CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 20-2014: A 65-Year-Old Man with Dyspnea and Progressively Worsening Lung Disease

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PRESENTATION OF CASE

Dr. Gregory K. Robbins: A 65-year-old man with a history of emphysema and inflammatory colitis was admitted to this hospital because of dyspnea, hypoxemia, and worsening lung disease.

The patient had been well until approximately 3 years before admission, when herpes zoster infection (shingles) occurred; shortly thereafter, episodes of bloody diarrhea developed, after which a diagnosis of inflammatory colitis was made at another hospital. Two years before admission, mesalamine was administered for treatment of the colitis, with improvement of his symptoms. During the next 2 years, progressive dyspnea on exertion occurred. One year before this admission, pulmonary-function tests were performed, and diagnoses of chronic obstructive pulmonary disease (COPD) and advanced emphysema were made. Tiotropium bromide was administered by inhalation. During the 6 months before this admission, numerous episodes of worsening dyspnea occurred. Supplemental oxygen (2 liters per minute through a nasal cannula, as needed), multiple courses of antibiotics, and tapering courses of prednisone were administered, with transient improvement. Approximately 5 months before this admission, cough with sputum production developed.

Dr. Carol C. Wu: A computed tomographic (CT) scan of the chest, performed at the other hospital, showed moderately severe centrilobular emphysema with bilateral lower-lobe basilar opacities, which may represent mild atelectasis, aspiration, or pneumonia. The main pulmonary artery was dilated, which can be seen in cases of pulmonary hypertension.

Dr. Robbins: Three months before admission to this hospital, a stress echocardiogram revealed fair-to-poor exercise capacity that was consistent with deconditioning, a left ventricular ejection fraction of 65%, diastolic dysfunction, and an estimated pulmonary-artery pressure of 45 mm Hg. The patient traveled to Florida for 1 month and felt relatively well on his return. Approximately 7 weeks before this admission, dyspnea on exertion worsened; supplemental oxygen (2 liters per minute through a nasal cannula) was administered.

Dr. Wu: A CT image of the chest obtained according to the pulmonary-embolism protocol at the other hospital showed emphysema with bronchial-wall thickening and new tree-in-bud and small nodular and reticular opacities in the lower lobes, the

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right middle lobe, and the lingula. A new, irregular nodular opacity in the right lower lobe measured 1.8 cm by 1.4 cm. The findings were thought to represent aspiration or pneumonia. There was no evidence of pulmonary emboli.

Dr. Robbins: Approximately 3 weeks before admission, dyspnea on exertion worsened and was associated with a nonproductive cough and temperatures to 37.8°C; the patient became unable to walk short distances in his home. Prednisone, tiotropium (by inhalation), mometasone furoate and formoterol fumarate dihydrate (in combination, by inhalation), and azithromycin were administered, without improvement. Oxygen saturation on exertion measured 75% while the patient was breathing 2 liters per minute, and supplemental oxygen was increased to 4 liters per minute through a nasal cannula, 24 hours daily. The administration of levofloxacin was begun, and 2 days later, he was admitted to the other hospital.

Medications at home also included metoprolol, lisinopril, and gabapentin. On examination, the temperature was 36.8°C, the blood pressure 119/73 mm Hg, the pulse 83 beats per minute, and the respiratory rate 30 breaths per minute; the oxygen saturation was 70% while the patient was breathing ambient air, and it rose to 95% with supplemental oxygen flow at 4 liters per minute. Examination of the chest revealed decreased breath sounds at the right base and diffuse wheezing in the upper lung fields. Blood levels of platelets, electrolytes, glucose, calcium, creatine kinase, and creatinine were normal; other test results are shown in Table 1. An electrocardiogram showed occasional premature ventricular complexes.

