Buruli ulcer and HIV co-infection in a Nigerian woman on antiretroviral therapy

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ABSTRACT

Introduction: Mycobacterium ulcerans infection (Buruli ulcer) is a re-emerging neglected tropical disease characterized by extensive destruction of the skin and soft tissue resulting in the formation of ulcers. Despite the increase in prevalence, Buruli ulcer (BU) is one of the least studied tropical diseases particularly in Nigeria where the disease was first described in 1967. With the high burden of human immunodeficiency virus (HIV) infections in sub-Saharan Africa, and West Africa being the epicenter of BU disease in the world, a co-infection of BU and HIV is invariably inevitable. Case Report: This communication describes the case of a woman on antiretroviral therapy before presenting with a WHO category III Buruli ulcer lesion that was successfully treated with Rifampicin/Clarithromycin therapy complemented by surgery. The patient presented in WHO stage 1 HIV infection with very low HIV Viral Load and moderate immunity. It was at a point of high HIV viraemia and lowered immunity that she developed the initial painless nodule that subsequently broke down to multifocal necrotic ulcer that turned out to be a BU lesion. Conclusion: In recent years, there have been several reports of BU/HIV co-infection, including treatment options and challenges with management. However, no such report has emanated from Nigeria.

Keywords: Buruli ulcer, Co-infection, Human immunodeficiency virus, Nigeria

INTRODUCTION

Buruli ulcer (BU), a necrotizing infectious disease of the skin and cutaneous tissue has been reported in over 33 countries globally [1]. The unique feature of the causative agent, Mycobacterium ulcerans is the production of mycolactone, an exotoxin that is responsible for its pathogenicity. This polyketide lipid molecule has immunosuppression and necrotizing properties with potent cytotoxicity on immune cells. Mycolactone usually diffuses from the site of infection, killing surrounding cells and causing tissue destruction and suppressing the immune response with no significant inflammatory or systemic symptoms like fever or malaise [2]. BU is regarded as the third most common mycobacterial
disease of humans after tuberculosis and leprosy [3]. There is a high burden of HIV infection in sub-Saharan Africa with its prevalence varying from country to country particularly in West Africa [4]. Currently the association between HIV infection and Buruli ulcer disease is not fully understood [5].

CASE REPORT

A 40-year old woman and a petty trader by vocation was diagnosed with HIV infection at the age of 28 years in 2006 while pregnant with her second child and was referred to the HIV Treatment Centre of the Nigerian Institute of Medical Research, Lagos. Her husband and the first child were tested and found to also be HIV infected. She presented in World Health Organization(WHO) clinical stage 1 of HIV infection (i.e. asymptomatic or with generalized lymphadenopathy only) with the following baseline laboratory parameters: HIV RNA Viral Load (VL) - 611 copies/mL; CD4 - 466 cells/µL; hemoglobin – 10.3g/dL; ALT – 9.3 U/L; and serum creatinine - 56.6 μmol/L.

She was not eligible for antiretroviral therapy (ART) for her own disease, according to the Nigerian HIV treatment guidelines at the time. However, she was commenced on Zidovudine and Lamivudine as part of the Prevention of Mother to Child Transmission (PMTCT) of HIV package. The antiretroviral drugs (ARV) given for PMTCT were discontinued one week after delivery as the woman remained ineligible for ART for her own disease. The child, on being tested for HIV at 6 weeks of age according to the Nigerian National Guidelines, was found to be uninfected by HIV.

She remained clinically stable, and although her HIV VL increased to 6905 copies/mL in August, 2009, her CD4 count remained above the national threshold for commencement of ART at 402 cells/µL. It was not until May 2012, when her CD4 count fell below 350 cells/µL that she was commenced on the national first line ART regimen with Zidovudine, Lamivudine and Nevirapine. After the ART was commenced her viral and immunologic parameters improved and by 2013, she had undetected viral load (detection level 50 copies/mL at the time) with a CD4 count of 514 cell/µL.

