

ORIGINAL ARTICLE

Concurrent PCP and TB pneumonia in HIV infected patients

JOSE G. CASTRO¹, GABRIEL MANZI³, LUIS ESPINOZA¹, MICHAEL CAMPOS² & CATHERINE BOULANGER¹

From the ¹Division of Infectious Diseases, University of Miami Miller School of Medicine, ²Division of Pulmonary Medicine, University of Miami Miller School of Medicine, and ³Jackson Memorial Hospital, Florida, USA

Abstract

We aimed to assess the incidence and clinical characteristics of patients with HIV infection with concurrent *Pneumocystis pneumonia* (PCP) and tuberculosis (TB). We carried out a retrospective record review of HIV infected patients admitted with pulmonary TB and PCP during the same hospital admission at a large county hospital in Miami, from 1995 to 2004. 2651 patients with HIV infection and possible TB or PCP were identified. There were 99 cases of PCP (81 presumptive and 18 confirmed) and 35 were new cases of TB. There were 17 patients who had a new, concurrent diagnosis of pulmonary TB and PCP. Approximately half of these patients were unaware of their HIV infections and half of them had a negative AFB in sputum. Most were men and had a CD4 count less than 100 cells/mm³. Chest X-ray disclosed bilateral infiltrates in most of the cases. All but 2 survived the hospital admission. Thus, concurrent TB and PCP in HIV infected patients were not uncommon in this large county hospital in Miami, Florida in the studied period, but its diagnosis was challenging.

Introduction

Soon after the beginning of the HIV pandemic, *Pneumocystis jirovecii* (formerly known as *Pneumocystis carinii*) and *Mycobacterium tuberculosis* (TB) became 2 of the most common etiologic agents of opportunistic infections associated with the acquired immunodeficiency syndrome. Today, after more than 2 decades of research, education, and treatment of HIV and its complications, respiratory opportunistic infections caused by these organisms are still major causes of morbidity and mortality among those infected with HIV. Interestingly, the distribution of these respiratory opportunistic infections varies geographically. While TB is the most common organism causing respiratory infections in HIV-infected individuals worldwide [1–6], in industrialized countries *Pneumocystis jirovecii* pneumonia (PCP) is the most prevalent [7–9]. The reasons for these differences are unknown, and may be related to limitations in diagnostic techniques in developing countries.

In HIV infected patients with severe immunosuppression, it is well recognized that more than 1 infection can coexist [10–13]. Concurrent pulmonary TB and PCP has been well described in reports

from African countries [6,14–16], but few studies have been performed in Europe or the US [13]. The aim of this study was to evaluate the frequency and main clinical characteristics of the coinfection of PCP and MTB in HIV infected patients presenting with respiratory symptoms hospitalized in a large county hospital in the US.

Methods

We conducted a retrospective computerized search by ICD-9 code of all patients admitted with HIV infection, TB or PCP from 1 January 1995 to 31 December 2004 at Jackson Memorial Hospital in Miami, Florida. The records of all patients who had presumptively the 3 diagnoses during the same hospital admission were reviewed. HIV infection was confirmed by documentation of both a positive ELISA and Western blot. The diagnosis of pulmonary tuberculosis was confirmed if either a positive culture for TB or a positive smear with a positive polymerase chain reaction (TB-PCR) was present. The diagnosis of PCP was confirmed by a positive direct fluorescent antibody test (DFA) or positive

cytology in respiratory samples such as sputum, bronchoalveolar lavage (BAL), or pulmonary biopsy. A presumptive diagnosis of PCP by the treating team was accepted if all the following requirements were met: history of respiratory symptoms, abnormal chest X-ray, arterial blood test with hypoxemia and a clinical response to specific therapy (Bactrim® or second-line therapy). A standardized case report form was created to capture from the medical records all pertinent demographic, clinical and radiological data, as well as the patient's clinical course.

The University of Miami Institutional Review Board approved the study.

Statistical analysis of the data was performed with descriptive statistics.

Results

A total of 2651 admissions of HIV-positive patients with confirmed or presumptive diagnoses of pulmonary tuberculosis, PCP or both, were identified. Of these, 155 (5.8%) subjects had presumptively both infections during the same hospital admission as identified by the computerized ICD-9 code search.

PCP

Review of these 155 records disclosed 99 cases of PCP; 81 were presumptive and 18 were confirmed (14 diagnosed by DFA in bronchoalveolar lavage, 2 by DFA in tissue biopsy, and 2 by sputum cytology).

