

CASE REPORT**AN AIDS PATIENT WITH MULTIPLE OPPORTUNISTIC INFECTIONS****Talha Mahmud**

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A patient was diagnosed having advanced acquired immunodeficiency syndrome (AIDS) who suffered from various pulmonary and extrapulmonary infective complications. A number of opportunistic infections were diagnosed and prompt treatment was initiated. Due to his low CD4+ lymphocyte count that carries a higher morbidity and mortality, he experienced clinical worsening even with treatment and could not survive through this Black Death.

Keywords: Human immunodeficiency virus (HIV), Pulmonary, Complications, Opportunistic infections, Acquired immunodeficiency syndrome (AIDS)

INTRODUCTION

The human immunodeficiency virus pandemic has spread to every country in the world including Pakistan.¹ The spectrums of infectious pulmonary and non-pulmonary complications in HIV infected individuals are entirely different from immune competent hosts and mostly these are low virulent organisms which are normally not encountered in the community or hospital based practice.² Like tuberculosis or hepatitis, AIDS is a new challenge on the rise in this part of the world where we will probably be in more encounter with such infections in the near future. In Pakistan, the HIV epidemic is currently in its early stages among people who sell sex, but there may be potential for a much greater spread given the levels of other sexually transmitted infections found and the existence of low levels of both protective knowledge and risk-reducing behaviours.³ The treating physicians have minimal training and experience of managing such pattern of infections. There should be precise measures aiming at the awareness of our medical community regarding basics of HIV and AIDS, dissemination of guidelines for its diagnosis and management, and the facilities of its treatment available under National AIDS Control Programme Pakistan or otherwise in private sector.^{4,5}

CASE REPORT

A 45-year-old businessman received pulmonary consultation while he was second time hospitalised under gastroenterology service due to severe dyspepsia. Besides epigastric discomfort, his presenting complaints included pyrexia, cough and sputum of one-week duration with a clear chest radiograph. Based on the diagnosis of infective bronchitis, he was given ceftriaxone one gram twice a day for two days followed by discharge from the hospital and oral cefixime 400 mg once daily for five days.

In his recent admission under gastroenterology service a month ago, he was diagnosed as having superficial rectal ulcers for which he received antibiotics with good recovery.

He was an ex-cigarette smoker and had history of heavy alcohol abuse. His past history included appendectomy twenty years ago, incision and drainage of foot abscess five years back and chronic hepatitis C for which he received interferons and ribavirin in 2006, and was seronegative. His family history was not significant.

In his follow-up after two weeks from hospital discharge, he presented in the pulmonary clinic with persistent symptoms including cough, high grade continuous fever and anorexia. Chest X-Ray posteroanterior view showed a small infiltrate in right lower zone, right apex and widened right para-tracheal stripe (Figure-1). Further details in his socioeconomic history revealed that he was a landlord at Shaikhupura, a town near Lahore and had history of frequent foreign travelling to Middle East (mostly UAE and Saudi Arabia) for business tours especially for buying instruments and spare parts utilised in agriculture and during his stay at foreign countries he displayed positive promiscuous sexual behaviour directed towards women. Clinical examination showed pulse 100/minute, BP 110/70 mmHg, temperature 39 °C, and respiratory rate 20/min with oxygen saturation on pulse oximeter (SpO₂) 95% on room air. He was pale, clubbed and had skin lesions on face consistent with molluscum contagiosum. Chest examination revealed bilateral vesicular breathing with fine occasional crackles in right upper part. Other systems examination revealed no abnormality except mild tenderness in the epigastrium. Owing to his chest radiographic findings, he was given oral levofloxacin 750 mg once a day and was advised to have investigations including anti HIV 1 and 2 by enzyme linked immunosorbent assay (ELISA), sputum for culture and sensitivity, and Zheil Neelson (ZN) staining, complete blood count (CBC), and repeat CXR-PA view.

