

## **Pneumocystis carinii Pneumonia in an Untreated Patient with HIV**

Gary is a 43 year old gay white man who presents to your office for the first time with a complaint of worsening shortness of breath over the previous 4-6 weeks. Gary claims he tested positive for HIV 7 years ago and has seen a doctor once or twice since that time. He admits that he preferred to ignore his diagnosis and suspects that it may have been wrong because he has felt well. The couple of doctors he saw in the interim pronounced him healthy but he acknowledges that he withheld both his sexuality and the previous HIV test results. He would like to blame this new shortness of breath on stress and lack of exercise but he admits he is concerned that this is, in fact, something HIV-related.

Gary is subtly short of breath while speaking to you. He notes a decreasing capacity to climb stairs, he cannot run to catch a bus, he has an occasional dry cough. He has noted intermittent fevers for 2 weeks although he hasn't taken his temperature. He has no other complaints. He denies weight loss or night sweats; he denies chest pain or chest pressure. His cigarette use has diminished somewhat but he notes that overall he does not feel ill.

Gary has been healthy all his life other than some childhood asthma. He takes occasional sinus medication and has no known allergies. He is a sexually active gay man who has had three relationships of more than 3 years duration but he is currently single. He is an infrequent participant in the club scene and usually uses condoms. He admits that there are times when he does not use a condom either because it is "inconvenient" or

“I forgot”. Gary is from Michigan and came to New York 12 years ago for his work in the garment industry. He has smoked 2 packs of cigarettes per day since age 20 and has done occasional recreational drugs. He has never injected drugs. His family history is non-contributory, he has a good relationship with his parents and 2 sisters who all live in Michigan. None are aware of his previous HIV test results.

On exam Gary is afebrile with a heart rate of 90 beats/min, respirations 18/min and blood pressure 120/80. His oxygen saturation on room air is 92%. He is somewhat pale, anicteric. Fundoscopic exam is normal. There is no thrush. He has shotty cervical and occipital adenopathy. His lungs have diminished breath sounds throughout. He coughs once or twice with deep inspiration and his cough is dry. His cardiac exam reveals a physiologically split S2. The rest of his exam is normal. You take him for a brisk walk in the corridor of your office. He becomes visibly winded and his oxygen saturation drops to 81%.

You strongly suspect that Gary has Pneumocystis carinii pneumonia (PCP). He has had untreated HIV for over 7 years and is likely quite immune suppressed. His complaints of dyspnea on exertion and his current findings put PCP first on a list that includes other infectious pulmonary processes such as bacterial pneumonia and tuberculosis as well as non-infectious causes such as pulmonary hypertension or cardiomyopathy. You recommend that Gary come into the hospital for further evaluation and treatment. At first Gary hesitates. Can't you give him some antibiotic that he could take at home? You tell him that yes, you could do that but you suspect he has more than a mild case of pneumonia and going home on antibiotics would not be effective enough therapy, particularly since his diagnosis is not entirely certain. You remind him that PCP

is an opportunistic infection that was the cause of many thousands of deaths in the early days of HIV. Even now, with effective prophylaxis and treatment for PCP available, patients continue to die of PCP. You suspect that Gary's immune system is very suppressed and that he is vulnerable to this kind of infection which should be treated and closely monitored in a hospital setting. He reluctantly agrees to follow your advice.

Gary's room air blood gas reveals a pH of 7.50, pCO<sub>2</sub> of 29mmHg and pO<sub>2</sub> of 76 mmHg. His LDH is 599 IU and his WBC is 6.2/mm. His Hgb is 12.1 and hematocrit is 35.4. His chest x-ray reveals bilateral airspace opacities and is highly consistent with a diagnosis of PCP [Figure 1]. Gary is started on intravenous trimethoprim-sulfamethoxazole (TMP-SMZ) as well as a macrolide to treat a possible community acquired atypical bacterial source. In addition, he is started on steroids given his hypoxemia and elevated A-a gradient. A pulmonary consult is obtained and on the 2<sup>nd</sup> hospital day Gary undergoes fiberoptic bronchoscopy with lavage and biopsy. He tolerates the procedure well. There is no post-procedure pneumothorax. His bronchoalveolar lavage results are negative for pneumocysts but his biopsy is positive. His CD4 cell count returns at 25/mm<sup>3</sup> and his viral load is 227,000 copies/ml.