Dr. Wu: Posteroanterior and lateral chest radiographs showed new hazy opacities in both lungs, most prominently in the right middle lobe (Fig. 1A and 1B). CT of the chest was then performed, which revealed bilateral ground-glass opacities (Fig. 1C and 1D), with more severe involvement of the right middle lobe, right lower lobe, and superior segment of left lower lobe and less severe involvement of the upper lobes. The tree-in-bud and nodular opacities noted on the previous CT scan had resolved, a finding consistent with resolved pneumonia. There was no evidence of mediastinal or hilar lymphadenopathy or pleural effusions. No evidence of traction bronchiectasis or honeycombing was found, which would have suggested interstitial fibrosis. The heart was not enlarged.

Dr. Robbins: Serologic testing, including testing for antinuclear antibodies, antineutrophil cytoplasmic antibodies, and rheumatoid factor, was negative. A blood test for galactomannan antigen was negative. Prednisone, gabapentin, mesalamine, ipratropium bromide by inhaler, albuterol sulfate by inhaler, and levofloxacin were administered. The patient remained afebrile and without sputum production. Two days before admission to this hospital, his respiratory status worsened. His supplemental oxygen needs increased to 80% oxygen through a face mask to maintain oxygen saturations between 85% and 90%. Prednisone was stopped, and methylprednisolone and trimethoprim–sulfamethoxazole were administered. An echocardiogram showed normal left ventricular function, an ejection fraction of 50%, and a positive bubble study (i.e., the injection of agitated saline showed evidence of right-to-left shunting across the interatrial septum). One day before admission, cardiac catheterization showed normal coronary arteries, a mean pulmonary-capillary wedge pressure of 13 mm Hg, and a pulmonary-artery pressure of 39/20 mm Hg (mean, 28), with no evidence of left-to-right shunting. On the ninth day, he was transferred to this hospital for further treatment.

The patient had hypertension, hyperlipidemia, and depression. Medications on transfer included methylprednisolone sodium succinate, trimethoprim–sulfamethoxazole, levofloxacin, escitalopram, gabapentin, heparin, metoprolol, pantoprazole, mometasone, acetaminophen, and lorazepam; he also was receiving 80% oxygen through a face mask. He had no known allergies. He was retired, having previously worked in sales. He lived with his wife and pet dogs and cats. Before this illness, he did yard work occasionally and had no known exposures to pet birds or hay and no occupational exposures, including asbestos. He drank two alcoholic beverages daily, did not use illicit drugs, and had smoked for 50 pack-years until stopping 8 months before admission because of dyspnea. His mother had COPD, and his children and grandchildren were healthy.

On examination, the temperature was normal, the blood pressure 130/90 mm Hg, the pulse 90 beats per minute, and the respiratory rate 24 breaths per minute. Breath sounds were diminished, without wheezes or crackles. Oxygen saturation was 67% on arrival, while the pa-

Table 1. Laboratory Data.*

Variable	Reference Range, Adults†	Other Hospital, 8 Days before This Admission	This Hospital, on Admission
Hematocrit (%)	41.0–53.0 (men)	42.9	38.0
Hemoglobin (g/dl)	13.5–17.5 (men)	13.6	12.3
White-cell count (per mm^3)	4500–11,000	9300	7500
Differential count (%)			
Neutrophils	40–70	86	96.4
Lymphocytes	22–44	9	2.8
Monocytes	4–11	4	0.7
Eosinophils	0–8	1	0
Mean corpuscular volume (μm^3)	80–100	87	84
D-Dimer	Negative	Negative	
Urea nitrogen (mg/dl)	8–25	29 (ref 7–20)	30
Total protein (g/dl)	6.0–8.3		5.7
Albumin (g/dl)	3.3–5.0		2.8
B-type natriuretic peptide (pg/ml)	0–300	988.5	
Blood gases (venous)			
Fraction of inspired oxygen			unspecified
pH	7.30–7.40		7.44
Partial pressure of carbon dioxide (mm Hg)	38–50		40
Partial pressure of oxygen (mm Hg)	35–50		60
Base excess (mmol/liter)			2.0

