BMJ Case Reports

TITLE OF CASE

A case of organizing pneumonia in human immunodeficiency virus infection

SUMMARY

A man in his fifties presented to his doctor with a fever, sore throat, cough, dysgeusia, and dyspnea of several days' duration. Tests for human immunodeficiency virus (HIV) antigen, HIV antibody, and HIV-PCR were positive. He was referred to our hospital for initiation of antiretroviral therapy and bronchoscopy to clarify the cause of an abnormal lung shadow on chest computed tomography. He was diagnosed with organizing pneumonia, with concurrent HIV infection. His pulmonary lesions were remitted spontaneously, and he was administered a fixed-dose combination of tenofovir (50 mg), emtricitabine (200 mg), and bictegravir (25 mg) for HIV. This is a rare report of organizing pneumonia with HIV infection. Physicians need to consider organizing pneumonia when lung opacity is observed in a patient with HIV infection.

BACKGROUND

The World Health Organization (WHO) estimated approximately 38 million people were infected with HIV worldwide, with 1.7 million new cases in 2019 [1]. In Japan, there were approximately 1,000 new HIV infections in 2019, of which >70% were in men who had sex with men [2]. Although starting antiretroviral treatment (ART) in the early HIV infection phase is important, individuals with HIV infection may be asymptomatic or may experience atypical symptoms [3,4], leading to diagnosic delay. Organizing pneumonia (OP), which is classified as interstitial pneumonia, has various aetiologies from cryptogenic to secondary bacterial infections, certain drugs, and collagen-related diseases [5]. Few reports on OP with concurrent HIV or acquired immune deficiency syndrome (AIDS) have been published [6-15].

CASE PRESENTATION

A man in his fifties presented to a clinic with a fever of 38.5°C, sore throat, cough, dysgeusia, and dyspnea on exertion one and a half month before he was reffered to our hospital. He also complained of backache, diarrhea, and loss of appetite. A loop-mediated isothermal amplification test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was negative, and the doctor prescribed antibiotics. He was admitted to a hospital with hemophagocytic syndrome and was discharged after three days when his hematology normalized. His chest X-ray during the hospital stay was normal. However, his fever increased to 39°C and he developed a sore throat after discharge. The doctor noticed oral thrush, a tattoo on his left upper arm, and several enlarged lymph nodes during the outpatient clinic. A positive hepatitis B core antibody test and *Treponema pallidum* hemagglutination assay led the doctor to suspect HIV infection. Both HIV antigen and antibody tests were reported as positive, with a CD4 lymphocyte count of 353/μL(15.2%) and a viral load of 1.3×10^6 copies/mL. Western blot was reported as GP160, P68/66, P55, P24/25, and P18/17 were positive, GP110/120, P40, and P34/31 were indeterminate, and P52/51 and GP41 were negative. Computed tomography (CT) showed bilateral peripheral ground glass opacity with thickening of interlobular septa. He was referred to our hospital to perform bronchoscopy for abnormal lung infiltration observed on CT, and for initiation of antitretroviral therapy (ART). His fever persisted at 39°C, and he complained cough and exertional dyspnea on admission. He did not receive any medical care, including complementary therapies, and had no drinking or smoking habits.

His blood pressure, heart rate, body temperature, and SpO_2 were 127/93 mmHg, 101 bpm, 37.2°C, and 95% (room air), respectively. On physical examination, palpable multiple lymph nodes were observed on his neck, posterior left ear and left axillary and inguinal regions. Inspiratory fine crackles were audible on the left side of the chest. Significant laboratory data included lactate dehydrogenase, 435 IU/L (Normal range; 124–222 IU/L); C-reactive protein, 3.27 mg/dL (Normal range; 0.00–0.14 mg/dL); and CD4 lymphocyte count 186/μL (14.0 %). HIV viral load was 8.5×10^5 copies/mL. PCR for SARS-CoV-2 and bacterial cultures of sputum including tuberculosis were negative. The results of interferon-gamma releasing assay, β-D-glucan, anti-nuclear antibody and some other collagen-related diseases were entirely negative.

INVESTIGATIONS

Three weeks before the refferal, CT showed dense consolidation lining on the upper lobes' bilateral pleura and patchy infiltration beside the pleura on the left lower lobe (Figure 1A). However, stronger consolidation was observed in the left lower lobe than in the bilateral upper lobes three weeks later (Figure 1B).

Bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial lung biopsy was conducted. BAL showed lymphocyte dominance (73%). Transbronchial lung biopsy revealed alveolar macrophages proliferated in alveoli, lymphocyte-dominant inflammatory cells infiltrated in interstitial tissue, and partly, organizing changes in airspaces (Figure 2). Ziehl-Neelsen and Grocott stainings, cultures for common bacteria and tuberculoisis, and *Pneumocystis jiroveci* pneumonia (PCP)-PCR were all negative.

DIFFERENTIAL DIAGNOSIS

Overall, bacterial pneumonia, tuberculosis, PCP, and malignancy were considered unlikely. Chest CT revealed migrant shadows from the bilateral upper lobes to the left lower lobe on admission compared with those seen three weeks before, and there was spontaneous remission during the clinical course (Figure 1), which suggested OP rather than other lung diseases, such as tuberculosis or PCP.

