

Factors That May Help In The Prediction Of Pulmonary Tuberculosis In HIV Infected Patients

Chrispin Kambili

A. Aim

The aim of this study is to identify factors which have a strong predictive value for the presence of tuberculosis (TB) in HIV infected patients when they present to the emergency department with possible pulmonary TB. Once these factors have been established they can be used to select patients for further, more sensitive testing. Introduction

The resurgence of tuberculosis has been directly linked to HIV (MMWR 40:869, 1991). HIV is probably the most significant factor not only in the reactivation of TB but also in the progression of primary infection to active disease and death. In New York City up to 40% of all TB cases have HIV infection (J Infect. Dis 165:87, 1992). As difficult as it is to diagnose TB in immunocompetent individuals, its manifestation in HIV infected persons is even more subtle and less specific. In the immunocompetent patient TB tends to be more atypical, 1) more likely to have extrapulmonary involvement, 2) more likely to have negative tuberculin skin test, 3) more likely to be resistant to antituberculous drugs, 4) more likely to progress to death rapidly, 5) less likely to have classical radiographic findings and 6) less likely to have positive AFB smears. In fact, only about 50% of HIV positive patients who have TB by culture have positive smears (Clin. Infect. Dis 22:683, 1996). Patients are usually "ruled out" for TB by negative sputum smears. When a patient has three negative smears he or she is taken out of isolation. If the smear, which is only 40 to 50 percent sensitive in HIV positive patients, fails to pick out a case of TB, the patient may go on and infect other patients and/or hospital staff. If TB is not suspected and promptly diagnosed the patient may remain infectious longer. One way to improve the sensitivity of the smear is to increase the number of smears examined. This may prove to be expensive because of the increased number of specimens in the lab and the increased number of days a patient has to remain in isolation. If one were able to select those patients more likely to have TB, one could perform more smears only in those patients thus increasing the sensitivity of the smear.

When a patient with known or suspected HIV infection presents to the emergency department with a cough it is prudent to assume that they have TB and take measures to isolate the patient and determine whether or not they indeed have TB. It may not always be practical to do this. For example, there may not be enough isolation beds in the hospital or the hospital budget may not permit excessive use or overuse of isolation beds. In some patients, one may want to initiate empiric antituberculous therapy while awaiting culture results because of the severity of the patient's illness. It is important, therefore, to establish factors that are associated with the diagnosis of TB in HIV patients when they first present to the emergency department.

I propose that it is possible to accurately predict which patients are likely to have TB by analyzing demographic, symptomatic and laboratory data when the patient initially presents to the emergency department with a cough and concomitant HIV infection. Although numerous papers have been published about atypical presentation of TB in HIV disease, no one has tried to stratify factors which are more predictive of TB in these patients (Am. Rev. Respir. Dis. 136:492, 1987; NEJM 324:1644, 1991; Clin. Infect. Dis. 22:683, 1996). These factors may be signs and symptoms a patient presents with, special risk factors for TB that a patient might have, or laboratory and radiologic findings. Once these factors have been established the admitting physician can determine which patients need to be isolated and be ruled out for TB and which patients would require more than the standard three sputum samples before declaring them free of TB.

B. Methods and patients

The study will be carried out in a large New York City hospital located in an area with high prevalence of both TB and HIV. There are about 60 to 100 cases of TB in this hospital out of about 600 patients admitted for "rule out TB" every year. Up to 60% of the TB cases have concomitant HIV infection (Am. Rev. Respir. Dis 144:745, 199 1),

Data will be obtained while the patient is being initially worked up in the emergency room. Fliers will be posted in the ER to remind ED physicians to page the study coordinator whenever a patient satisfying the enrollment criteria is admitted. Frequent visits will be made to the ER to remind the ED staff of the on-going study. All patients presenting to the emergency room with cough and history of HIV infection will be eligible for enrollment. The patient must have "rule out TB" as one of their admitting diagnosis. A written consent will be obtained from each eligible patient. If the patient is unable to give consent, consent will be obtained from the next of kin. A standard questionnaire will be used to obtain demographic data. ED notes will be used to obtain presenting vital signs. The computerized laboratory information system will be used to obtain laboratory results including I-HIV status of the patient and the results of sputum cultures. A positive result will be the one in which *Mycobacterium tuberculosis* has been isolated by sputum culture.

C. Statistical Analysis

The variables that are obtained at the initial presentation will then be examined for association with presence or absence of TB. X² test will be used to determine the two tailed statistical significance of associations in two by two tables. Odds ratios and 95% confidence intervals will be derived from logistic regression coefficients to provide estimates of statistical association between a given variable and a positive TB culture. An α level of 0.05 will be used as the indication of statistical significance.

If patients were selected in such a way that the sensitivity of the sputum smear is improved from the current 50%, the clinical implications would be enormous since even a single missed case of TB can be disastrous especially in a setting where other HIV infected patients are present (NEJM 328:521, 1993). One would achieve the increased sensitivity by doing more smears in patient more likely to have TB. For example, an increase from 25 of 50 true cases to 35 of 50 would represent a percentage increase from 4.2% of presentations to 5.8% of presentations. This would represent a 40% increase in case identification rate. A χ^2 test hypothesis of 40% improvement as outlined above, power of 80% and type I error of 5% together yield an effect size of 0.115 and a target sample size of 586 subjects which almost exactly matches the 600 patients expected to be available over one year. With 600 patients and a projected TB case rate of 8% to 15%, logistic models will have sufficient power to accommodate the three or four predictors that would be the maximum considered for a final predictive model. These predictors will be chosen from the variables listed in table 1.

Demographic variables	Race	black Hispanic white
	drug use	LVDU crack use
	Homelessness	
	history of living in a homeless shelter	
	history of incarceration	
Signs and Symptoms	Duration of cough	
	fever	
	chills/night sweats	
	weight loss	
	dyspnea	
Lab Data	CD4 count	>200 50-200 <50
	infiltrate on CXR	interstitial upper lobe lower lobe Cavitary
	mediastinal adenopathy	
	hypoxemia (Po ₂ < 70mmHg)	

References

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