Doxycycline Pleurodesis for Pneumothorax in Patients With AIDS*

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Since first described in 1984, nontraumatic pneumothoraces in patients with AIDS has become more common. When compared with spontaneous pneumothorax in the general population, pneumothoraces in patients with AIDS are often complicated by prolonged air leaks as well as higher recurrence rates. Chemical pleurodesis has an important role in the management of these complications. The most experience with chemical pleurodesis uses tetracycline hydrochloride as the sclerosing agent; however, this agent is no longer available. Doxycycline has been used in pleurodesis of malignant effusions, but its use in managing pneumothoraces is limited. We present five patients who have AIDS with a total of seven pneumothoraces. Each patient experienced a persistent air leak. Six of the pneumothoraces were managed successfully with doxycycline. Although the follow-up period was limited, there were no recurrences noted and the only side effect seen was chest pain in four which was easily controlled with narcotics. Doxycycline sclerotherapy can be used effectively for pleurodesis in the management of nontraumatic pneumothorax in the patient with AIDS.

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S\^{}pontaneous pneumothorax in patients with AIDS was first reported in 1984.\(^1\) Since then, it has become an increasingly common, and at times, a problematic event. Not only can prolonged air leaks develop, but also the risk of recurrent pneumothoraces is increased.\(^2\,3\) To decrease the incidence of recurrence of pneumothorax, some authors have recommended performing chemical pleurodesis with tetracycline hydrochloride for initial spontaneous pneumothoraces for patients without AIDS.\(^4\,5\) Unfortunately, tetracycline is no longer available for this purpose and doxycycline has been recommended as a substitute agent. Doxycycline has been used successfully for pleurodesis in the management of malignant pleural effusion, but experience with its use in the management of pneumothoraces is limited.\(^6\) We present five patients with AIDS in whom pneumothoraces were complicated by persistent air leaks and who were managed successfully with doxycycline pleurodesis (Table 1). In each case, the pleurodesis was performed in a similar manner. Each patient had between 100 to 300 mg of lidocaine instilled through the chest tube initially for local anesthesia and then had 500 mg of doxycycline mixed in 30 mL of sterile saline solution instilled. The chest tube remained clamped for 2 hours post procedure and then was returned to water seal.

CASE REPORTS

Case 1

A 29-year-old black man with a history of intravenous drug use,\(^*\) positive serology for human immunodeficiency virus (HIV) 2 years before admission, and no prior history of Pneumocystis carinii pneumonia (PCP) or PCP prophylaxis was admitted with shortness of breath of 3 weeks' duration. A chest roentgenogram showed diffuse interstitial infiltrates with predominant upper lobe involvement. He was given empirically trimethoprim and sulfamethoxazole (TMP/SX) and prednisone with subsequent confirmation of PCP by bronchoscopy lavage specimen. On the 11th hospital day, the patient developed a nontraumatic pneumothorax on the right side and underwent tube thoracostomy. The initial air leak resolved, and on the 18th hospital day, sclerotherapy with doxycycline was performed. He experienced severe chest pain requiring 75 mg of meperidine intravenously (IV) for control. The chest tube was successfully removed on the following day. The hospital course was also complicated by development of a left-sided pneumothorax on the 16th hospital day which required a second tube thoracostomy. He had a prolonged air leak, but despite this, the patient eventually underwent uncomplicated sclerosis with 60 U of bleomycin on the 33rd hospital day. Bleomycin was chosen as the sclerosing agent because of the patient's prior discomfort with doxycycline. The left-sided tube was removed successfully 3 days after pleurodesis. The patient died 2 months later of sepsis without any recurrence of pneumothoraces.

Case 2

A 37-year-old black man with a history of intravenous drug use had a 2-day history of right-sided pleuritic chest pain, shortness of breath, and fever. The chest roentgenogram showed a moderate sized right-sided spontaneous pneumothorax. Tube thoracostomy was performed and subsequent chest roentgenograms showed subcutaneous emphysema, bilateral interstitial infiltrates, and bullous changes in both apices and the left base. He was given empirically TMP/SX with the addition of prednisone once confirmation of PCP was obtained by a bronchoscopy lavage specimen. Subsequent HIV antibody test was positive. Because of a small persisting apical pneumothorax, a second chest tube was placed on the fifth hospital day with complete resolution of the pneumothorax. The patient underwent pleurodesis with doxycycline. He experienced chest pain post pleurodesis which required a total of 7 mg of morphine IV for control. Both chest tubes were successfully removed on the ninth hospital day and he was eventually discharged. Ten months after discharge, the patient was free of recurrence of the pneumothorax.