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. The abbreviation ref denotes reference range at the other hospital.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

tient was breathing oxygen (4 liters per minute) through a nasal cannula; it rose to 89 to 90% with the administration of oxygen (10 liters per minute) through a face mask, and approximately 2.5 hours later, it increased to 93% with the use of a high-flow face mask that delivered a fraction of inspired oxygen of 60%. The remainder of the examination was normal. An electrocardiogram showed sinus rhythm at a rate of 91 beats per minute, with occasional premature ventricular complexes and possible premature atrial complexes with aberrant conduction. Approximately 3.5 hours after the patient's arrival, blood levels of electrolytes, calcium, phosphorus, magnesium, globulin, and creatinine were normal, as were the platelet count and results of tests of liver function and coagulation; other test results are shown in Table 1.

Dr. Robbins: Diagnostic tests were performed.

DIFFERENTIAL DIAGNOSIS

Dr. Kathleen M. Finn: The patient is a 65-year-old grandfather, with 2 years of progressive dyspnea on exertion and a 50-pack-year history of smoking. The patient was transferred to this hospital with worsening dyspnea, nonproductive cough, low-grade fever, and hypoxemia that was unresponsive to prednisone and antibiotics.

Initially, I assumed that the 2 years of progressive dyspnea and the current illness were related. Most patients with chronic dyspnea have