She had however developed a painless nodule on her right ankle in August, 2009 which she did not take seriously and did not report to the clinical team. There was no personal or family history of diabetes mellitus and tuberculosis. The nodule slowly progressed to an ulcer which kept increasing in size and severity. She was told by traditional healers, whom she sought for care, that the ulcer was as a result of fetish poison she stepped on and could only be treated by traditional medicine. She was further warned that using orthodox medicine for the treatment of the ulcer would prove fatal. She therefore took care to conceal the wound by wearing long skirts or trousers whenever she came to the treatment centre.

The traditional treatment was not effective as the lesion continued to increase in size and depth. By 2017 she was no longer able to walk unaided. It was at this point that her son reported her condition to the clinic with a photograph of the wound. A clinical impression of Buruli ulcer(BU) was entertained and the molecular Parasitology Research Laboratory within the Neglected Tropical Diseases (NTD) Research Unit of the Institute was contacted. A team went to her home and reviewed her. Examination of the right lower limb revealed multifocal large ulcers on the right leg and foot, with the largest on the lateral aspect of the lower one third of the leg and the ankle measuring 15cm by 10 cm. There was noticeable surrounding inflammation but no evidence of osteomyelitis deep to the lesions. There was no significant finding on general and other systems examinations.

Swab specimens were taken from the ulcers for IS2404 Nested PCR and smear microscopy. The PCR result was positive for *M. ulcerans* while the Ziehl-Neelsen staining was negative.

She received anti-BU treatment with oral Rifampicin 600 mg daily and Clarithromycin 500mg twice daily for three months. No paradoxical reactions were experienced by the patient during the treatment. She also underwent skin grafting procedures and physiotherapy sessions at the National Orthopaedic Hospital, Lagos. She is now fully mobile and remains virally suppressed on the first line antiretroviral regimen of Zidovudine, Lamivudine and Nevirapine. Figure 1 and Figure 2 demonstrate the pre treatment and post treatment of her right leg.

Figure 1: Leg with ulcer before treatment.

Figure 2: Leg showing healing scars after treatment.
DISCUSSION

The WHO had developed treatment regimens for HIV and BU as separate disease entities but ran into a dilemma when BU/HIV co-infection gradually emerged particularly in areas of sub-Saharan Africa where both diseases overlap [6, 7]. The application of both regimens to treat cases of BU/HIV co-infection threw up a plethora of management challenges due to the limited knowledge of the clinical and epidemiological interactions between BU and HIV infection [8]. While awaiting more urgently needed evidence, current management practice of both diseases has been useful in building simple preliminary guidance on how to manage BU/HIV infections and that was the template we deployed in the management of our case study [6].

At the time of her presentation with the HIV infection she had moderate immunity but subsequently had high HIV viraemia and lower immunity. It was at this stage that she developed the multifocal necrotic BU lesion. In this case report, it appears BU presented as an opportunistic infection while immune reconstitution did not seem to have any positive effect on the course of the disease in this patient.

This case supports the current test and treatment strategy for HIV infection recommended by the WHO and adopted by Nigeria in December, 2016 which leads to viral suppression, immune preservation/reconstitution, prevention of opportunistic infections and conditions and improved quality of life [9].

Our treatment outcome in this study could have derived from the fact that we did not have to debate which treatment to start first as the woman was already on ART (2012) before her BU episode was established (2017) and treatment commenced immediately.

This case report further highlights the hypothesis that an underlying HIV infection can determine the progression and severity of BU disease [10,11,12]. Secondly, that multifocal BU would benefit more from a combined antibiotic therapy and skin grafting than relying on either alone. Lastly, and in view of the increasing incidence of BU/HIV co-infection, this first reported co-infection case in Nigeria is an ideal opportunity to alert, remind and improved quality of life [9].

CONCLUSION

As a result of the limited knowledge of the clinical and epidemiological interactions between the two infections it is expedient to comply with the screening of BU patients for HIV infection before commencing treatment. The BU in this patient presents more as an opportunistic infection probably due to the lowered immunity.

REFERENCES

Author Contributions
Adewale Adegboyega Oke – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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Agatha Nkiruka David – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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Guarantor of Submission
The corresponding author is the guarantor of submission.

Consent Statement
Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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