MAI = Mycobacterium avium intracellulare; PCP = Pneumocystis carinii pneumonia; FTX = pneumothorax; TMP/SX = trimethoprim and sulfamethoxazole

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Table 1—Spontaneous Pneumothorax in AIDS Patients*

<table>
<thead>
<tr>
<th>Pt. No.</th>
<th>Active Pulmonary Infection</th>
<th>Prior PCP</th>
<th>Aerosol Pentamidine</th>
<th>Side of PTX</th>
<th>Complication of PTX</th>
<th>Pleurodesis Agent</th>
<th>Complications of Pleurodesis</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PCP</td>
<td>No</td>
<td>No</td>
<td>Right</td>
<td>Persisting air leak bilaterally</td>
<td>Doxycycline on right</td>
<td>Pain</td>
<td>Died 2 mo later with sepsis</td>
</tr>
<tr>
<td>2</td>
<td>PCP</td>
<td>No</td>
<td>No</td>
<td>Left Right</td>
<td>None</td>
<td>Bleomycin on left doxycycline</td>
<td>None</td>
<td>Alive at 10 mo without recurrence Died at 3 mo</td>
</tr>
<tr>
<td>3</td>
<td>MAI</td>
<td>Yes</td>
<td>No</td>
<td>Right</td>
<td>Persisting air leak</td>
<td>Doxycycline</td>
<td>None</td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td>4</td>
<td>PCP</td>
<td>No</td>
<td>No</td>
<td>Left</td>
<td>Persisting air leak bilaterally</td>
<td>Doxycycline</td>
<td>Pain</td>
<td>Died with Pseudomonas Sepsis after 2 wks</td>
</tr>
<tr>
<td>5</td>
<td>PCP</td>
<td>No</td>
<td>Yes</td>
<td>Left Right</td>
<td>Persisting air leak bilaterally</td>
<td>Doxycycline on both sides</td>
<td>Pain</td>
<td>None</td>
</tr>
</tbody>
</table>

*PTX = pneumothorax.

**CASE 3**

A 30-year-old black man with AIDS and a prior history of PCP and disseminated *Mycobacterium avium intracellulare* (MAI) infection was admitted with altered mental status. A right lower lobe infiltrate was seen on his chest roentgenogram. He had been maintained previously with TMP/SX prophylaxis, but had been noncompliant. He was given empirically IV TMP/SX. On the second hospital day, he developed a right-sided nontraumatic pneumothorax requiring tube thoracostomy. Subsequent bronchoscopy and lavage specimens were negative for PCP but revealed acid-fast smear-positive organisms which cultured for MAI. Despite a persistent air leak, pleurodesis with doxycycline was performed on hospital day 6. By the 8th hospital day, the air leak resolved, the chest tube was removed, and the patient was eventually discharged from the hospital. Three months after discharge, the patient died from his HIV disease without recurrence of his pneumothorax.

**CASE 4**

A 25-year-old white man with a prior history of HIV infection had sudden onset of dyspnea and pleuritic chest pain. He was afebrile and tachypneic with an otherwise unremarkable physical examination. Admission laboratory data showed a mildly elevated lactate dehydrogenase level of 461 IU and a widened alveolar to arterial oxygen gradient of 70 mm Hg. His chest roentgenogram showed a moderate left-sided pneumothorax and mild interstitial infiltrates. A tube thoracostomy was performed, and on the following day, he underwent bronchoscopy with bronchoalveolar lavage specimen positive for PCP. An IV TMP/SX was begun. He had a persistent air leak despite adequate re-expansion of the left lung. On the 8th hospital day, pleurodesis with doxycycline was performed. He experienced chest discomfort, which was controlled with 75 mg of meperidine given intramuscularly. The air leak resolved and the chest tube was removed on the 10th hospital day. The patient was discharged the next day and moved to Mexico.

**CASE 5**

A 22-year-old black man with prior history of HIV infection, cytomegalovirus retinitis, and aerosolized pentamidine prophylaxis was admitted with a 1-month history of nonproductive cough and a 1-day history of sudden severe chest pain. He denied fevers, chills, or night sweats. On examination, he was febrile to 43°C and had decreased breath sounds over the left chest. Chest roentgenogram showed a left-sided tension pneumothorax. Tube thoracostomy was performed with complete re-expansion of the lung. On the second hospital day bronchoscopy and lavage specimen confirmed the diagnosis of PCP and IV TMP/SX was begun. Despite a persistent air leak, on the 10th hospital day pleurodesis with doxycycline was attempted; however, the air leak persisted. On hospital day 12 he developed a nontraumatic pneumothorax on the right side requiring tube thoracostomy. There were now bilateral air leaks. On the 20th hospital day, successful pleurodesis on the right side with doxycycline was performed. Four days later, a repeat left-sided pleurodesis with doxycycline was successful and the air leak resolved. Both chest tubes were eventually removed and the patient was discharged home. Two weeks later he was readmitted for Pseudomonas sepsis and died 1 week later.