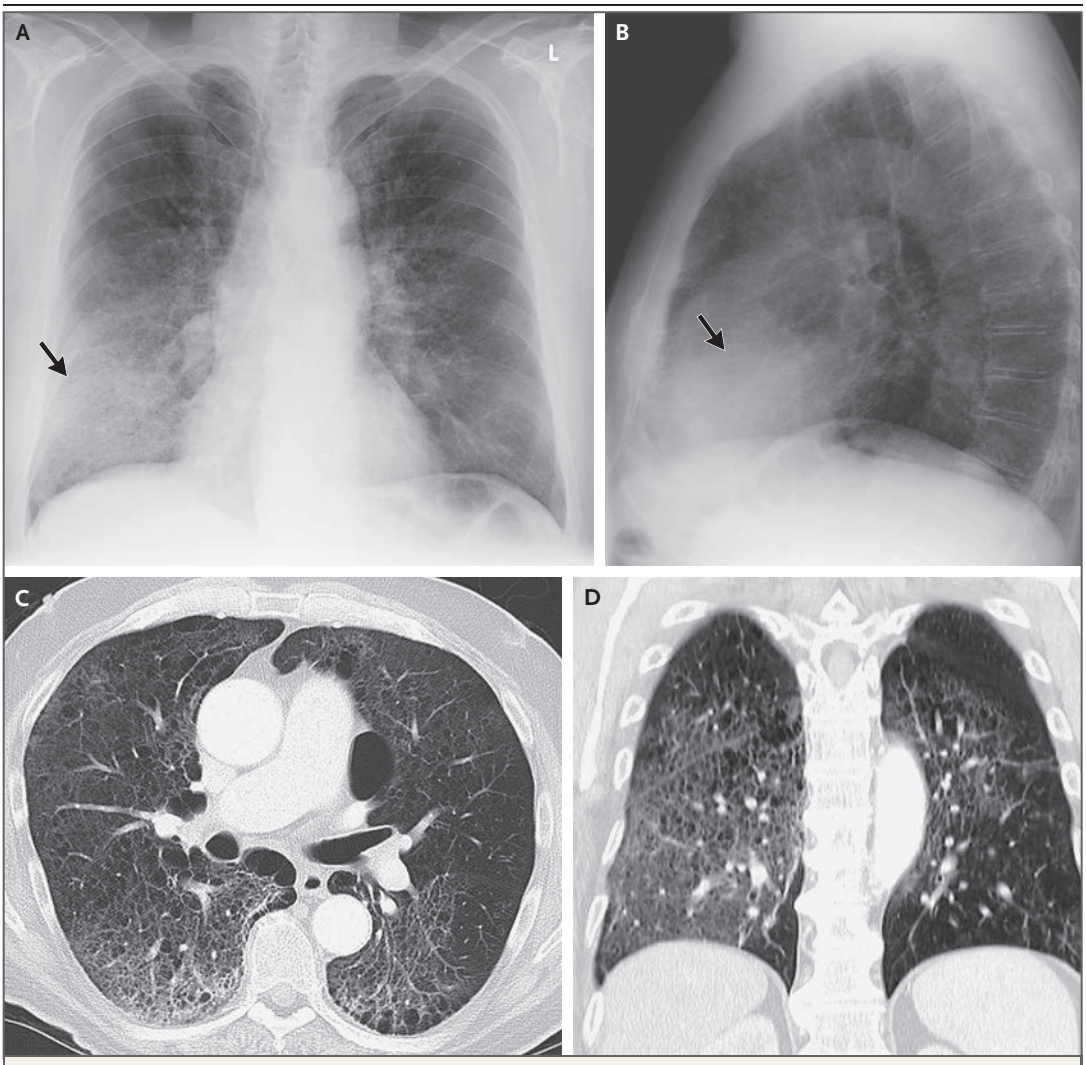

Figure 1. Chest Imaging.

A chest radiograph shows new bilateral hazy opacities that are most predominant in the right middle lobe (Panels A and B, arrows). CT images of the chest show diffuse, bilateral ground-glass opacities without evidence of lymphadenopathy or pleural effusions (Panel C, axial image, and Panel D, coronal image).

a condition that falls into one of five broad categories: asthma, obesity or deconditioning, cardiac diseases, COPD, or interstitial lung disease.[1] This patient had no history of asthma, and obesity or deconditioning would not cause this magnitude of hypoxemia. He had an extensive cardiac evaluation that did not reveal a reason for his dyspnea. His pulmonary-capillary wedge pressure is consistent with heart failure, although I would expect the wedge pressure to be higher with this degree of hypoxemia. On examination, there was no jugular venous distention. Chest imaging revealed no pleural or pericardial effusions. Although the B-type natriuretic peptide level was markedly elevated, at 988.5 pg per milliliter, patients with a history of left ventricular dysfunction can have an elevated level that is unrelated to their dyspnea.[2]

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Could a diagnosis of COPD explain this patient's chronic dyspnea? His substantial smoking history increases the likelihood that COPD was the cause of dyspnea (likelihood ratio, 8.0 to 19.0).[3] Also consistent with a diagnosis of COPD is his previous improvement when he was treated with antibiotics and glucocorticoids. However, I am bothered by the abrupt acceleration of these re-

cent dyspneic events. Recurrent upper respiratory tract infections triggering an exacerbation of COPD could partially explain his condition, but these exacerbations are new for him. Why were the symptoms of COPD manifested now? The patient also recently quit smoking, which is often a red flag that a patient is feeling poorly.

Because I assumed that the patient had a chronic, progressive process, I was surprised to find that three CT scans of the chest obtained over a 6-month period showed no progression of disease. Instead, the most recent CT scan showed entirely new, diffuse, isolated ground-glass opacities. Ground-glass opacities are abnormalities below the spatial resolution of the CT scan that do not obscure bronchial or vascular margins, unlike opacification due to a consolidation. They can be focal, patchy, or diffuse.[4] Histologically, they represent partial filling of air spaces by exudate, fluid, or blood, increased pulmonary-capillary blood volume, partial collapse of alveoli, or interstitial thickening.[5] The differential diagnosis of these opacities is therefore quite broad. However, they are usually associated with other CT findings. For example, the halo sign that is associated with aspergillosis consists of ground-glass opacities surrounding a focal area of consolidation. Unusual in this case is that the opacities are isolated, meaning that they are not associated with any other radiologic findings. The list of diseases that cause acute or subacute, isolated ground-glass opacities is relatively short (Table 2).[4]

Table 2. Causes of Diffuse, Isolated Ground-Glass Opacities.

