**Pneumocystis carinii** Pneumonia*

The Time Course of Clinical and Radiographic Improvement

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Objectives: The purpose of this study was to compare the time course of clinical and radiographic improvement in patients with *Pneumocystis carinii* pneumonia (PCP), and evaluate the usefulness of early follow-up chest radiographs (CXRs) in these patients.

Design: Retrospective, chart review.

Methods: The medical records of 36 episodes of confirmed PCP among 28 patients were reviewed. Clinical parameters of improvement were defined as follows: (1) a decrease in temperature by 0.5°C, (2) a decrease in respiratory rate by 25%, and (3) a 2% improvement in arterial oxygen saturation, as measured by pulse oximetry, in the setting of an unchanged amount of supplemental oxygen or a reduction in supplemental oxygen. A patient was defined as clinically improving when all three of these criteria were met. All CXRs were graded by radiologists, specifically for the study, as normal or abnormal and improved, worsened, or unchanged from the initial CXR.

Results: Clinical improvement was noted during 30 of 36 episodes of PCP (83%) at a mean of 4.5 ± 2.5 days (± SD). There was improvement in the CXR finding during the hospital stay during 15 of 36 episodes (42%), at a mean of 7.7 ± 4.5 days. Radiographic resolution preceded clinical resolution in only four cases (11%). Excluding seven patients who received ventilatory support, the median number of CXRs per patient was four (range, two to nine CXRs).

Conclusion: We conclude that radiographic improvement of PCP lags behind clinical improvement.

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Key words: AIDS; chest radiograph; *Pneumocystis carinii* pneumonia

Abbreviations: PCP = *Pneumocystis carinii* pneumonia; CXR = chest radiograph

While the overall incidence of *Pneumocystis carinii* pneumonia (PCP) in patients with AIDS has declined in recent years, it still remains a common cause of pneumonia in these patients.1 We have noted that in our institution, patients admitted with PCP often undergo several chest radiographs (CXRs) during their hospital stay. Appropriate reasons for performing CXRs after PCP is diagnosed might include suspicion of a complication such as pneumothorax or to establish a new baseline prior to discharge. Another potential reason for obtaining a follow-up CXR might be to obtain objective evidence of improvement in a patient being treated empirically for PCP. However, performing CXRs for this reason would be of benefit only if patients commonly demonstrate radiographic improvement before clinical improvement occurs.

It is well known that clinical improvement of bacterial pneumonia precedes radiographic resolution, which often takes > 8 weeks.2,3 We are aware of no studies that have investigated whether radiographic resolution of PCP similarly lags behind its clinical resolution. Whether frequent follow-up CXRs are of any benefit in patients with PCP who are clinically improving has also not been studied. The objective of the present study was to compare the timing of clinical improvement with radiographic improvement in patients with PCP.
An electronic search of the medical records at the University of Connecticut Health Center was performed, searching for discharges with a diagnosis of PCP between 1990 and 1996. Episodes without a confirmation of the diagnosis by direct fluorescent antibody testing of sputum (expectorated or induced) or BAL were excluded from further analysis, as were patients without HIV infection. The age, gender, risk factors for HIV, duration of HIV disease, last known CD4 count prior to hospital admission, history of prior PCP, presence of concurrent opportunistic infection, use of PCP prophylaxis, and clinical symptoms and their duration were noted for all patients. The hospital admission PaO2 or pulse oximetric saturation, as well as amount of supplemental oxygen (if any), were also abstracted.

