Advanced HIV Case – Challenging the Occam's Razor, Yet Again

Tay SY[1], O'Hern J[2], Gunathilake M[3], Krause V[3], Marshall C[1]
[1]Department of Infectious Diseases, Royal Darwin Hospital, Darwin, Australia
[2]Department of Infectious Diseases, Launceston General Hospital, Launceston, Australia
[3]Centre for Disease Control, Northern Territory Department of Health, Darwin, Australia

Introduction: Patients with advanced HIV can often present with multiple simultaneous infections or pathologies, where the principle of parsimony (Occam's razor) does not stand. Here, we describe a case of a late HIV presenter with seven simultaneous infections including disseminated Mycobacterium simiae immune reconstitution syndrome (M. simiae IRS) associated with mesenteric spindle cell pseudotumour.

Case: A young previously healthy female Papua New Guinean presented with 9 months of recurrent episodes of diarrhoea, nausea, vomiting, fevers and 12kg weight loss. She was found to have gastroenteritis secondary to Cryptosporidiosis and Salmonella spp., oral candidiasis, Escherichia coli urinary tract infection, Staphylococcus aureus vulvar cellulitis, hyperchloremic metabolic acidosis and renal impairment (eGFR 19mL/min) which was likely multi-factorial in aetiology. She was diagnosed with HIV and had a CD4 T-cell count of 28 cells/uL.

Most of her symptoms resolved on antibiotics and nitazoxanide except for her fevers. Basic investigations including a CT scan of her chest, abdomen and pelvis (CTCAP) did not reveal other significant pathology. She was discharged home on antiretrovirals (ART) via compassionate access as she was on a student visa.

Two weeks later, she was readmitted from clinic with anaemia (haemoglobin 60g/L), worsening liver derangement (ALP 417 U/L, ALT 135 U/L, GGT 170 U/L), ongoing fevers and a new mild central abdominal pain. A repeat CTCAP revealed scattered pulmonary nodules, retroperitoneal and mesenteric lymphadenopathy. Sputum PCR was positive for Pneumocystis jiroverci. Despite treatment with trimethoprim/sulfamethoxazole, she remained febrile.

As disseminated mycobacterial infection was strongly suspected, mycobacterial blood culture, liver and bone marrow biopsies were performed. The biopsies only revealed one para-trabecular granuloma in the bone marrow sample with negative ziehl-neelsen stain. A subsequent PET/CT scan confirmed widespread FDG-avid lymphadenopathy with an enlarging coalescing mesenteric nodal mass (see figure). This also correlated with a development of an approximately 10x12 cm palpable central abdominal mass. Additionally, pelvic ultrasound showed bilateral hydrosapingitis and an enlarged right ovary. MRCP of liver showed intra-hepatic stricture.

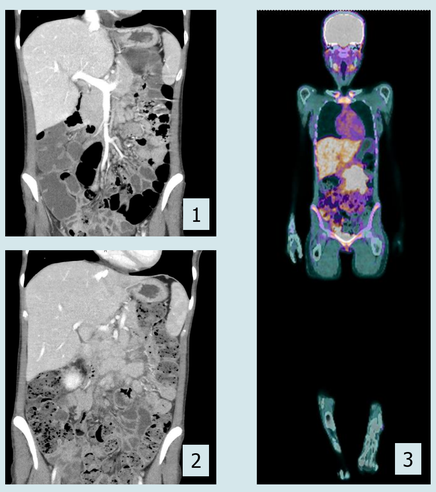

Fig.1-2. Rapid development of coalescing mesenteric lymph nodes seen on CT abdomen and pelvis 3 June (Fig.1) and 27 June 2017 (Fig.2).

Fig.3. PET/CT scan showing increased FDG uptake in large mesenteric mass. Normal FDG uptake of liver seen.

As her mycobacterial cultures were still negative at 3 weeks, she underwent laparoscopic mesenteric nodal, tubal and ovarian biopsies. Histology of the proximal small bowel mesenteric node was consistent with a mycobacterial spindle cell pseudotumour with abundance of acid-fast bacilli (AFB) seen.

Concurrently, an AFB was also identified on cultures of blood, mesenteric lymph nodes, bowel bowel, liver, bone marrow, right ovarian and bilateral fallopian tube samples at 3 – 4 weeks of incubation. Aspirates of fallopian tubes, peritoneal biopsy and peritoneal fluid were culture negative. Initial DNA probe of the AFB was positive for Mycobacterium avium complex (MAC) but subsequent DNA sequencing of all positive isolates identified M. simiae.

Approach: This patient was initially started on Genvoya (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide).

Two months in her presentation and prior to final identification of the AFB, she was empirically commenced on treatment for disseminated MAC and also possible drug-resistant tuberculous infection given the findings of oophorosalpingitis. Rifampicin, ethambutol, moxifloxacin and clarithromycin were added.

ART selection was difficult to avoid potential drug interactions, and with consideration to her low weight (36kg), renal impairment and lack of Medicare access. A decision was made to change her ART to tenofovir/emtricitabine and efavirenz. Due to her low weight, it is not possible to prescribe this as atripla as dose reduction was required for efavirenz to 400mg.

Her medical adherence was challenging due to polypharmacy, drug intolerance, development of a distressing HIV-related eosinophilic folliculitis and also complex psychosocial issues including patient's and family's acceptance of her diagnoses. Strategies employed to improve adherence includes sequential recommencement of mycobacterial treatment via directly observed therapy to identify causative agent causing gastrointestinal upset. Clarithromycin was substituted to azithromycin with resolution of her symptoms. On M. simiae identification, her treatment was subsequently streamlined to Genvoya, trimethoprim /sulfamethoxazole 800/160mg twice daily, Moxifloxacin 400mg daily, Azithromycin 250mg daily and Folic acid 5mg daily. Regular ECG was performed whilst on potential QT prolonging medications of moxifloxacin, clarithromycin and efavirenz.

Outcome: Despite sub-optimal adherence to her mycobacterium treatment, the patient's disseminated mycobacterial infection improved as her CD4 count increased with ART. Her viral load has reduced to 389 copies/ml and CD4 count continues to rise to 349 at 15 months follow-up. Her central abdominal mass is no longer palpable and her anaemia has almost normalised. Her mycobacterium treatment will continue for 12 months from time when therapy was more consistent.

Discussion: This case highlights the diagnostic and management challenges that remain in those presenting with advanced HIV, particularly in those with culturally diverse backgrounds, despite our current range of available ART.

Nontuberculous mycobacterial IRS (NTM-IRS) is well-recognised and majority of NTM-IRS are casused by MAC infection. Disseminated M. simiae related IRS, such as in this case, has been documented on immune restoration with anti-retroviral therapy (ART). Limited data exist on clinical features and management of disseminated M. simiae infections, they are often regarded to be similar to MAC infections[1]. Blood cultures are positive (90%) in disseminated MAC infection[1]. In our case, mycobacterial-specific blood culture but not conventional blood culture was able to isolate M. simiae infection. Of note, DNA-probe for MAC was not able to distinguish M. simiae infection from MAC in this case. Treatment with clarithromycin, quinolone (such as moxifloxacin) and trimethoprim/sulfamethoxazole appears promising[1,2,3]. In most NTM infections, clarithromycin and azithromycin are generally regarded as inter-exchangeable, with greater drug tolerance in azithromycin use[1]. Prognosis of disseminated M. simiae appears poor, treatment response seems to correlate with immune reconstuition with ART[2]. Hence, priority of treatment should be placed on commencement of ART.

References:
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