Opportunistic infections
Pneumocystis pneumonia
Cytomegalovirus pneumonia
Herpes simplex virus pneumonia
Respiratory syncytial virus bronchiolitis
Interstitial lung diseases
Desquamative interstitial pneumonia
Respiratory bronchiolitis-associated interstitial lung disease
Nonspecific interstitial pneumonia
Acute interstitial pneumonia
Hypersensitivity pneumonitis
Cryptogenic organizing pneumonia
Alveolar diseases
Pulmonary edema
Diffuse alveolar hemorrhage
Acute respiratory distress syndrome
Drug toxicity

ACUTE AND SUBACUTE INTERSTITIAL LUNG DISEASES

Interstitial lung diseases are a group of disorders characterized by cough, dyspnea, and hypoxemia, similar to this patient's presentation. Several types of interstitial lung disease are associated with diffuse, isolated ground-glass opacities. Desquamative interstitial pneumonia and respiratory bronchiolitis are possible diagnoses in this case, especially given the patient's smoking history.[6] Each of these diseases can develop over a period of weeks, but it is more likely that they will be manifested over a period of months. A few features of this case make these diagnoses unlikely. First, these diseases tend to occur in the fourth to fifth decade of life, and this patient is in his seventh decade. Second, progression of desquamative interstitial pneumonia often stabilizes in conjunction with smoking cessation and treatment with glucocorticoids, which did not occur, and respiratory bronchiolitis is associated with a clinical course that is more benign than that in this case.

Nonspecific interstitial pneumonia can occur over a period of weeks, but it is more likely to develop over a period of months.[7] Approximately one third of patients with this disease have influenza-like symptoms, and most patients have fine crackles on examination, neither of which this patient had. Nonspecific interstitial pneumonia is frequently associated with connective-tissue diseases or the presence of elevated levels of rheumatoid factor or antinuclear antibodies.[8] This patient had no symptoms suggestive of a connective-tissue disease, and tests for both rheumatoid factor and antinuclear antibodies were negative.

Acute interstitial pneumonia is a consideration in this patient, especially given his rapidly progressive respiratory failure. However, most patients with this disease report an influenza-like syndrome, and although diffuse, isolated ground-glass opacities may be the initial finding on CT of the chest, progression to consolidation (similar to that in the acute respiratory distress syndrome) occurs quickly, unlike in this case.[9] Hypersensitivity pneumonitis is also unlikely in this patient, since he had no history of inhalation of agricultural organic antigens or occupational exposures.

Finally, cryptogenic organizing pneumonia (formerly known as bronchiolitis obliterans with organizing pneumonia) needs to be considered because of an association with inflammatory bowel disease.[10] We are told that this patient had a diagnosis of inflammatory colitis. However, diffuse, isolated ground-glass opacities are rare in patients with this disorder, who classically present with patchy consolidation and have a rapid clinical improvement in association with the administration of glucocorticoids.[11]

DRUG TOXICITY

Various medications have been implicated in ground-glass opacities. This patient was receiving metoprolol, lisinopril, gabapentin, and mesalamine when this recent episode started. Of the medications on this list, only mesalamine has been associated with dyspnea, nonproductive cough, and low-grade fevers.[12] Symptoms of pulmonary toxic effects of mesalamine can occur from days to years after starting the medication. This patient had been receiving the drug for 2 years. However, patients who have toxic effects associated with the use of mesalamine usually have evidence of consolidation, infiltrates, and effusions and do not have diffuse, isolated ground-glass opacities. Therefore, it is unlikely that mesalamine was the cause of the patient's symptoms.