Gary improves slowly in the hospital but remains easily winded with any exertion. On the seventh hospital day he develops sharp right-sided chest pain and his oxygen saturation falls abruptly into the eighties. A chest x-ray reveals a right-sided pneumothorax [Figure 2]. A small chest tube is placed with successful re-expansion of the lung and improved oxygenation. The following day the patient experiences left-sided chest pain and a chest x-ray reveals a new, left-sided pneumothorax [Figure 3]. A second thoracovent is placed and both lungs are re-expanded in the follow-up film [Figure 4].

The right chest tube remains in place for 10 days while the left is successfully removed after 5 days. The patient remains on TMP-SMX for 7 days whereupon he is switched to intravenous clindamycin with oral primaquine due to rising liver function tests. His breathing and oxygenation improve and remain stable. He is discharged on the 25<sup>th</sup> hospital day on prophylaxis for PCP, Mycobacterium avium and toxoplasmosis with dapson, azithromycin and pyrimethamine, respectively. One week before discharge he is started on efavirenz and lamuvidine/retrovir for treatment of his HIV. He tolerates these antiretrovirals well.

For someone who was trying to deny his HIV status, Gary was jolted by what happened to him. He feels angry at himself for avoiding medical care for so long, especially as he well knows that it is now possible to take effective medications for HIV. Before leaving the hospital at one point he asked you if his course was typical for people with HIV.

### **Risk and Incidence of Pneumocystis carinii pneumonia in patients with HIV**

PCP is an opportunistic infection that emerged as the dominant disease of HIV-infected individuals in the 1980's. Prior to the implementation of routine measures to prophylax against it, PCP was diagnosed in up to 75% of patients with AIDS [1,2]. PCP was both the most frequent index diagnosis in patients with HIV and the most common opportunistic infection (OI) of HIV-infected patients. After 1987, prophylaxis became the standard of care and the incidence of PCP decreased. The Multicenter AIDS Cohort (MAC) study followed 4954 US homosexual men prospectively from 1988 – 1991 and found that among those taking prophylaxis, 14.5% presented with an index diagnosis of

PCP whereas 46.3% of those not on prophylaxis developed PCP as their presenting (OI) [1,3].

You tell Gary that his low CD4 cell count made him extremely vulnerable to contracting PCP. Had he been under medical care, he would have started PCP prophylaxis when his CD4 cell count fell below 200 cells/mm<sup>3</sup>. Daily TMP-SMX is the first choice for both primary and secondary prophylaxis of PCP [4]. Oral dapsone and inhaled pentamidine are also effective and are frequently used given that more than 25% of patients are intolerant to TMP-SMX. [5]. Gary was given dapsone upon discharge from the hospital due to his TMP-SMX intolerance. Prophylaxis is recommended in all patients with a prior history of PCP whose cell counts are below 200 [6]. In a 1995 study in the New England Journal of Medicine, Bozette et al. noted that in patients with CD4 cell counts under 100, pentamidine was found to be less effective than either dapsone or TMP-SMX [7].

You tell Gary that his antiretroviral therapy will also hopefully reduce his risk of recurrence of PCP by giving his CD4 cell count a chance to recover. It is now recognized that patients on HAART who suppress their viral loads to undetectable levels and whose CD4 cell counts rise above 200 can safely discontinue their PCP prophylaxis [8].

### **Clinical Presentation and Manifestations of PCP**

Gary presented to you after several weeks of non-specific illness which is fairly typical for the presentation of PCP in patients with HIV. A 1984 comparison of PCP in immunocompromised patients with and without HIV revealed that the HIV-seronegative patients presented more acutely than those with HIV. Gary's presentation of a few weeks

