CASE REPORT

Never too early for the opportunists!

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SUMMARY

Primary HIV infection can occur in 40–90% of individuals recently infected with HIV. Variable symptoms usually suggestive of a flu-like illness as well as high-level HIV viraemia and steep decline in CD4 cell count are often noted. We report a case of a previously healthy homosexual man who presented with symptoms suspicious of primary HIV infection as well as non-productive cough associated with chest CT finding of diffuse ground glass appearance in lungs. Recent HIV seroconversion was confirmed. Diagnosis of *Pneumocystis jirovecii* pneumonia was made on transbronchial lung biopsy. The symptoms improved rapidly after initiation of treatment with trimethoprim-sulfamethoxazole. It is important to recognise that although *Pneumocystis* pneumonia is generally seen in the setting of AIDS, it can occasionally also occur during primary HIV infection.

BACKGROUND

Pneumocystis jirovecii pneumonia (PCP) is one of the most common opportunistic infections in patients with AIDS. Since those who develop primary HIV infection are often young and healthy persons, they are generally perceived as having low risk of opportunistic infections such as PCP. However, significant changes in the immune system can occur during HIV seroconversion exposing patients to such opportunistic infections. Our case highlights the importance of recognising that opportunistic infections such as PCP can occur in patients with primary HIV infection.

CASE PRESENTATION

A 56-year-old previously healthy homosexual man presented to the emergency department with 7-week history of malaise, non-productive cough and 10-pound weight loss and 4-week history of progressive dyspnoea and fatigue. He had also noted a maculopapular rash on his face and trunk that erupted with his malaise and cough but had resolved after 3 weeks. His last sexual encounter, which was unprotected, had occurred 11 weeks prior. He carried with him a report of his last annual HIV antibody ELISA test performed 5 weeks earlier, which was negative. He had not taken any prescription or over-the-counter medications in the preceding 6 months.

On examination, he was afebrile and breathing comfortably at rest, and vital signs revealed neither tachypnoea nor hypoxia on pulse oximetry. Several subcentimeter, non-tender lymph nodes were palpable in right anterior cervical and epitrochlear regions. Chest auscultation revealed few mid-zone

and lower zone crackles. Liver and spleen were not enlarged.

INVESTIGATIONS

Initial laboratory assessment revealed only mild normocytic anaemia. CT scan of the chest demonstrated a diffuse ground glass appearance with scattered linear infiltrates in bilateral middle and lower lobes (figure 1). HIV seroconversion was suspected, and HIV antibody ELISA (third-generation assay) was repeated. ELISA was found to be positive for HIV-1, which was confirmed by western blot. CD4 cell count was 158/μL (15%). HIV-1 viral load was 4.1 million copies/mL. He remained dyspnoeic with exercise, so bronchoscopy with lavage and transbronchial biopsy were performed. Gomori methenamine silver (GMS) stain and acid-fast stains of induced sputum and bronchoalveolar lavage (BAL) specimen were non-revealing. Transbronchial lung biopsy showed interstitial pneumonia characterised by lymphoplasmacytic infiltrates and macrophages within alveolar septa. GMS stain showed occasional focal clusters of cysts of *P jirovecii* (figures 2 and 3).

DIFFERENTIAL DIAGNOSIS

Apart from primary HIV infection and opportunistic infections such as PCP, disseminated cryptococcosis, atypical mycobacterial infections, cytomegalovirus disease and disseminated histoplasmosis, the other major differential diagnoses considered were viral infection syndromes including infectious mononucleosis or respiratory viral infection and bacterial pneumonia including those caused by *Legionella*, *Chlamydia* and *Mycoplasma* species.

Figure 1 CT scan of chest.

To cite: Subedee A, Kimmel W, Donato AA. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009612

Figure 2 H&E stain of transbronchial lung biopsy (×20) showing lymphoplasmacytic infiltrates and macrophages within alveolar septa.

TREATMENT

The patient was started on trimethoprim-sulfamethoxazole for the treatment of *P jirovecii* pneumonia and discharged to home.

OUTCOME AND FOLLOW-UP

His symptoms resolved rapidly and he was started on antiretroviral therapy as outpatient 1 week later. Follow-up evaluation in 6 weeks showed appropriate viral load suppression to 27 600 copies/mL and elevation of CD4 count to 346/μL. Repeat viral load at 12 weeks was 52 copies/mL.

DISCUSSION

P jirovecii (formerly *Pneumocystis carinii*) is an opportunistic fungus recognised as one of the most common opportunistic pathogens in subjects with established AIDS. Primary HIV infection was first described as 'infectious-mononucleosis-like illness' in 1985 in 11 of 12 homosexual men who had seroconversion for HIV antibodies.¹ 40–90% of individuals recently infected with HIV may develop variable, non-specific and usually self-resolving features, such as fever, sweats, myalgia, severe fatigue, pharyngitis, diarrhoea, truncal exanthem, lymphadenopathy, leukopenia, thrombocytopenia and transaminitis.^{2–4} Diagnosis may be made by the presence of markedly elevated HIV viral load coupled with negative HIV antibody enzyme immunoassay. Combined antigen-antibody tests (fourth-generation tests which detect both antibody and p24 antigen) can reduce the window period of acute HIV infection by up to 2.35 days compared

with antibody only assays.⁵ It is possible that acute HIV infection could potentially have been diagnosed sooner, had a fourth generation been used in our case. We did not perform HIV avidity assay or detuned ELISA test to document recent seroconversion, which had clearly occurred in this patient who had been undergoing yearly HIV antibody tests and had a negative test 5 weeks earlier. CD4 T-cell counts have been shown to decline sharply in humans and in animal models during the acute infection period.^{6–9} PCP occurring concomitantly with primary HIV infection, as in the current case, has been reported in several case reports and case series.^{7–11} Other opportunistic infections such as *Candida* oesophagitis,^{8–10} cryptococcal meningitis¹⁰ and toxoplasmosis¹² have also been reported in the literature in the setting of primary HIV infection. Emerging evidence strongly suggests that early initiation of antiretroviral therapy in primary HIV infection would improve CD4 recovery and delay disease progression.^{13–14}

In our case, the diagnosis of PCP was missed by fungal staining studies of induced sputum and BAL and was made only by transbronchial biopsy. Studies have reported sensitivities of 90–99% for diagnosis of PCP with traditional staining studies, including direct fluorescent antibody staining, on BAL without transbronchial biopsy. The sensitivities are 95–100% with transbronchial lung biopsy.¹⁵ PCR test on respiratory samples appears to have higher sensitivity or specificity compared with traditional staining methods. Had this been performed in our case, it could potentially have led to the diagnosis sooner, but it is unclear if PCR can accurately distinguish between colonisation and infection.¹⁵

Our case highlights the importance of considering and pursuing the diagnoses of not only primary HIV infection but also opportunistic infections traditionally associated with advanced AIDS in the right clinical setting.

Learning points

- ▶ 40–90% of patients who develop primary HIV infection are symptomatic. Physicians should have a high index of suspicion for this diagnosis in patients with risk factors of HIV infection.
- ▶ High-level HIV viraemia and a steep CD4 decline are often seen in primary HIV infection.
- ▶ Opportunistic infections such as *Pneumocystis* pneumonia can occur during primary HIV infection.

Figure 3 Gomori methenamine silver stain of transbronchial lung biopsy (×40) showing cysts of *Pneumocystis jirovecii* organisms.

Contributors All the authors contributed substantially to the diagnosis and management of this case as well as to the drafting and revising of this article. All the authors reviewed and approved of the submitted version of the article..

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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