OPPORTUNISTIC INFECTIONS

The infections associated with diffuse, isolated ground-glass opacities include respiratory syncytial virus (RSV), cytomegalovirus (CMV), herpes simplex virus, and pneumocystis pneumonia. RSV is a serious cause of infection in the elderly, affecting 3 to 7% of elderly persons annually.[13] Those with COPD are at higher risk for RSV infection. Because RSV affects the bronchiolar epithelium, leading to obstruction and increased airway resistance, wheezing (which this patient initially had) is common. However, the infection starts in the nasopharynx, with coryza, rhinorrhea, sinusitis, or conjunctivitis, and spreads to the lungs 1 to 3 days later. This patient had none of these symptoms, making RSV infection unlikely.

CMV pneumonia is very unusual in immunocompetent hosts; patients with CMV pneumonia typically have fever, dyspnea, and nonproductive cough occurring over a 2-week period, with severe hypoxemia.[14] However, these patients usually have multiorgan involvement, including retinitis, hepatitis, or colitis, none of which this patient had. Herpes simplex virus pneumonia is seen almost exclusively in immunocompromised hosts. Although the symptoms are similar to those of CMV pneumonia, herpes simplex virus spreads from either extension or aspiration of the virus from an oral lesion or hematogenous spread from genital lesions.[15] We are not told that this patient had any oral or genital lesions. This leaves pneumocystis pneumonia, the last item on my list.

PNEUMOCYSTIS PNEUMONIA

Does this patient have pneumocystis pneumonia? When considering this possibility, we need to keep in mind that there are two distinct clinical manifestations of pneumocystis pneumonia, depending on whether a patient has or does not have human immunodeficiency virus (HIV) with the acquired immunodeficiency syndrome (AIDS).[16] Although patients in both categories present with a nonproductive cough, dyspnea, hypoxemia, and low-grade fever, patients with HIV–AIDS typically have a much longer prodrome (weeks instead of days), a higher organism load, and less severe hypoxemia. Diffuse, bilateral, isolated ground-glass opacities are common in both groups of patients, but especially in patients with HIV infection.[17] Which pattern does this patient have? The duration of his prodrome would suggest that he has HIV infection, but his hypoxemia is rather severe, so it is difficult to determine.

Why would this 65-year-old grandfather have pneumocystis pneumonia? In this patient, we need to consider glucocorticoid-induced immunosuppression and defects in T-cell–mediated immunity.

GLUCOCORTICOIDS

We are told that numerous courses of prednisone were administered to the patient during the previous 6 months, and glucocorticoid use is associated with a higher risk of the development of pneumocystis pneumonia. In reports of HIV-negative patients with pneumocystis pneumonia, 92% were taking glucocorticoids within 1 month before diagnosis.[18,19] However, nearly all patients had other underlying conditions related to immunocompromise (e.g., cancer, autoimmune disease, or vasculitis) or had undergone organ transplantation, and the median prednisone dose was 30 mg for 12 weeks. Although I cannot entirely rule out

glucocorticoid use as a cause for pneumocystis pneumonia, the patient did not take prednisone while he was in Florida, which makes it less likely to be the culprit. In addition, pneumocystis pneumonia in a patient with COPD and intermittent glucocorticoid use is rare.

DEFECTS IN T-CELL–MEDIATED IMMUNITY

We next need to consider an underlying defect in T-cell–mediated immunity. Eight days before his transfer to this hospital, the patient had lymphocytopenia, which I initially attributed to his prednisone use. However, when I calculated the absolute lymphocyte count, it was astonishingly low (837 cells per cubic millimeter). One study showed that a lymphocyte count less than 800 per cubic millimeter had 100% specificity for a CD4 T-cell count less than 200 per cubic millimeter.[20] Although most causes of lymphocytopenia (Table 3) have already been ruled out, we still need to consider primary immunodeficiency, idiopathic CD4+ lymphocytopenia, and HIV infection.