TB

TB infection was confirmed in 56 and excluded in 99 patients. The patients who had TB excluded were: 9 with *M. kansasii* infection, 9 with *Mycobacterium avium intracellulare* complex infection/colonization in sputum and 81 patients who were 'ruled out' with a negative acid fast bacilli smear in sputum and a negative culture. It is a common practice in this hospital to 'rule out' TB (with 3 negative smears in sputum) in HIV infected patients who are admitted with pneumonia. Of the 56 patients who had confirmed TB, 21 were excluded from the analysis because their diagnosis and treatment occurred before the index admission. The remaining 35 patients had a new diagnosis of TB and were included in the analysis; 34 were diagnosed by culture and 1 by TB-PCR.

Coinfection

There were 17 patients with concomitant diagnosis of PCP and pulmonary tuberculosis in the same

hospital admission during the study period. Additionally, there were 2 patients with *M. kansasii* infection and confirmed PCP and 3 patients with disseminated MAC infection and confirmed PCP. The clinical characteristics of the patients with PCP and TB are summarized in Table I. Most of the subjects were male (12/17) with an average age of 43 y and advanced HIV infection (average CD4+ cell count of 83 cells per mm³). Most of the subjects (65%) were newly diagnosed with HIV infection: 8 subjects (47%) who were diagnosed at the time of admission, and 3 additional subjects who were diagnosed less than 3 months before admission. The chief complaints on admission were dyspnea (70%), fever (47%) and cough (24%). Radiologic abnormalities were described as bilateral interstitial infiltrates in 15 of the 17 cases and lobar infiltrates in 2 other cases. There were no cases with isolated upper lobes infiltrates. PCP was confirmed in 4 cases by DFA (in bronchoalveolar lavage in 3 cases and sputum in 1 case). Pulmonary tuberculosis was confirmed by culture in most (16/17) of the cases. The cultures were obtained from sputum (15), pleural fluid (2), blood (2) and bronchoalveolar secretions (1). The only subject with a negative culture had a positive AFB smear in sputum with a detectable PCR test. In this group of patients with confirmed TB, there were 8 subjects (47%) who had negative AFB smears in sputum. Most of the patients (88%) survived the hospital admission.

Discussion

In the present study 17 HIV infected patients were admitted to hospital with a new, concomitant PCP and TB infection. About half of these patients were not aware of their HIV infection and about half of them had a negative AFB in sputum (with subsequent delay in the TB diagnosis). We believe this information is important for several reasons: it highlights the need to increase the awareness of the occurrence of this dual infection in HIV infected patients, it supports the practice to exclude pulmonary TB in all HIV infected patients admitted to the hospital with respiratory symptoms, and underscores the need for better and faster diagnostic tests for the diagnosis of both entities. Additional known reasons are: both infections can mimic clinically and radiologically each other [17,18], both are potentially fatal and if not recognized promptly, and tuberculosis has the risk of transmission to health care personnel and other patients [19,20]. Currently there is limited information about this simultaneous infection in Western countries because most reports of dual TB and PCP infection in HIV infection come from African countries characterized by high rates of

Table I. Characteristics of HIV patients with pulmonary TB and PCP.

Case	Age/ Gender	Symptoms	Time HIV	AFB sputum	CD4 ¹	TB DX ²	PCP DX	Chest X- ray	Outcome
1	46/M	SOB ³	6 weeks	Negative	18	Sputum CX ⁴	DFA BII ⁵		Survived
2	33/M	SOB	Admission	Positive	48	Sputum CX	DFA BII		Survived
3	29/M	Fever	Admission	Positive	48	BAL CX	DFA BII		Survived
4	41/M	SOB	Admission	Negative	76	Sputum CX	DFA BII		Survived
5	51/F	SOB cough	4 y	Negative	212	Sputum/pleu CX	Clinical BII/cystic		Survived
6	43/F	SOB, fever	2 y	Few	113	AFB+PCR	Clinical BII/granulomas		Survived
7	41/M	Cough/fever	4 y	Positive	42	Sputum CX	Clinical BII		Survived
8	37/F	SOB, fever	5 y	Negative	1	Sputum CX	Clinical BII bases		Survived
9	46/M	SOB, fever	4 weeks	Few	8	Blood/sputum CX	Clinical BII/diffuse		Survived
10	42/F	SOB, fever	10 y	Negative	72	Pleural fluid sputum CX	Clinical Middle lobe		Expired
11	45/M	SOB	Admission	Rare	190	Sputum CX	Clinical BII		Survived
12	40/M	Cough/fever	10 y	Negative	71	Sputum CX	Clinical Infiltr left lobe/pl effus		Survived
13	37/M	Cough/sweats	3 months	Positive	93	Sputum CX	Clinical BII		Survived
14	59/M	SOB	Admission	Few	75	Sputum CX	Clinical BII		Expired
15	34/F	Fever	Admission	Negative	151	Sputum CX	Clinical BII		Survived
16	48/M	SOB, fever	Admission	Rare	189	Sputum CX	Clinical BII		Survived
17	66/M	SOB	Admission	Negative	6	Blood/sputum CX	Clinical Bilat patchy infiltrates		Survived

¹CD4 cells/mm³.²DXN: diagnosis.³SOB: shortness of breath.⁴CX: culture.⁵BII: bilateral interstitial infiltrates.

