Correspondence

Title: Urinary lipoarabinomannan detection and disseminated nontuberculous mycobacterial disease

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Dear Editor

We read with interest the article entitled "Does disseminated nontuberculous mycobacterial disease cause false-positive Determine TB-LAM lateral flow assay results? A retrospective review" by Nel *et al* [1]. The authors present an important finding relevant to clinicians managing patients with advanced HIV. Although we agree that disseminated nontuberculous mycobacterial (NTM) disease needs to be considered in patients with positive Determine TB-LAM lateral flow assay (LF-LAM) results, we urge that the implications for clinical practice be considered in the context of what is known about the relative incidence of tuberculosis and NTM disease in high HIV burden settings. Disseminated NTM is almost exclusively observed in patients with extreme immunosuppression (median CD4 count consistently <50 cells/µL, often <10 cells/µL) [2], has always been uncommon in HIV-infected patients in Africa, and has become rarer in the era of combination antiretroviral therapy (ART).

Disseminated NTM accounted for only 1.5% of ID consults, and 4% of annual mycobacterial disease diagnoses in the Author's hospital, vastly outweighed by *Mycobacterium tuberculosis* (MTB). Even in this reported case series, 12% of NTM isolates occurred in patients also culture positive for MTB [1]. In a recent study from Cape Town [3], only 1 of 410 (0.2%) unselected HIV-positive patients admitted to medical wards and who had a mycobacterial blood cultures taken had evidence of disseminated NTM, compared to 132/410 (32.2%) with Xpert or culture-confirmed MTB. This individual had NTM mycobacteraemia, was strongly positive on urine LF-LAM, but also positive on two urinary Xpert MTB/RIF tests, implying mixed MTB/NTM disease (Xpert being specific for MTB). Similarly, a study from Malawi using systematic blood and sputum culture to investigate 467 sputum smear-negative HIV-positive patients starting ART with WHO Stage 4 disease isolated NTM in 4 (0.9%), compared to MTB in 48 (10.2%), and non-typhoid salmonella species in 29 (6.2%) [4].

Given current evidence, disseminated NTM accounts for a very small proportion of mycobacterial disease in LAM-positive HIV patients in Southern Africa, greatly outnumbered by MTB disease. Mixed MTB/NTM disease also needs to be considered.

We suggest use of Xpert MTB/RIF on concentrated urine to distinguish NTM from MTB disease in patients with positive LF-LAM results who have the risk-profile for NTM disease, including CD4 <50 cells/µL. Misdiagnosing MTB or mixed MTB/NTM as NTM disease has serious consequence for patients, with NTM treatment being inadequate for MTB, and requiring prolonged use of expensive treatment not covered by National TB Programmes.

We, therefore, agree that disseminated NTM should be considered as a cause of positive LF-LAM, but only when MTB and mixed MTB/NTM disease have been rigorously excluded. In addition to urine and sputum Xpert MTB/RIF testing, urine, blood or bone marrow mycobacterial culture (if available) can provide supportive evidence for this decision. The relative non-specificity between MTB and NTM should not detract from the routine use of LF-LAM to diagnose TB in appropriately selected HIV-positive populations, nor the treatment of LF-LAM positive patients with standard TB drug regimens [5]. In resource-limited settings, treatment of HIV-positive patients with positive urine LF-LAM using standard MTB regimens with no further investigations has been shown to reduce mortality [6].

References

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Conflicts of Interest

We report no conflicts of interest for all authors.