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CASE REPORT

Multi-Organ Failure in a Known Tuberculosis and Diabetic Patient with Advanced HIV Disease

Mwamba Precious[1], Mphaka Satch[1], Nsofwa Jubedah Mwansa[1], Mukubesa Terry Mutale[1], Mofya Yorum,[1] Gamal Maksoud[1], Mwinsa Chimese[2], Kennedy Gondwe[3], Christopher Nyirenda[1]*

[1]The Copperbelt University, School of Medicine, Internal Medicine, Ndola, Zambia.
[2]Ndola Teaching Hospital, Department of Internal Medicine, Zambia.
[3]The Copperbelt University, School of Medicine, Internal Medicine, Kitwe, Zambia.

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Corresponding Author: Christopher Nyirenda, The Copperbelt University, School of Medicine, Internal Medicine, Ndola, Zambia.

Abstract

People living with HIV are at an increased risk of not only infectious co-morbidities but also the co-existence of HIV with other chronic illnesses, notably non-communicable diseases (NCDs). Confronting the dual epidemic of HIV and its co-existence with both infectious and NCDs is a public health priority especially in countries with higher HIV burden. It is in this population that extra pulmonary or disseminate forms of tuberculosis contributing to high morbidity and mortality are likely to be reported more so in late presentation. One such presentation of a disseminated type of disease in TB may involve the meningitis to cause tuberculous meningitis. The clinical presentation of tuberculous meningitis in HIV-infected individuals may include headaches, seizures and, cranial imaging may reveal space occupying lesions such as a tuberculoma and the yield of culture of cerebrospinal fluid may also be greater. Given that delayed initiation of therapy is a strong predictor of mortality in cases of tuberculous meningitis, health care providers must consider tuberculosis in the differential diagnosis of the HIV-infected individual with lymphocytic meningitis. The presentation in this case report is further compounded by the state of nephropathy associated with encephalopathy probably secondary to obstructive uropathy in BPH, viral Hepatitis B and diabetes mellitus

Keywords: TB meningitis, $CD4^+$ count, Viral load, Diabetes, BPH, Obstructive uropathy, Acute kidney Injury.

1. Introduction

HIV continues to be a major global public health issue, having claimed about 33 million lives so far. However, with increasing access to effective HIV prevention, diagnostic, treatment and care, including for opportunistic infections, HIV infection has become a manageable chronic health condition. This has enabled people living with HIV to lead long and healthy lives [1]. The risk of developing tuberculosis (TB) is estimated to be between 16- 27 times greater in people living with HIV than among those without HIV infection [2]. In addition, HIV positive persons who become infected with hepatitis B or C virus are at increased risk of developing chronic hepatitis. Consequently, persons who are co-infected with HIV and hepatitis can have serious medical complications including an increased risk of liver related morbidity and mortality.

We present an elderly male patient who was brought to medical filter with history of fever and convulsions in a known PTB patientand newly diagnosed HIV disease pre-cART also presenting with features of prostatism. A provisional diagnosis of tuberculousmeningitis in HIV stage 4 pre cARTin suspected benign prostatic hypertrophy (BPH) with obstructive uropathy was made.

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2. History and Physical Examination (Case Presentation)

The patient was a 68-year-old Zambian male, known diabetic and newly diagnosed HIV positive patient on treatment for Pulmonary Tuberculosis but not yet on anti-retroviral therapy. He presented to medical filter with complaints of convulsions for 1 day and fever for 2 days.

The history of presenting complaints was that the patient was in usual state of health until 2 days prior when he developed fever anda day later presented with 3 episodes of fits; the 1st episode lasted about 20 minutes, involved rhythmic jerking of the patient's 4 limbs and trunk, and the patient regained consciousness immediately after.The 2nd episode happened a few minutes after the 1st one and lasted just as long as the 1st one with similar features, and the 3rd episode was terminated with some medication at the referring hospital. There was no loss of bowel and bladder control in all the episodes. However, there was visual disturbance, headache, projectile vomiting, and dizziness.