HIV and TB where PCP has been thought to be infrequent [14–16]. Most of these reports used highly sensitive methods for detection of *Pneumocystis jiroveci* that could detect subclinical infections, but then it was unclear what percentage of patients had active diseases. On the other hand, in this country there is a renewed interest in the study of TB for the following reasons [21]: deceleration of the decline in the overall national TB rate, the persistent disparities in TB rates between whites and racial/ethnic minorities and the worldwide increase in multidrug-resistant TB cases. This study was conducted in the county hospital that serves a city that, in 2004, had the fifth highest number of AIDS cases and had a MTB rate that was twice (10 per 100,000) the national average. We think that the 17 cases found in this report are enough to highlight the potential presence of this double pneumonia in HIV infected patients, but probably are an underestimate of the magnitude of the problem. There are several potential reasons for missing cases. This is a retrospective review that relied on ICD-9 codes for the identification of potential cases and the criteria for the diagnosis of PCP were more strict than what is clinically accepted. Most patients who are admitted to this hospital with presumptive PCP are treated empirically and did not meet our inclusion criteria for PCP diagnosis. This approach of low threshold for the treatment of PCP, although not validated by large, prospective trials, represents a reasonable alternative

in a well-defined subpopulation of HIV-positive patients, especially when convenient and cost-effective diagnostic facilities are not always available [22]. In many instances, but not in all the cases, there is an additional effort to obtain expectorated sputum or induced sputum as the initial diagnostic modality. In an ideal setting, this is an extremely valuable diagnostic modality for PCP that possesses the advantages of being rapid and non-invasive while having a high diagnostic sensitivity. However, in clinical practice many patients cannot produce sputum and the diagnostic yield is lower in some patients (receiving aerosolized pentamidine for PCP prophylaxis) [23]. Additionally, not all available methods used for the diagnosis of PCP (silver stain, modified Giemsa stain, modified toluidine blue, immunofluorescence and PCR assay) have the same yield and have not been used uniformly throughout the study period in this hospital. Fiberoptic bronchoscopy (with its better diagnostic yield for PCP) is reserved for patients who do not respond to therapy as expected. It is well known that PCP can worsen the first few days after the initiation of appropriate therapy (even with the use of steroids) and, because of this, many patients who have PCP who receive adequate treatment subsequently undergo BAL. The diagnostic value of BAL for PCP, however, decreases inversely with the number of days of therapy [24]. Also, in this hospital, DFA for PCP in sputum has not been available throughout all the years of the study.

The epidemiological characteristics of the patients are, not surprisingly, consistent with the characteristics of all 3 conditions: middle age men of minority ethnic backgrounds. As described in these cases, the typical radiographic appearance of 'reactivation MTB', with upper lobe infiltrates, is not commonly seen in patients with low CD4 cell counts. The presence of 2 concomitant pneumonias makes it difficult to assign the radiological characteristics to only 1 disease.

Almost all the patients described in this report survived the hospital admission and were discharged to the outpatient clinic despite the potentially lethal conditions, which was even more surprising if we take into consideration that almost half of the patients were not even aware of their HIV status. This good outcome in all these severely ill patients is remarkable and is probably in part related to the aggressive early use of PCP treatments. The downside of this practice is the lack of specific diagnosis (presumptive) and probably the over-treatment of many cases with the potential of excess toxicity [25]. A similar situation has been reported from the Memorial Sloan-Kettering Cancer Center in New York where only 57% of AIDS patients with suspected PCP actually had *P. jiroveci* recovered from bronchoalveolar lavage (BAL) fluid or transbronchial biopsy specimens; 43% of patients would have received inappropriate empiric anti-Pneumocystis therapy for other conditions (Kaposi's sarcoma, bacterial pneumonia, bronchitis, etc.) [26]. As new technology becomes available it is expected that the sensitivity of new tests for the diagnosis of PCP and TB will increase and will limit unnecessary treatments.

Conclusions

Concurrent TB and PCP in HIV infected patients was not uncommon in this large county hospital in Miami, Florida in the studied period, but its diagnosis was challenging.

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