**DiSCUSSION**

The overall incidence of spontaneous pneumothorax in patients with AIDS is reportedly as high as 2 percent. Three risk factors identified for the development of nontraumatic pneumothorax in this population are concomitant active PCP, a history of aerosolized pentamidine prophylaxis, and a history of PCP episodes. The AIDS patients with acute PCP have a reported incidence of pneumothorax ranging from 6 to 9 percent, and 95 percent of AIDS patients with a nontraumatic pneumothorax have active PCP at the time of presentation. In the five cases presented here, four had active PCP, only one had a history of PCP and only one was receiving aerosolized pentamidine prophylaxis.

Reported recurrence rates for nontraumatic pneumothorax in the general population varies from 23 to 52 percent. Patients with persistent air leaks or who develop recurrences are usually referred for surgical intervention. Chemical pleurodesis through closed tube thoracostomy has been tried as a method of decreasing the incidence of recurrence. In one study, chemical pleurodesis was successful in decreasing the recurrence rate from 41 to 25 percent. Chemical pleurodesis avoids the risks of surgery and general anesthesia; and therefore, it has been suggested by some authors as the standard treatment of an initial nontraumatic pneumothorax.

In patients with AIDS, recurrence after initial
nontraumatic pneumothorax is more common than the general population with rates reported from 36 to 65 percent. When these pneumothoraces occur, they may present as tension pneumothoraces or bilateral pneumothoraces. Indications for surgical intervention in these patients are similar to those in non-AIDS patients; however, this intervention is less effective and has a higher morbidity than in the general population. This may be related to the underlying immunodeficiency state causing an increase in complications and a decrease in healing. Chemical pleurodesis, therefore, provides an attractive alternative for management of the initial nontraumatic pneumothorax in the AIDS population, as it should reduce the chance of recurrence.

Most cases of chemical pleurodesis for pneumothorax have reported tetracycline as the sclerosing agent. Unfortunately, the injectable tetracycline hydrochloride is no longer available and experience with alternative agents is limited. Because of the similarities to tetracycline, doxycycline may be a suitable alternative. In one of the largest studies with doxycycline, Mansson reported 18 patients with malignant effusions in whom pleurodesis was attempted with 500 mg of doxycycline. In five of the patients, the initial attempt at pleurodesis was successful. In ten patients, multiple attempts were necessary before a successful outcome. In only three patients was pleurodesis unsuccessful despite multiple attempts. The side effects of doxycycline, similar to tetracycline, included fever and pain, and they were seen in a minority of the patients. It would seem, therefore, that doxycycline is preferred for chemical pleurodesis in the management of pneumothoraces.

We have presented seven pneumothoraces occurring in five patients with AIDS, of which six episodes were successfully managed with pleurodesis with doxycycline (Table 1). None of the cases developed recurrences. Despite lidocaine instillation into the pleural space, four of the patients still experienced pain, but in no case was this impossible to be controlled with supplemental narcotics. The follow-up period in each case is limited, as the majority of the patients died of diseases unrelated to either the pneumothorax or pleurodesis. It is difficult to comment, therefore, if the pleurodesis decreased the incidence of recurrence. Doxycycline pleurodesis did, however, successfully manage persistent air leaks and allowed all the patients to be discharged from the hospital. Four of the patients had active PCP at the time of presentation. In such case, it is important to treat the underlying infection as well as the pneumothoraces to achieve a favorable result.

In two cases, the patients had bilateral pneumothoraces and underwent bilateral pleurodesis. A late potential complication of bilateral pleurodesis is the small risk of inducing clinically significant restrictive lung disease. In the AIDS population, however, because of the underlying disease, the usual survival period is limited and thus, this potentially late complication may not be an important concern.

Bleomycin and talc have been reported as sclerosing agents as well. However, bleomycin is an expensive agent and talc is difficult to place through a chest tube, often requiring direct visualization by means of a thoracoscope. Therefore, doxycycline offers some advantages over these agents.

In summary, because of the high recurrence rate and significant morbidity from pneumothoraces, we suggest that serious consideration be made with regard to performing pleurodesis on all initial nontraumatic pneumothoraces in subjects with AIDS. We have successfully treated with doxycycline pleurodesis five patients who have AIDS and nontraumatic pneumothoraces complicated by persistent air leaks. This agent can be effectively used in lieu of tetracycline for this purpose.

REFERENCES

9 McClellan MD, Miller SB, Parsons PE, Cohn DL. Pneumothorax with Pneumocystis carinii pneumonia in AIDS. Chest 1991; 100:1224-28