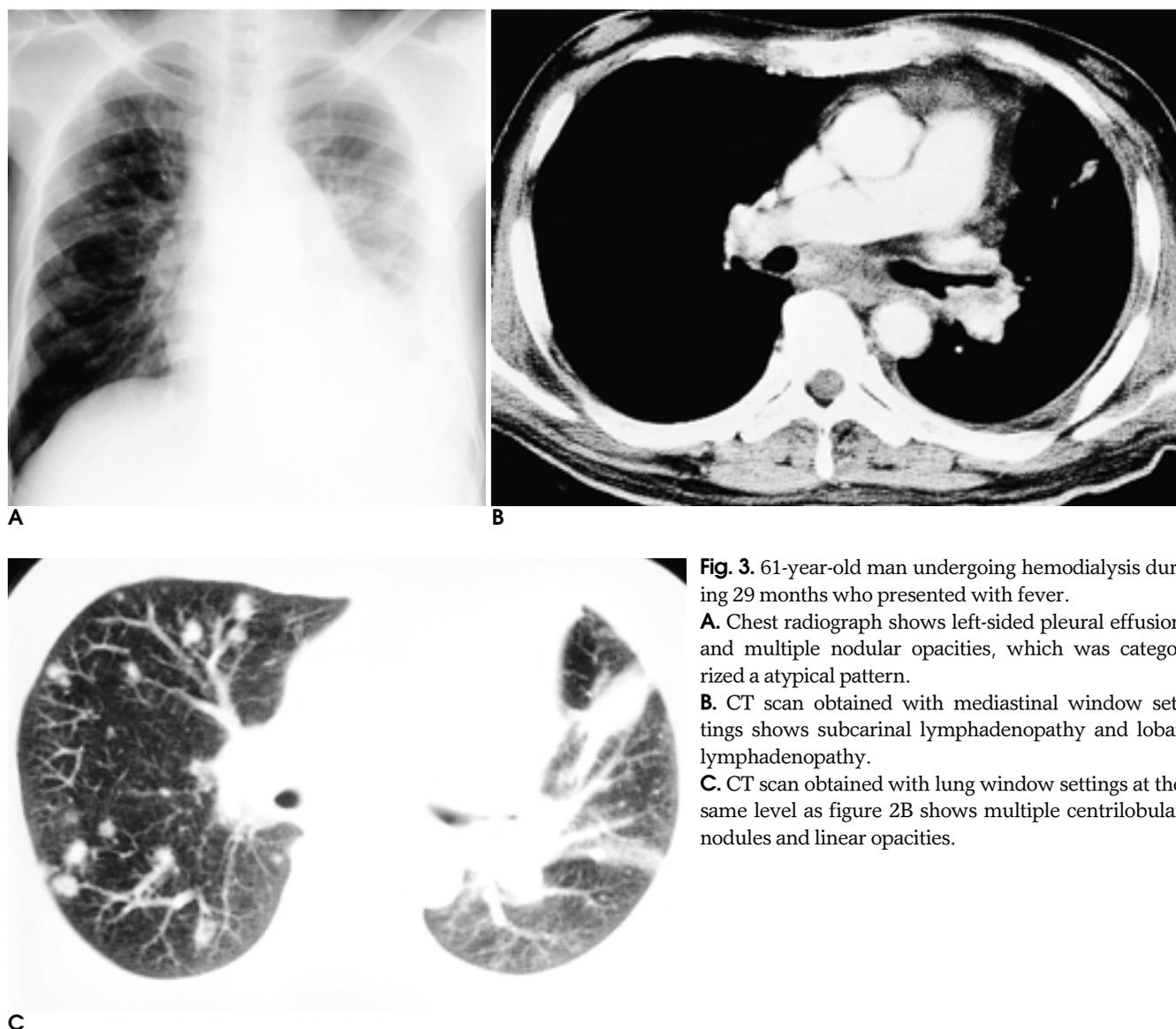


Fig. 3. 61-year-old man undergoing hemodialysis during 29 months who presented with fever.
A. Chest radiograph shows left-sided pleural effusion and multiple nodular opacities, which was categorized a atypical pattern.
B. CT scan obtained with mediastinal window settings shows subcarinal lymphadenopathy and lobar lymphadenopathy.
C. CT scan obtained with lung window settings at the same level as figure 2B shows multiple centrilobular nodules and linear opacities.

was 4.8%, about five times that of the general population of our country (9).

The inordinately high percentage of patients with AIDS whose radiographic findings are more typical of primary than of postprimary tuberculosis has been well documented (1, 2). In our series, tuberculosis with ESRD showed a pattern similar to that of AIDS. The primary pattern, manifesting as pleural effusion or segmental consolidation, was seen in twelve patients (43%), in ten of whom pleural effusion dominated. Pleural effusion in uremic patients may result from heart failure, uremic pleurisy, parapneumonic effusion, or atelectasis (10), but tuberculous pleural effusion can usually be distinguished from these other types by microscopic and chemical examination of pleural fluid prior to the result of pleural fluid acid-fast bacilli smear and culture. In some patients pleural biopsy may confirm the diagnosis, as in two of our cases.

It has been reported that cavities had formed in 46% of patients with pulmonary tuberculosis who were diabetic or otherwise immunocompromised [diabetes (n=31), malignancy (n=6), or steroid therapy (n=2)], and about half of them had multiple cavities (11). In our series, five patients showed evidence of cavitory lung lesions, a proportion similar to that observed in relation to the rare phenomenon of cavity formation in patients with AIDS (1, 2) and in contrast to the high prevalence of cavitation seen in patients with intact immunity (12).

Prior to the epidemic of HIV infection, approximately 13% of newly reported cases of tuberculosis involved extrapulmonary sites (13). In HIV-infected patients, however, both absolute and relative rates of extrapulmonary involvement have increased by up to two thirds (14), in our series, extrapulmonary tuberculosis accounted for 36% of all cases. Multiorgan involvement is probably a much more common than is usually recognized: once M. tuberculosis is identified in any specimen, other sites are generally not evaluated.

Since presenting symptoms may be non-specific and protean, the diagnosis of tuberculosis in patients with ESRD can be difficult (5, 6). In many patients tuberculosis is diagnosed at a time when symptoms such as dyspnea, malaise, and fever could be readily attributed to uremia, volume overload, pyogenic reaction to dialysate or the relatively common bacterial infections of vascular access sites that occur in patients undergoing dialysis. The failure of the radiologist to alert the physician to the possibility of pulmonary tuberculosis frequently leads to long delays in the institution of therapy. Unfortunately,

there are no radiologic findings, alone or in combination, that are pathognomonic of tuberculosis, and for correct diagnosis, especially in those patients at increased risk, it is important that a degree of suspicion is maintained.

Our study has several limitations. First, CD4+ T-lymphocyte counts were not checked in any patient. We made no objective measurements reflecting the immune status of patients with ESRD. Second, radiologic findings such as pleural effusion may result partly from heart failure, a common complication of ESRD, though the pleural fluid encountered was exudate consisting principally of lymphocytes. Third, only 13 patients, in nine of whom the radiographic pattern was primary, underwent chest CT scanning.

In conclusion, the results of the present study indicate that there is a high incidence of tuberculosis in patients with ESRD, and that the radiologic appearance of pulmonary tuberculosis in ESRD commonly shows a primary pattern, with frequent extrapulmonary involvement. Tuberculosis should be considered in the differential diagnosis of any patient with ESRD presenting with pleural effusion, any kind of pulmonary infiltrate not responding to common antibiotics, or extrapulmonary manifestations.

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