Dual diagnostic dilemmas in advanced HIV

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History and Symptoms

- 44 year old male
- Referred by General Practitioner with newly diagnosed HIV
- 4 month history of dry cough, shortness of breath, fatigue, headaches, weight loss and occasional night sweats
- Transient episode of bilateral blurred vision two weeks previously, resolving spontaneously
- Identified as homosexual
- Last negative HIV test 4 years earlier and not sexually active since
- No injecting drug use, recent travel or other risk factors for blood borne viruses
- Computerized Tomography (Chest Abdomen Pelvis) with GP: - clear chest - para-aortic and mesenteric lymphadenopathy (largest 4.4mm in diameter) - hepatosplenomegaly

Clinical Examination

- Vital signs and temperature within normal limits
- Small, soft, sub-centimetre lymph nodes (anterior cervical and inguinal regions)
- Neurological examination unremarkable (cranial nerves, gait, cerebellar examination, upper and lower limb tone, power, reflexes and sensation)
- Visual Acuity 6/6 bilaterally
- Cardiovascular, respiratory and gastrointestinal system examinations unremarkable
- Urinalysis: no abnormalities

Investigations

- CD4 count 20 (x10^7/L); 3%
- HIV-1 Viral load 1,031,690 copies/ml (6.01 log10)
- HIV-1 subtype B, fully susceptible genotype.; HLA B*5701 not detected
- FBC revealed pancytopoenia with lymphopoenia; Renal and liver function unremarkable
- Syphilis, viral hepatitis, toxoplasma serology, serum cryptococcal antigen and interferon gamma release assay were unremarkable.
- Serological evidence of immunity to Hepatitis B but not to Hepatitis A
- Cytomegalovirus (CMV) IgG positive, IgM negative
- Induced sputum: CMV DNA positive; *Pneumocystis jirovecii* PCR negative; culture negative
- Blood (and Mycobacterial) cultures and Urine culture negative.
- Peripheral blood CMV DNA positive: 19,045 copies/ml (4.3 log10)
- Computerised Tomography (CT) contrast scan of brain: normal.
- Admitted to hospital
- Fundoscopy: left CMV retinitis (with CMV DNA in vitreous fluid). See images 1 and 2

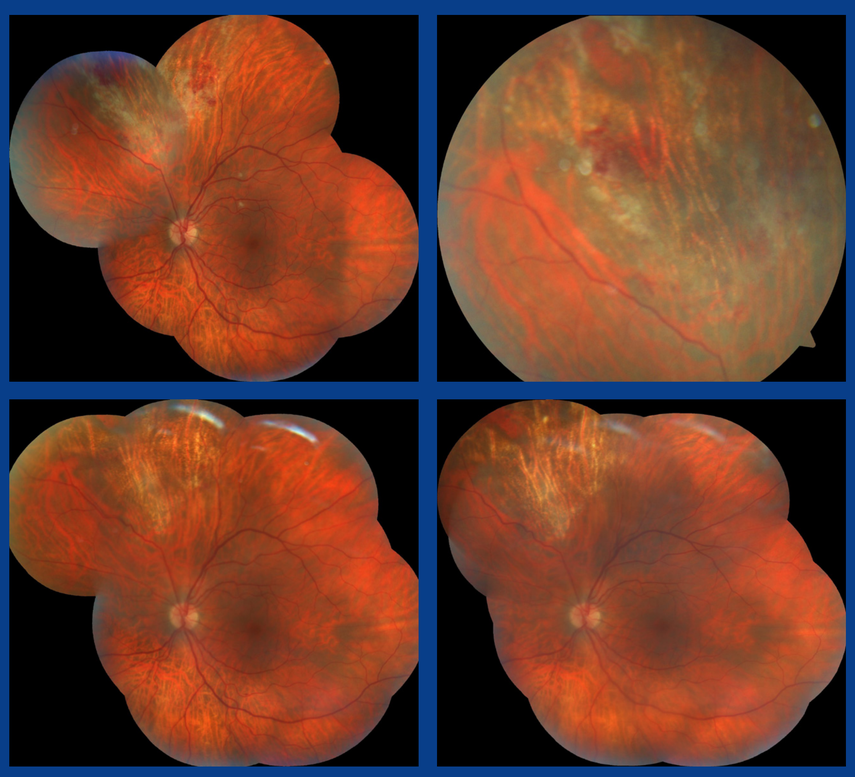

Image 1: Left eye: Superonasal changes. Macula & Disc spared. Day 10 CMV therapy

Image 2: Left eye: At 2 month (left) and 5 month (right) follow-up (CD4 count 70)

- Positron Emission Tomography (PET): glucose avid lesions above and below the diaphragm suggesting an infiltrative process. See images 3 and 4
- Lymphoma requiring prompt treatment was considered and a gated heart pool study showed normal left ventricular function
- Para-aortic lymph node (core biopsy) - insufficient for flow cytometry; reactive change, tissue stains consistent with *Mycobacterium Avium* Complex infection.