In his second outpatient follow up after another seven days, he was still suffering from high-grade continuous fever, dry cough and a 6 kg weight loss. Follow up lab work up revealed positive anti HIV testing, and CBC showed Hb 10.5 g/dL, WBC 4.84×10³/μL, Platelets 377×10³/μL, Differential

WBC count (Neutrophils 78.8%, Lymphocytes 13.2%, Monocytes 7.4%, Eosinophils 0.4% and Basophils 0.2%). His absolute counts were: Neutrophils $3.81 \times 10^3/\mu\text{L}$, Lymphocytes $0.64 \times 10^3/\mu\text{L}$, Monocytes $0.36 \times 10^3/\mu\text{L}$, Eosinophils $0.02 \times 10^3/\mu\text{L}$ and Basophils $0.01 \times 10^3/\mu\text{L}$. Serum biochemistry was normal except for a raised serum lactate dehydrogenase (LDH) to 383 IU. Sputum for pyogenic culture revealed no growth after 48 hours of incubation and three sputa smears were negative for ZN staining.

He was advised to take an appointment from national AIDS treatment centre in Lahore and was hospitalised in a private room with a provisional diagnosis of HIV/AIDS with an opportunistic pulmonary infection that could be bacterial, fungal, viral or mycobacterial. His high resolution computerised tomography (HRCT) of chest was carried out on the same day of his hospitalisation and then empirically, he was started with cefotaxime 1 gm IV q8h and amikacin 750 mg IV qid. HRCT chest showed consolidation in right upper lobe mostly involving apical segment having small cavities/cysts along with findings suggestive of paratracheal, right hilar and sub-carinal lymphadenopathy (Figure-2 and 3). His bronchoscopic survey of all airways up to sub-segmental level revealed normal mucosal colour and texture with patent orifices and sub-carinae. Upper lobe apical segmental bronchoalveolar lavage (BAL) was carried out. During hospitalisation further investigations were carried out including a repeat anti HIV 1 and 2 serology that was positive. Lymphocyte count revealed; absolute T-cell count $475/\mu\text{L}$ (720–2320), absolute B cell count $68/\mu\text{L}$ (100–430), CD4+T-helper lymphocytes 2.74% (29–60%), CD4+T-helper lymphocytes absolute count $17/\mu\text{L}$ (430–1010) and reversed CD4+/CD8+ ratio. Two days after sending his BAL, a microbiologist alert call was received about the presence of heavy growth of *Nocardia* species in the specimen for which cotrimoxazole intravenous infusion 6 hourly was started. BAL was negative for ZN staining, fungal smear and silver staining for pneumocystis jirovecii. His blood culture was negative and there was growth of candida species in the urine. Four days after his hospitalisation, he developed newer symptoms including intractable headache and vomiting for which he was given symptomatic treatment. His spinal tap was done on the same day and CSF was sent for biochemistry and cell counts along with fungal smear (India ink), cryptococcal antigen (CRAG), pyogenic culture and Gram and ZN staining. Keeping in view of his very low CD4+ lymphocytes counts ($17/\mu\text{L}$) and the neurological symptoms (classic signs for meningeal irritation were absent), he was empirically started with amphotericin 50 mg/day infusion (for cryptococcal meningoencephalitis), the commonest form of central nervous system (CNS) infection in AIDS patients. His cytomegalovirus virus (CMV) IgG antibodies were positive and IgM were

negative. Toxoplasma antibodies were also negative. Two days later, another microbiologist alert call was generated confirming about the positivity of India ink stain for cryptococcus neoformans.

With all these measures, headache, fever and vomiting frequency was reduced while he was also receiving supportive treatment including omeprazole, metoclopramide and acetaminophen. CSF analysis showed Glucose 88 mg/dL, Protein 9 mg/dL, Chloride 121 mEq/L, WBC $4/\text{mm}^3$, RBC $16/\text{mm}^3$, negative AFB smear and positive CRAG.

One week after hospitalisation, he was called for his appointment from AIDS treatment centre at Shaukat Khanum Hospital, Lahore and anti-retroviral treatment was started by the infectious disease department including lamivudine 150 mg BD, nevirapine 200 mg OD and stavudine 30 mg BD.

Three days after starting anti-retroviral treatment, a set of newer symptoms jumped in with further worsening of the clinical picture. The patient experienced episodes of altered sensorium, diplopia and loss of vision lasting for 5–10 minutes. CT and MRI Brain scans were normal, while optic funduscopy showed a few retinal granular lesions and haemorrhages. On the basis of these clinical features in the presence of very low CD4+ lymphocyte count, fundoscopic findings and positive CMV IgG, a provisional diagnosis of CMV retinitis/encephalitis was made and ganciclovir 250 mg (5 mg/kg) IV q12h was added to the ongoing treatment.