TREATMENT

Since esophageal candidiasis was diagnosed using a gastrointestinal fiberscope, 400 mg fluconazole was prescribed for two weeks. He was administered a fixed-dose combination of tenofovir alafenamide (50 mg), emtricitabine (200 mg), and bictegravir (25 mg) for HIV, and trimethoprim-sulfamethoxazole as PCP prophylaxis due to his low CD4 count (186 cells/μL) ten days after admittion.

OUTCOME AND FOLLOW-UP

He was discharged two weeks later, after ensuring that the medication had no obvious side effects. His symptoms improved, the lung consolidation regressed, and the viral load decreased to less than 20 copies/mL over the course of outpatient follow-up. Three months following discharge, GP110/120 and P40 became negative (at first, both were indeterminant), both of P34/31 and P52/51 were positive (at first, former was indeterminant and latter was negative) on Western blot.

DISCUSSION

This is a rare report for OP with concurrent HIV/AIDS.

The patient presented with fever of over a month's duration, exertional dyspnea, and enlarged lymph nodes. As symptoms of early (acute and recent) HIV infection are usually non-specific and of short duration [3,4], individuals with HIV infection often do not present to doctors during these critical phases. However, his protracted symptoms led to multiple hospital visits, enabling early diagnosis. The World Health Organization (WHO) recommends ART initiation on diagnosis in individuals with HIV infection (Treat All). Early initiation of ART should be considered to protect others against HIV infection and improve prognosis. Patients exhibit high viral load, high infectivity, and preserved immunity in this phase than in the chronic phase [16,17]. The European AIDS Clinical Society (EACS) guidelines recommend ART initiation irrespective of the CD4 and suggest prompt ART initiation for patients with acute or early-phase HIV infection if the symptoms are severe or prolonged, with neurological involvement, low CD4 cell count and pregnancy [16]. The present case took one month from the diagnosis of HIV to ART since the patient wanted to wait for the result of HIV-PCR to make sure that he was infected with HIV, and needed time for inspection, such as bronchoscopy, and the result after admission. The EACS Guidelines document that “acute” infection is defined as HIV detection (p24 and/or HIV RNA) without HIV antibody, and “recent” infection is as HIV antibody detection up to six months after infection [16]. According to these guidelines, the average duration lacking p31 reactivity is 69.5 days. Since p31 of this patient was indeterminant in the first western blotting, and turned to positive four months later, a recent HIV infection (Fiebig stage IV) was suggested.

The diagnosis of esophageal candidiasis via gastrointestinal fiberscope suggested that the patient had AIDS. The Centers for Disease Control and Prevention (CDC) reported in 2007 that 36% of new HIV cases developed AIDS within one year [18].

OP was suspected since his chest CT exibited migrant shadows, lung biopsy (and BAL) showed lymphocyte-dominant inflammatory cells infiltrated in interstitial tissue, and organizing changes in airspaces, and his pulmonary lesions were remitted spontaneously [5, 19]. Little is known about OP with HIV infection, and most reported cases have occurred in individuals with low CD4 counts or AIDS [6-15]. The duration of OP varied from several days to several months from onset to diagnosis [20]. Three cases [6,7,8] are the only previously reported cases in which OP and HIV infection were diagnosed concurrently

and, in two of the three cases, the patients had chronic HIV infections [6,8]. The other case [7] was under the treatment of tuberculosis for four months before HIV/AIDS was detected. Rapaka et al. [9] reported a case of acute respiratory distress syndrome caused by severe acute fibrinous OP and simultaneous diagnosis of acute HIV infection. Miller et al. [21] reported that open lung biopsy was needed in 23 of 754 patients with HIV infection, of which 3 of the 23 were diagnosed with bronchiolitis obliterans OP. (One had concurrent PCP, and another had concurrent pseudomonal pneumonia.). According to the study results, 1 of 754 patients (0.13%) with lung abnormalities requiring lung biopsy had OP alone. There could be more OP patients with HIV/AIDS who have not been reported.

The present patient did not require steroid therapy, while many of the reported cases required it. Most of them were treated with steroids successfully, although one case, whose CD4 was as low as 2/mL, died of aspergillosis after receiving steroids [10]. Treatment with systemic corticosteroids usually results in a rapid and marked improvement in a manner like that in HIV disease. However, caution is advised when using immunosupressants in this population because of the increased risk of opportunistic infection particularly with advanced HIV disease [20]. The appropriate timing for using steroids, before, after, or at the same time with ART, should be further investigated.

LEARNING POINTS/TAKE HOME MESSAGES

・Physicians need to consider organizing pneumonia when lung opacity is observed in a patient with HIV infection.

・OP responds rapidly to corticosteroids with good prognostic, but physicians should take precautions especially when administering steroids to patients with low CD4 counts because of the increased risk of opportunistic infection.

・The appropriate timing for using steroids, before, after, or at the same time with ART, should be further investigated.

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FIGURE

Figure 1. Chest computed tomography (CT) images of the patient's lungs

A) The CT scan performed three weeks before admission shows dense peripheral consolidation of both upper lobes (arrows) and patchy peripheral infiltration of the left lower lobe. B) The CT scan performed on admission shows increased consolidation of the left lower lobe (arrow), which is more prominent than the consolidation of the upper lobes. C) The CT scan performed on two weeks after discharge shows less consolidation than on the two Figure 1.

Figure 2. Pathology of the patient's lungs

A) Alveolar macrophages proliferated in alveoli and lymphocyte-dominant inflammatory

cells infiltrated in interstitial tissue. H.E staining (x 10). B) Organizing changes are shown partly in airspaces. H.E staining (x 40).

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