of worsening dyspnea on exertion was typical. Patients without HIV but with PCP in the setting of immunocompromise had a shorter duration of symptoms (5 days vs. 28 days), more fever (92% vs. 76%), more tachypnea (30 vs. 23.4 breaths/min) and lower room-air oxygenation levels (52 vs. 69 mm Hg) [9]. This is not to say that all PCP presents slowly. A 1987 retrospective look at 145 patients admitted with PCP to New York City's St. Vincent's Hospital noted that 49 % of the patients had symptoms for less than 2 weeks [10]. While fever is common, Gary's lack of it did not point away from PCP. It did, however, make a bacterial or mycobacterial source for his complaints less likely. Dyspnea, dry cough and a fever are the most commonly reported complaints in HIV-seropositive patients with PCP; other symptoms include chest pain, malaise, weight loss, headache, night sweats, chills and fatigue. Many of these symptoms are features of active pulmonary tuberculosis, which makes MTB important to rule out in the differential diagnosis of patients with PCP. Six – seven percent of AIDS patients with PCP may be entirely asymptomatic [11, 12].

The laboratory values for patients with PCP frequently reveal an elevated LDH. Nearly 90% of patients will have LDH levels over 50 IU above baseline and a level greater than 450 IU is predictive of PCP over another pulmonary process [13]. The ABG will usually show hypoxia, increased A-aO<sub>2</sub> gradient, hypocarbia and respiratory alkalosis. Gary's presentation had all of these features.

### **Chest X-Ray in PCP**

The most commonly described radiographic appearance in PCP is of diffuse, interstitial infiltrates. Two percent – 34% of patients with PCP and HIV will have normal chest x-rays. A 1992 study which reviewed 65 series and over 2400 cases of PCP found

that the classic “ground-glass” interstitial pattern was found nearly 80% of the time [14]. Aerosolized pentamidine chemoprophylaxis has been associated with radiographic prominence of upper lobe disease in PCP [15, 16]. Many other chest x-ray abnormalities have been reported, including mass lesions, cavitary lesions, pleural effusions and pneumothoraces among others. Gary’s typical presentation had taken a somewhat atypical turn when he developed a pneumothorax. He wants to know more about it.

### **Pneumothorax in PCP**

Pneumothorax develops in patients with PCP in approximately 5% of cases [17]. A 1996 retrospective study at Bellevue Hospital in New York City revealed that 67 of 1360 (4.9%) patients hospitalized with PCP developed pneumothorax. Pneumothorax developed as a consequence of mechanical ventilation or an invasive procedure in 56% of the cases and 22 (44%) were spontaneous. Patients who developed pneumothorax in the course of mechanical ventilation had 100% mortality whereas most of the others were successfully treated with tube thoracostomy [18]. Risk factors for spontaneous pneumothorax in-patients with PCP have been identified as cigarette smoking, history of pentamidine chemoprophylaxis and pneumatoceles identified on chest x-ray [19]. Pneumothorax is felt to develop primarily in the setting of rupture of cystic lesions that may be present in active disease or left over from a prior infection. Multiple studies revealed that patients receiving inhaled pentamidine had increased incidence of upper lobe disease on radiographic appearance [15, 16]. For a time this was thought to be due to the preferential deposition of drug in the lower lobes. In fact, a study done by Braughman et al. in Cincinnati assessed the relative distribution of *P. carinii* in the lungs.

Lavage specimens from the middle lobe were compared with specimens from the apical segment. When comparing groups who had received pentamidine or not there was no difference found. Both groups demonstrated significantly higher numbers of P. carinii clusters in the apical segment compared with the middle lobe lavage specimen [20]. Therefore, while those receiving pentamidine may have predominance of upper lobe disease more frequently than those receiving other forms of prophylaxis, the explanation for this phenomenon is not entirely clear. In lungs damaged by PCP-induced pneumothoraces, histologic examination reveals subpleural necrosis and bleb formation due to direct tissue invasion. Perhaps in Gary's case, profound immunosuppression led to high levels of organisms in the apical area. That and his heavy tobacco use led to greater tissue destruction. Bilateral pneumothoraces have been described in a small subset of patients in the studies previously mentioned. Gary's case is thus atypical but not unique. His pneumothoraces were aggressively and successfully managed with chest tubes and his course of therapy led to resolution of his symptoms. His radiograph continued to demonstrate diffuse infiltrates after 21 days of therapy, but his oxygenation was normal and his exercise tolerance was markedly improved from admission. It will now be his task to participate in his health care and adhere to the medical regimens prescribed.