Primary immunodeficiencies presenting in adulthood are rare and are mostly humoral deficiencies. Idiopathic CD4+ lymphocytopenia is a condition defined by the Centers for Disease Control and Prevention (CDC) as depletion of CD4+ T-lymphocytes to less than 300 per cubic millimeter, in the absence of HIV infection or other immunodeficiency.[21] It is a clinically rare and heterogeneous disorder that occurs in a range of patients, from those who are asymptomatic to those with recurrent opportunistic infections. It has been associated with inflammatory bowel disease. However, the diagnosis of idiopathic CD4+ lymphocytopenia can be considered only in HIV-negative patients. Could this patient have HIV infection despite having no known risk factors? On the basis of CDC guidelines for universal HIV screening, his age is not even within the recommended range of 13 to 64 years. It is Arthur Miller's play *Death of a Salesman* that suggested to me a risk factor in this retired salesman; he is human, and affairs are common.

It is the 30,000-ft view of the patient's medical history that provides clues that he has HIV–AIDS. Herpes zoster infection developed 3 years before the patient's presentation, and although it is common in patients older than 50 years, it suggests waning immunity; had he been younger at the time of that diagnosis, he might have been tested then for HIV. The bloody diarrhea, which was attributed to inflammatory bowel disease, could suggest infections or mucosal immune dysfunction. The rapid progression of COPD over a period of 2 years is unusual, but accelerated COPD has been reported in patients with HIV infection.[22] The numerous episodes of shortness of breath, starting 6 months before presentation, suggest recurrent infections. It is even possible that pneumocystis pneumonia developed earlier and was partially treated each time the patient received glucocorticoid therapy, although the two previous CT images do not suggest this. Another clue is the low albumin level, which suggests a chronic inflammatory process. As physicians, we are all subject to "framing bias" (in which diagnostic possibilities are limited by how we perceive a grandfather with dyspnea) and unfortunately do not always think of new HIV infections in older patients. As a result, HIV in this population is frequently diagnosed late.

My diagnosis is HIV infection and pneumocystis pneumonia; I would test for HIV antibodies and obtain an induced-sputum sample to test for *Pneumocystis jirovecii*.

Table 3. Causes of Lymphocytopenia.

Infections
Bacteria
Viruses (human immunodeficiency virus)
Fungi and parasites
Primary immunodeficiency
Common variable immunodeficiency
IgA deficiency
Medications and radiation
Glucocorticoids
Chemotherapy
Autoimmune diseases
Lymphoma and malignant conditions
Other
Renal failure
Aplastic anemia
Cushing's disease
Heavy alcohol use
Malnutrition
Protein-losing enteropathy
Idiopathic CD4+ lymphocytopenia

Dr. Eric S. Rosenberg (Pathology): Dr. Ginns, what was your impression when you evaluated this patient?

Dr. Leo C. Ginns: It was evident that this patient had COPD with elements of emphysema and bronchiectasis. Superimposed on this, I suspected that another event, such as aspiration, had occurred and partially resolved itself. The development of an interstitial process had prompted the patient's transfer to this hospital for further evaluation and management. The referring physician thought that the patient had a progressive interstitial lung disease of unknown origin for which lung biopsy and eventual lung transplantation might be indicated. When I evaluated this patient, the diffuse radiographic changes seen on his most recent chest imaging were classic for pneumocystis pneumonia. Before consideration of bronchoscopy or other more invasive procedures, I ordered an HIV test and obtained an induced-sputum sample for pneumocystis testing.

CLINICAL DIAGNOSIS

Interstitial lung disease, probably due to pneumocystis pneumonia.

DR. KATHLEEN M. FINN'S DIAGNOSIS

Pneumocystis pneumonia and advanced HIV infection.