His final diagnoses were advanced AIDS with opportunistic infections including *Nocardia* Pneumonia, cryptococcal neoformans meningitis, cytomegalovirus retinitis/meningo-encephalitis, oral and urinary candidiasis, fungal nails infection and molluscum contagiosum.

Besides this treatment, he was still having worsening in his neurological symptoms and had developed slight disorientation. These symptoms were probably due to raised intracranial pressure due to CNS infections (though CT/MRI brain scans were normal and no papilloedema on fundal examination), he was offered repeated spinal taps which the patient and his family refused. The same scenario could have been seen in immune reconstitution inflammatory syndrome (IRIS) in AIDS patients, so methyl prednisolone 40 mg IV q8h was started that led to only mild improvement in the clinical state.

After next two days (two weeks after hospitalisation), he experienced a severe bout of vomiting leading to aspiration. The patient became exhausted and ended up having acute respiratory failure. His family was unwilling for mechanical ventilatory support and they decided not to resuscitate him any more and he passed away in next few minutes.



Figure-1: CXR-PA of the patient showing a small infiltrate in right lower zone, right apex and widened right para-tracheal stripe.



Figure-2: HRCT chest of the patient showing consolidation in right upper lobe mostly involving apical segment having cavities.

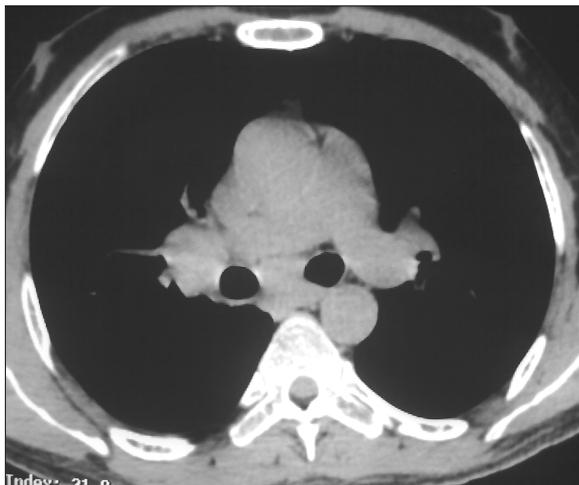


Figure-3: HRCT chest mediastinal window showing paratracheal, right hilar and sub-carinal lymphadenopathy.

DISCUSSION

The sequence of pulmonary infections (bacterial, viral, fungal and/or mycobacterial) occurring in HIV infected individuals parallels the depletion of CD4+ lymphocytes.⁶

The commonest infections include bacterial pneumonias which can occur at any CD4+ lymphocytes count. Nocardiosis, an opportunistic gram-positive infection whose isolation from respiratory tract is almost always indicative of infection has frequently been misdiagnosed initially as tuberculosis (since upper lobe involvement is common and nocardia species are weakly acid-fast). Most authorities recommend trimethoprim-sulfamethoxazole as part of first-line therapy for nocardiosis but combination therapy with other agents is warranted in patients with severe infections.⁷ Cytomegalovirus infections are the commonest viral infections in persons with AIDS. In the presence of positive serology, CMV retinitis can be diagnosed by an experienced ophthalmologist on the basis of characteristic retinal changes (yellow-white, fluffy, or granular retinal lesions associated with haemorrhage).⁸ For majority of patients, intravenous ganciclovir, or intravenous foscarnet is a preferred treatment.⁸ Pulmonary cryptococcal infection (the only encapsulated yeast that causes disease in humans) is usually clinically silent and its commonest manifestation is meningitis that occurs when the CD4+ lymphocyte count is 100–200 cells/ μ L.⁹ India ink stain or mucicramine stain can detect its polysaccharide capsule. Treatment for cryptococcal meningitis includes intravenous Amphotericin B plus oral Flucytosine as induction therapy for 14 days. If there is clinical improvement with CSF sterilisation during induction therapy, fluconazole should be used and Amphotericin B and Flucytosine can be discontinued.⁸

Non-infectious pulmonary complications of AIDS include neoplasms, interstitial pneumonias and other associations like COPD, pulmonary hypertension, and alveolar proteinosis etc.

Immune reconstitution inflammatory syndrome (IRIS) is paradoxical worsening of pre-existing infectious processes following the initiation of highly active antiretroviral therapy (HAART). Unfortunately, in most of cases, HIV-infected patients come under attention when the clinical symptoms of immune deficiency occur, often being deeply immunocompromised.¹⁰

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