The clinical course of each patient during the hospital stay was reviewed, and the following parameters were abstracted: the daily maximum temperature, the mean daily respiratory rate (computed as the mean of all available readings during the day), daily maximum oxygen concentration required, and the daily mean oxygen saturation. Clinical parameters of improvement were defined as follows: (1) a decrease in temperature by 0.5°C, (2) a decrease in respiratory rate by 25%, (3) any reduction in supplemental oxygen (defined as either a decrease in the percentage of oxygen delivered by mask, a decrease in the flow rate of oxygen delivered by nasal cannula, or a switch from mask to nasal cannula) or an increase in pulse oximetric saturation by 2%, as compared to the values on the first day of hospitalization in the absence of a change in oxygen supplementation (all patients defined as improving by this parameter actually had an improvement of ≥ 3%). A patient was considered as clinically improving when all three of these parameters were met. If any of the three parameters was normal at presentation, clinical improvement was defined as improvement in the other parameters. The occurrence of complications, such as respiratory failure requiring ventilatory support or pneumothorax, was noted. The type of anti-Pneumocystis therapy received, duration of hospitalization, and outcome (death or survival to hospital discharge) were also abstracted.

All CXRs obtained on each patient during the hospitalization were reviewed independently by two of three radiologists (E.M.H., H.K., S.B.) specifically for the study, and graded as normal or abnormal. In addition, all but the initial CXR were also scored as either improved, worsened, or unchanged compared to the initial CXR. The radiologists were blinded as to the clinical course of the patients, but not to the temporal sequence of the CXRs. Radiographs with discordant judgment were later reviewed together so that a consensus could be reached. The time required for clinical improvement was compared with that required for radiographic improvement.

### RESULTS

Twenty-eight patients with 36 episodes of PCP were studied. The ratio of male to female gender was 8:1. The mean age of the patients was 36.3 ± 9.4 years (± SD). The mean duration of known HIV infection was 3.8 ± 2.9 years. The mean CD4 count prior to hospital admission was 75.2 ± 8.8/μL. Risk factors for HIV infection were as follows: (1) IV drug use, 39%; (2) homosexuality, 36%; (3) heterosexual contact, 11%; (4) transfusion, 8%; and (5) multiple risk factors, 6%. Fourteen of 36 patients (39%) had prior PCP, while 22 patients (61%) did not. Twenty-three of 36 patients (64%) had been prescribed PCP prophylaxis prior to the time of presentation.

Fever was the most common symptom at presentation, noted in 31 of 36 episodes (86%). Nonproductive cough was present in 29 patients (81%), dyspnea in 27 patients (75%), weight loss in 14 patients (39%), and chest pain in 2 patients (6%). The mean PaO2 was 66 ± 19.7 mm Hg in the 31 patients who had arterial blood gases measured while breathing air. The diagnosis of PCP was confirmed by direct fluorescent antibody staining of expectorated sputum in 18 patients (50%), induced sputum in 4 patients (11%), and BAL in 13 patients (36%).

Sixteen of 36 episodes (44%) were treated with trimethoprim-sulfamethoxazole, 15 episodes (42%) were treated with IV pentamidine, and 5 episodes (14%) were treated with clindamycin and primaquine. Twelve of 36 episodes (33%) were treated with corticosteroids.

The mean number of days required for the patients’ temperature to decrease by 0.5°C was 2.9 ± 2.5 days. The time until improvement in the respiratory rate occurred was 3.4 ± 2.5 days, while the mean time taken for either a 2% improvement in oxygen saturation or a decrease in the level of oxygen supplementation was 3.2 ± 1.6 days. Clinical improvement during the hospital stay, defined as improvement in all three of the above parameters, was seen in 30 of 36 episodes (83%), while 6 patients (17%) showed no clinical improvement and ultimately died. The mean time until clinical improvement occurred was 4.5 ± 2.5 days. Seven patients (19%) required ventilatory support during the course of their stay (four of whom died and three recovered).

In 16 of 36 episodes (44%), there was improvement in the CXR during the hospital stay, while the rest (56%) showed no radiographic improvement. In patients who did show radiographic improvement, the mean time until improvement was noted was 7.7 ± 4.5 days. Figure 1 demonstrates the timing of clinical and radiographic improvement in the 30 episodes in which clinical improvement occurred. During these episodes, a total of 83 follow-up CXRs were performed during the hospital stay (excluding CXRs performed after initial radiographic improvement was noted), of which 11 CXRs were performed prior to the definitive diagnosis of PCP being obtained. Radiographic improvement preceded clinical improvement in only four episodes (by 1 day in two episodes, and by 2 days and 3 days in one episode each). The CXRs in five of the six patients who died showed progressive infiltration. In all five of these patients, clinical worsening preceded radiographic worsening. In one patient, there was improvement of...
the CXR although his clinical status did not improve, and he ultimately died in the hospital.