Bone marrow tissue samples: - no evidence of lymphoproliferative disorders; reactive changes, tissue stains consistent with Mycobacterium Avium Complex infection

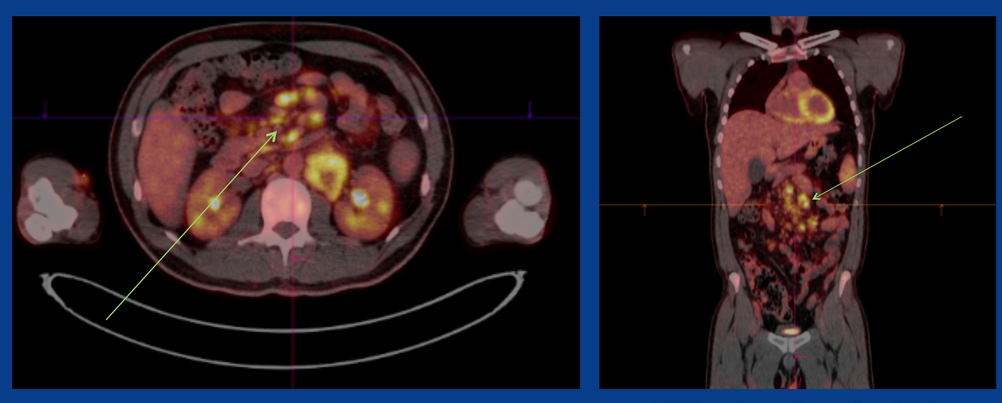

Image 3: PET shows multiple glucose avid mesenteric lesions with a peak SUV of 9.1

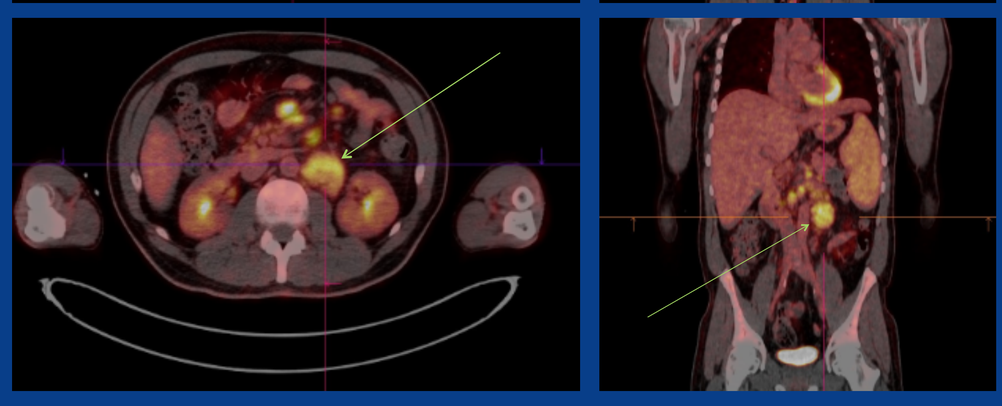

Image 4: PET shows a 44mm left para-aortic region mass with a peak SUV of 8.6

Diagnoses

- Advanced HIV with profound immunosuppression (CD4 count of 20 at diagnosis)
- Two CDC category C conditions: - *Mycobacterium Avium* Complex /MAC infection - Cytomegalovirus / CMV Retinitis

Management and Outcomes

- CMV therapy commenced with Foscarnet (2.4mg /0.1ml intra-vitreal) and Gangliclovir (oral 900mg BD, + intra-vitreal) and ongoing ophthalmology review.
- Antimycobacterial therapy: oral Clarithromycin 500mg BD & Ethambutol 1200mg OD
- Both modes of therapy tolerated well
- HIV Antiretroviral therapy commenced two weeks later: Tenofovir Alafenamide / Emtricitabine (25/200mg daily) and Dolutegravir (50mg daily)
- Remained well at follow-up with good medication adherence and tolerability
- Symptoms resolved within 4 weeks of commencing antimicrobials
- Remained on maintenance treatments and (Cotrimoxazole 400/80mg OD) PJP prophylaxis
- Followed up with Counselling, Immunology, Haematology, Ophthalmology, Sexual Health
- Vaccinated for Hepatitis A, Influenza and Pneumococcal disease

Significance

Advanced HIV with profound, life-threatening immunosuppression is still seen in Australia. This case was diagnosed in the primary care setting. Clinicians must be alert to opportunistic infections, which often have multi-system manifestations and require an index of suspicion for diagnosis. A multi-disciplinary approach was essential in the management of this case