The patient gave a history of a gradual onset of productive cough associated with fevers, chills, night sweats and loss of appetite for a month at this institution where he was diagnosed with PTB and HIV with suspected prostate Cancer. He was admitted, started on medication, and discharged 4 days later.

At the time of presentation there was no cough, breathlessness,chest pain, loss of appetite, weight loss or night sweats.

Review of systems revealed presence of urgency and nocturia in the genitourinary system. The other systems were unremarkable.

Past medical and surgical history showed that the patient was recently diagnosed with HIV disease and Pulmonary TB (onsputum smear) and was being evaluated for suspected Prostate cancer. He was a known diabetic since 2005.

The patient was on 4-fixed dose combination (4FDC) of the anti-tuberculosis drugs,pyridoxine, septrin, paracetamol, metformin and silodosin but not yet on anti-retroviral drugs.

There was a positive family history of TB in the patients' sister.

The patient was married with 3 children. He did not smoke or consume alcohol. There was no history of recent travel.

In summary, this is a history of R.N M/68 known diabetic and newly diagnosed HIV disease pre-cART, with Pulmonary TB, who presented with fever for 2 days and tonic-clonic convulsions for 1 day. There was a positive history of nocturia and urinary urgency. The patient was on 4FDCs, metformin, Silodosin, paracetamol, septrin and pyridoxine. However, there was no history of photophobia, headache, projectile vomiting or dizziness. There was also no history of cough, night sweats, chest pain, weight loss, anorexia, frequency, dysuria or hematuria.

3. Provisional Diagnosis

Tuberculous Meningitis in a known diabetic andHIV stage 4 pre-cART with convulsive disorder and suspected prostate cancer.

4. Differential Diagnosis

i. Cryptococcal meningitis

ii. BPH r/o Ca prostate

iii. Tuberculoma

iv. Cryptococcoma

v. New onset epilepsy

5. Physical Examination

Physical examination in a propped-up position revealed the following;

General Condition: Stable, not in respiratory distress, oriented to time, place and person, afebrile and appeared wasted. GCS- 15/15

Vitals: BP – 114/78 mmHg, pulse rate- 115 bpm, respiratory rate- 22 breaths/min, temp- 36.6ºC and SPO_2-95% on room air.

Arm: Negative axillary lymphadenopathy bilaterally

Neck: No cervical lymphadenopathy bilaterally, no supraclavicular nodes

Face: Hadcentral pallor$^+$ but no jaundice,

Mouth: Fair oral hygiene, mucosal moist and clear.

Chest: No scars or chest deformities. Bilateral chest expansion and moving with respiration. Bi-basal crackles heard.

Precordium: No thrills or heaves, apex beat 5th ICS left midclavicular line, S_1S_2 heard, regular but tachycardic and no added sounds.

Per Abdomen: No scars, not distended, moving with respiration, non-tender, and no palpable masses. Tympanic percussion note, and bowels sounds were heard. No inguinal masses.

Urinalysis: sticks were unavailable

RDT: Negative

DRE: i. Normal anal sphincter and peri-anal region

ii. Enlarged and firm prostate

Musculoskeletal: no rash, edema, hyperpigmentation or joint deformities.

In summary, we examined male adult in semi-recumbent position. He was mildly pale, bilateral basal crackles, and tachycardia. The prostate was enlarged and firm. However, there were negative signs of meningism. Fundoscopy was not done.

6. Working Diagnosis

i. TBM in HIV stage 4, pre-cART

ii. Known DM patient with suspected BPH

7. Differential Diagnoses

i. Cryptococcal meningitis

ii. BPH r/o Ca prostate

iii. Acute Kidney Injury in Obstructive Uropathy

8. Diagnostic Features and Assessment

Per the patient's presentation of fever and convulsions, in a background of pulmonary tuberculosis with suspected prostate cancer in HIV disease, the initial impression was tuberculous meningitis secondary to pulmonary tuberculosis in HIV stage 4. A full blood count was done and it showed that the patient had a low white cell count of $3.90x10^9$/l with a normal platelet count of $231x10^9$/l. Hemogram also revealed a normocytic hypochromic anaemia with haemoglobin of 11.1g/dl. Erythrocyte sedimentation rate was markedly elevated at 122mm/lh. Therandom blood sugar was 5.4mmol/L. The malaria parasite slide analysis came out negative. The CD4 count was 120 cells/µL, Viral load of 4,340,000 copies/ml, HBsAg reactive, RPR serology non-reactive, normal ALT but elevated AST of 78.0U/l and decreased albumin of 21.5g/dl. Total serum PSA was elevated at 33.96ng/ml. Urea and Creatinine were high with values at 12.0mmol/l and 513.0µmol/l respectively.