We attempted to determine the indications for the follow-up CXRs; however, in 50% of the cases, the reason was not documented. In 25%, CXRs were obtained because of concern regarding clinical deterioration. Other indications included assessing for improvement on therapy and continued or recurrent fever. There were no cases where we could determine that the follow-up CXRs resulted in a change in management.

DISCUSSION

Our impression that patients with PCP frequently have several CXRs performed prior to discharge from the hospital was confirmed by this study. Even among patients with an uncomplicated case of PCP, a median of four CXRs was performed prior to discharge from the hospital. The other important finding of this study is that radiographic improvement in patients with PCP rarely occurs before clear evidence of clinical improvement. In only 4 of 36 episodes (11%) did radiographic improvement occur before clinical improvement was apparent. Finally, the many CXRs performed on these patients resulted in no changes in medical management that were discernible from our review of the medical records.

It has previously been reported that the CXR abnormalities due to PCP improve over the course of 1 to several weeks and occasionally may persist for several months after successful therapy.4 In addition, the CXR findings may at times worsen during the first week of therapy, despite clinical improvement.5 While there have been no case series directly comparing the time course of clinical and radiographic improvement, in one patient treated with pentamidine and steroids, clinical and radiographic resolution was reported to occur in 4 days.6 Rankin and Pella7 reported radiographic resolution within a week of therapy including steroids, while clinical resolution occurred in 4 days. DeLorenzo et al8 examined the radiographic resolution of PCP and reported that during a 3-week follow-up, the CXR had worsened at the end of the first week in 46%, while only 17% had improved. By 3 weeks, only 35% had improved. Over a 5-month period, it was found that complete resolution occurred in 43%, partial resolution occurred in 16%, worsening occurred in 18%, and 22% were unchanged; however, this study did not correlate the radiographic resolution with clinical resolution. In contrast, we saw improvement in the CXR during hospitalization in 44% of the episodes, occurring at a mean of 7.7 ± 4.6 days. In addition, none of our patients showed evidence of the radiographic deterioration that has been reported to sometimes occur during the initial 48 to 72 h of therapy. This may have been partly because concomitant steroid therapy had been instituted in a third of our cases.

Our study has some limitations due to its retrospective nature. We were frequently unable to determine the reason why the follow-up CXRs were performed, but there may have been reasons that were not documented in the chart. Similarly, although there appeared to be no alterations in therapy based on the CXRs, perhaps changes in therapy were being contemplated that were not instituted based on the CXR results. Since the study was retrospective, and since CXRs were not performed on a regular basis on each patient, we could not determine exactly when radiographic improvement occurred in each patient. Finally, due to the relatively small number of patients who received corticosteroids, we could not do any meaningful analysis of how corticosteroids influence the rate of radiographic resolution of PCP. However, none of these limitations detracts from the main finding of this study; radiographic improvement lags behind clinical improvement in most cases of PCP.
Given our finding that the radiographic improvement in PCP generally lags behind clinical improvement, it seems that early follow-up CXRs performed on patients with uncomplicated PCP are unlikely to yield useful clinical information. We suggest that in patients being treated for proven PCP, early follow-up CXRs be reserved for patients with clear evidence of clinical decline or a suspected complication such as pneumothorax. Since some patients with PCP have permanent radiographic abnormalities, it might be useful to obtain a CXR to determine the new “baseline.” The results of DeLorenzo et al suggest that the time of discharge may not be the best time to this, as patients will often continue to improve radiographically > 3 weeks after treatment is instituted.

REFERENCES