CASE REPORT

Pericardial effusion with *Mycobacterium avium* complex in HIV-infected patientsThajunnisha Mohamed Buhary,¹ Sedki Latif Gayed,¹ Irfan Hafeez²¹Department of GUM, East Lancashire Hospitals NHS Trust, Burnley, UK²Department of General Medicine, East Lancashire Hospitals NHS Trust, Blackburn, UK**Correspondence to**
Dr Thajunnisha Mohamed Buhary, thajunbasheer@gmail.com

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SUMMARY

Disseminated atypical *Mycobacterium* infection is a well-known opportunistic infection in HIV-infected patients with advanced immune deficiency before the introduction of combination antiretroviral therapy. Although the disseminated infection is now rare, few cases of localised infections are reported. A 38-year-old man was diagnosed with HIV infection during asymptomatic sexual health screening. Although he was asymptomatic on diagnosis, he had advanced immunodeficiency; therefore, combination antiretroviral therapy was started immediately. After 5 months of treatment, he developed pericardial effusion. *Mycobacterium* was detected from a culture of the pericardial fluid and *Mycobacterium avium* complex was identified using a gene probe test. He was treated with combination therapy for *Mycobacterium* infection and he fully recovered. Treatment continued for 4 years until he achieved adequate immune recovery.

BACKGROUND

Mycobacterium avium complex (MAC) refers to the infections caused by either of the two non-tuberculosis mycobacterial species, namely *M. avium* and *M. intracellulare*. Although the nomenclature of MAC was developed early in the HIV epidemic, the number of cases of MAC dramatically dropped in the post-highly active antiretroviral therapy (HAART) era because of the highly effective combination therapy and prophylaxis against MAC infection.^{1 2} Before the introduction of HAART, MAC was commonly presented as a disseminated disease.³ Although localised disease is uncommon, substantial numbers of cases with focal lymphadenitis were reported shortly after the introduction of HAART. Pericardial involvement in MAC infection is uncommon and only very few cases were reported in the past.^{4 5}

CASE PRESENTATION

A 38-year-old man presented to our GUM clinic for asymptomatic sexual health screening. His serological test for HIV infection was found to be positive. Subsequently his CD4 T lymphocyte count (CD4 cells) was 30 cells/mm³ and the HIV viral load (VL) was 380 000 copies/mL; a combination of HAART was immediately started.

After undergoing HAART for 5 months, he was admitted with a 2-week history of fever, progressive shortness of breath, productive cough and lethargy. His CD4 count at this point was 36 cells/mm³ with undetectable VL. Blood pressure was 95/50 and the pulse rate was 120 bpm. No heart murmurs or

pericardial rubs were heard. Lung fields were clear. Oxygen saturation was 96% and the chest X-ray (CXR) taken on the day of admission was normal. Haemoglobin was 10.3; white cell count was $6.5 \times 10^9/L$; C-reactive protein was 187; erythrocyte sedimentation rate was 120. Liver function and kidney function parameters were normal. An ultrasound scan of the abdomen did not show hepatomegaly, splenomegaly or intra-abdominal lymphadenopathy. An antibiotic for suspected bacterial pneumonia was started with co-amoxiclav.

Pneumocystis carinii pneumonia was excluded from bronchoscopy and bronchoalveolar lavage. The stain for acid fast bacillus (AFB) and the bacterial culture from the alveolar washing were negative.

ECG showed widespread ST elevation with PR depression which is suggestive of pericarditis. Repeat CXR after 1 week of hospital admission showed cardiomegaly (figure 1). Doppler echocardiography revealed a moderate pericardial effusion with no echo evidence to suggest tamponade or diastolic dysfunction. Pericardial aspiration was performed under echo guidance and clear serous fluid of 70 mL was aspirated.

INVESTIGATIONS

Stain for AFB and PCP and the bacterial culture of the pericardial fluid were negative. *Mycobacterium* had been recovered from the culture and the gene probe identified that the isolate was MAC. Pericardial fluid cytology showed amorphous proteinaceous material with small lymphocytes, scattered neutrophils and histiocytes with no malignant cells.

Pericardial fluid analysis with or without pericardial biopsy is frequently helpful, although in most cases the cause of pericardial effusion is suspected by the clinical setting in which it occurs. The bacteriological, immunological, biochemical and cytological analysis are helpful to determine the aetiology of the effusion. The most helpful and frequently used diagnostic studies are Gram stain and bacterial and fungal culture, cytology, AFB stain, and mycobacterial culture with adenosine deaminase, interferon γ , or lysozyme, and the PCR.