Considering the patients elevated levels of urea, creatinine and PSA coupled with the associated co-morbid conditions, a diagnosis of obstructive uropathy secondary to BPH to rule out prostate cancer in a known PTB patient was made. A renal ultrasound and prostate biopsy were indicated. CSF analysis was non-revealing. Neuroimaging modalities such as CT scan and/or MRI and EEG were not available to help further establishthe diagnosis.

9. Management Approach

The general and pharmacological aspects of the management included the following:

9.1 General

Supportive management of the patient included iv insertion of two large bore cannulas, insertion of a foley urinary catheter, commencement of IV fluid for rehydration and proper monitoring of urine output. Initiation of cART was delayed in this patient to avoid immune reconstitution inflammatory syndrome (IRIS) as per treatment guidelines, however, the patient was counselled in readiness for possible initiation of cART in due course. Furthermore, the patient was encouraged to have enough bed rest and the nutritional department was consulted to advise on the appropriate dietfor the patient. In addition, a consultation was sent to urology for input.

9.2 Pharmacotherapy

The patient was on the following therapies

Anti-tuberculosis therapy being 3 tablets per day of the 4 fixed dose combination. This was latter adjusted per renal function. Patient also received iv antimicrobials and silodosin for urosepsis and BPH respectively. For diabetes, Metformin 850mg PO q12hr was administered. The patient was on septrin 960mg od po as prophylaxis against toxoplasmosis, pneumocystis jerovici, and GI opportunistic infections. Other medications included, fluconazole 200mg od po as prophylaxis against cryptococcal meningitis, paracetamol 1g tds po, and magnavit 1 capsule od po.

10. Follow-Up and Outcome

When the patient was initially admitted, his white cell count was at $3.90x10^9$/l but it later improved to $4.70x10^9$/l. His haemoglobin and platelet count had reduced from11.1g/dl to 9.5g/dl and 231-to-$128x10^9$/l respectively. Despite the appropriate measures instituted and good adherence to treatment, the patients' condition had deteriorated following subsequent reviews in hospital. He later developed acidotic breathinglikely a result of acute kidney injury secondary to uro-sepsis and obstructive uropathy as evidenced by his persistently elevated urea and creatinine levels. The derangements culminated into mortality after two weeks in admission to the hospital.

11. Discussion

Tuberculosis is a multi-systemic disease caused by inhalation of mycobacterium tuberculosis aerosols, hence being an airborne disease. The infection goes to the lungs where it forms a ghon focus. Later, a ghon complex forms involving the ghon focus and hilar lymph nodes (8). This outcome is what is referred to as primary pulmonary TB. Secondary pulmonary TB mayoccur either with reactivation of an old, previously latent infection or with reinfection secondary to a second exposure to the mycobacteria.

Additionally, dissemination to other organ systems may occur in advanced TB via a hematogenous route that often results in a miliary pattern within each affected organ. This pattern is likely to signify a disseminated form of tuberculosis and is common in immunocompromised persons such as those with advanced HIV infection. On the other hand,extra-pulmonary tuberculosis (EPTB) is defined as any

bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs(4).

Sites that may become involved include meninges; cervical lymph nodes (scrofula) and larynx; liver/ spleen, kidneys, adrenals, and ileum; lumbar vertebrae (Pott disease); bone marrow and fallopian tubes and epididymis. The clinical presentation of mycobacterium tuberculosis includes fevers and night sweats, weight loss, cough, and hemoptysis(7).

Nontuberculous mycobacteria, M. avium complex (MAC) typically occurs in AIDS patients with CD4 counts <50 cells/mm3 and presents as disseminated disease. The diagnosis of TB requires identification of the bacilli. Positive sputum smear necessitates culture for species identification.