PATHOLOGICAL DISCUSSION

Dr. John A. Branda: An immunofluorescence assay specific for *P. jirovecii* performed on an induced-sputum specimen collected on the first hospital day was positive (Fig. 2). This confirmed the diagnosis of pneumocystis pneumonia. In addition, a 1,3-β-D-glucan assay performed on serum collected on the first hospital day was positive at 370 pg per milliliter (reference range, <60) and supports the diagnosis of pneumocystis pneumonia.[23-26] The second diagnostic test was HIV antibody testing, which was positive, establishing the diagnosis of HIV infection.

MANAGEMENT

Dr. Robbins: At the time of diagnosis, this patient's CD4+ T-cell count was 15 per cubic millimeter (4.1%), which supported the diagnosis of HIV–AIDS. The HIV RNA (viral load) was 200,000 copies per milliliter, and genotype testing revealed no HIV drug-resistance mutations. Since patients presenting with a CD4+ T-cell count of less than 50 per cubic millimeter and an active opportunistic infection are at a significantly increased risk for additional infections, careful screening for other infections was performed.[27] The viral load for CMV was 1070 copies per milliliter.

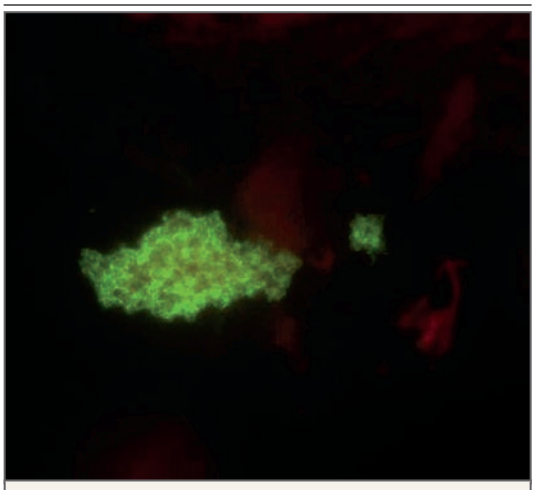

Figure 2. Immunofluorescence Staining of an Induced-Sputum Specimen.

A direct immunofluorescence antibody stain specific for *Pneumocystis jirovecii* highlights a cluster of cysts in sputum. The morphologic features of the cysts, coupled with apple-green fluorescent staining, are diagnostic of *P. jirovecii* infection.

The administration of high-dose oral trimethoprim–sulfamethoxazole was initiated. We continued the administration of prednisone, which was slowly tapered over a 3-week period.[28-30] Observing an acceptable side-effect profile after the patient had received trimethoprim–sulfamethoxazole for several days, we began antiretroviral therapy and prophylaxis for *Mycobacterium avium–intracellulare* infection. For the initial treatment of HIV infection, we elected to start with elvitegravir, cobicistat, tenofovir, and emtricitabine.[31] With respect to the patient's CMV viremia, current guidelines do not recommend treating asymptomatic infection.[28,32]

Despite rapid virologic suppression in the patient, his CD4+ T-cell count was slow to rebound. Failure of CD4+ T-cell reconstitution (i.e., immunologic failure) occurs in approximately 10 to 15% of patients with HIV infection and has been associated with poor outcomes.[33-35] This patient's treat-

ment was also complicated by transient adrenal insufficiency. Currently, the HIV is fully suppressed, but he continues to struggle with pulmonary disease. I have no doubt that if his HIV infection had been diagnosed earlier, many of these complications could have been avoided.[36,37]

In hindsight, this case clearly shows numerous missed opportunities for HIV testing, such that the patient was placed at increased risk for progressive pulmonary disease, opportunistic infections, and death. Patients are not always forthcoming with their physicians about risk factors, especially those that may have occurred years earlier, which is why it is critical that all adults be tested for HIV. Since 2006, the CDC has recommended universal testing up to the age of 64 years,[38] but as the epidemic ages, this case and others[39] suggest that we should routinely test older patients too.

FINAL DIAGNOSIS

HIV infection with AIDS and pneumocystis pneumonia.

This case was presented at the Medical Case Conference.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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