DIFFERENTIAL DIAGNOSIS

Although there are few case studies that described increased prevalence of pericardial effusion in HIV-infected patients, number of cases reported dramatically declined due to HAART and MAC prophylaxis. The differentials of pericardial effusions in HIV-infected patients are broad. They include infections and neoplastic aetiologies such as lymphoma and Kaposi's sarcoma. Mycobacteriae

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Figure 1 An anteroposterior chest radiograph showing cardiomegaly.

are the most common infective pathogens isolated,^{6 7} and the rare causes of *Cryptococcus*, *Nocardia*, *Listeria monocytogenes*, *Rhodococcus equi* and *Chlamydia trachomatis* should be excluded.

In our case, a presumptive diagnosis of *Mycobacterium tuberculosis* was made and antituberculosis treatment was started and continued until the definitive diagnosis of MAC was made.

TREATMENT

Therapy was started with rifampicin (600 mg/day), clarithromycin (500 mg two times per day) and ethambutol (1 g/day) with prednisolone (40 mg/day). After 2 weeks of having this combination, rifampicin was replaced with ciprofloxacin 500 mg two times per day to minimise the drug interaction and the isolate was identified as resistant to rifampicin.

Treatment of MAC should consist of two or more antimicrobial drugs to prevent or delay the emergence of resistance. It should include a macrolide and ethambutol with or without rifabutin. British HIV Association and British Infection Association guidelines for the treatment of opportunistic infections in HIV seropositive individuals (2011) and the Department of Health and Human Services guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents recommend clarithromycin as the preferred macrolide as it has been extensively studied in patients with AIDS. The addition of a third or fourth drug should be strongly considered in patients with advanced immunosuppression (CD4 count <50 cells/mm³), severely symptomatic disseminated MAC infection and a scenario where constructing an effective HAART regimen is not possible. There are limited data for the use of other drugs as third or fourth agents such as injectables like amikacin or streptomycin, or fluoroquinolones and they are only considered when the first-line drugs cannot be used because of drug interaction, resistance or intolerance.

OUTCOME AND FOLLOW-UP

His symptoms improved dramatically and he was discharged from the ward after 4-week treatment and was followed up in

the outpatient chest and HIV clinics. Treatment for MAC was continued for 4 years until his CD4 count >200 cells/mm³ for 6 months with undetectable VL.

DISCUSSION

MAC disease usually occurs in patients with CD4 count <50 cells/mm³. In these patients with severe immune depression who are not taking HAART, MAC infection typically presents as a disseminated, multiorgan infection.⁸ Patients most commonly report fever, night sweat, fatigue, weight loss, anorexia and diarrhoea. Common signs include hepatomegaly and lymphadenopathy. Laboratory abnormalities include anaemia, leucopenia, hypoalbuminaemia and elevated liver alkaline phosphatase level, whereas the radiological features include hepatosplenomegaly and intra-abdominal lymphadenopathy.⁹

Isolated organ involvement in MAC disease has been reported often in patients who have responded to HAART with improved CD4 count. This is suggested to be a manifestation of immune reconstitution inflammatory syndrome (IRIS), as in our case. IRIS in MAC disease is similar to IRIS or paradoxical reaction described in *M. tuberculosis* where bacteraemia is absent. Isolated organ involvement includes mesenteric or cervical lymphadenitis, pneumonitis, pericarditis, osteomyelitis,¹⁰ skin or soft tissue abscesses, genital sores or central nervous system involvement.¹¹

Diagnosis of MAC disease needs the isolation of MAC from cultures of blood, lymph node, bone marrow aspirate, or other normally sterile tissue or body fluids. Species identification is performed using specific DNA probes,^{12 13} high-performance liquid chromatography or biochemical tests. Rapid identification of MAC is also possible using low-cost multiplex PCR as an alternative to DNA probe method.¹⁴

Antimycobacterial treatment of MAC infection needs combination therapy that should include a macrolide and ethambutol, with or without rifabutin. A combination of at least two new drugs including fluoroquinolones, amikacin and other agents are used to treat in case of treatment failure or resistance. Treatment should be continued until the patient shows adequate immune response to HAART; otherwise, the treatment should be lifelong.

Learning points

- ▶ MAC infection should be included in the differential diagnosis in cases of pericardial effusion.
- ▶ MAC pericardial effusion can be a manifestation of IRIS in the setting of immune recovery with HAART.
- ▶ It is very tempting to avoid MAC prophylaxis with weekly Azithromycin with availability of very potent combination ARV medications. However, this case shows the importance of MAC prophylaxis to every patient with CD4 count <50 cells/mm³.

Contributors TMB conducted the literature search related to the topic. This involved online searches through databases and websites such as PubMed, Medscape and Up-to-date. In addition, TMB then planned and wrote the entire article, referring to in-ward patient notes, with the advice of SLG and IH. SLG managed the patient while he was in the ward as well as during the follow-up period, in addition to organising the diagnostics material. IH managed the patient while he was in the ward, as well as advising TMB in organising the manuscript.

Competing interests None declared.

Patient consent Obtained.

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