HIV/AIDS and its associated opportunistic infections has emerged as a major public health concern. Despite the collaborative efforts by the international community to contain the pandemic, infections continue to be on the rise, more so in sub-Saharan Africa. The need for the continued research and sensitization of the public with regards to this deadly disease cannot be over-emphasized. In developing countries, especially Sub-Saharan Africa, HIV co-infection with TB has a strong association such that the diagnosis of one of these two warrants investigation of the other. TB-HIV/AIDS co-infection is a common presentation and we have to payparticular attention on the impact of HIV on the death of tuberculosis patients(5)

During the initial presentation of the patient, a hemogram was done and the initial WCC was low, then it later started to increase. The hemogram also showed a normal platelet count, with a normocytic hypochromic anemia, which could have been caused by the long standing infections. The ESR was markedly elevated, as a result of chronic inflammation possibly from the TB infection, and possibly other opportunistic infections. The RBS was normal and MPS negative.

A low CD4 and high VL may have resulted from delayed diagnosis and initiation of cART which may have predisposed the patient to opportunistic infections such as tuberculosis. Of the liver enzymes, ALT was normal, AST elevated and albumin levels decreased. The HBsAg test was reactive. The given outcomes probably suggested an acute on chronic disease process.

The derangements could be explained by the underlying HIV infection, which lowers the immunity and predisposes patients to infections that may affect different body systems especially pre-cART initiation. The trend in which HIV continues causing deaths despite availability of various treatment options,may probably be due to stigma and ignorance in the population about their HIV status, resulting in late hospital presentations. For some patients the poor clinical outcomes may be due to non-adherence to treatment.

The elevated total serum PSA, Urea and Creatinine, suggested an acute kidney injury in obstructive uropathy secondary to BPH. For this reason, a renal ultrasound and prostate biopsy were planned, but the patient demised before the tests were done.

The largely non revealing CSF analysis made the possibility of encephalopathy arising from obstructive uropathy in BPH more likely than the initially thought of tuberculous meningitis.The possibility of a brain space occupying lesion could not be explored due to lack of diagnostic neuroimaging modalities such as CT scan and/or MRI at the attending institution. Despite the reported CSF status, it remains possible that in this known PTB – HIV and DM patient the tuberculosiswould have disseminated to other organs rather than the brain.

In terms of prognosticators, the patient was a geriatric, known DM, PTB and HIV with multiple organ affectation and presenting relatively late for care. Patient deteriorated in admission despite the various modalities of care instituted as appropriate. HIV-

associated tuberculosis may pose challenges to care and result in high mortality(1). Further, HIV infection and older age appear to be the main risk factors associated with EPTB, as in our patient, mortality being significantly higher in patients with EPTB(4).

Dealing with HIV pandemic and its related complications continues to be a challenge in sub-Saharan Africa settings like Zambia because of limited resources and public ignorance. The lack of equipment such as a CT Scian & MRI and sometimes reagents that are considered basic necessities for the practice of modern medicine compromises the quality of care administered by health practitioners.

It is also possible that some patients may be ignorant of the available services and the need to seek medical attention early, while those who do know may not be able to afford some costs attached to the medications or diagnostics requiring outsourcing.

12. Conclusion

Late diagnosis of HIV and associated opportunistic infections and the corresponding delayed initiation of antiretroviral therapy may result in poor clinical outcomes in HIV care. Further, patients with HIV-TB and other co-infections need proper evaluationfor organ function, drug-drug and drug-disease interactions and should pay attention to appropriate dosingand monitoring for side or adverse effects. It is thus recommended that communities be sensitized on the benefits of timely presentation and access to care. Further, HIV care settings should be supported with the necessary diagnostic and monitoring tools and qualified human resource for optimal management and desirable clinical outcomes.

Patient Consent

Informed consent for clinical evaluation and write-up with the possibility of publication was sought and obtained from the patient.

Conflict of Interest

The authors declare that there was no conflict of interest regarding the publication of the manuscript

Author Contributions

All authors contributed towards the concept, design, reviews and ultimate write up of the manuscript

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