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Association of slow recovery of Mycobacterium africanum-infected patients posttreatment with high content of Persister-Like bacilli in pretreatment sputum

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ABSTRACT

Objectives/Background: Mycobacterium africanum that causes 40% of tuberculosis (TB) in West Africa grows more slowly in culture and has similar transmission capacity compared with Mycobacterium tuberculosis, but M. africanum-exposed contacts progress more slowly to active disease. The presence of lipid body (LB) containing M. tuberculosis complex (MTBC) cells in sputum samples has been associated with mycobacterial transcriptomes indicating slow or no growth and persister-like antibiotic tolerance. Slow-growing bacilli have been found to display a persister-like phenotype with the accumulation of LBs and drug tolerance. Our previous study showed that the body mass index and lung damage resolution on chest X-ray were significantly improved slower in M. africanum-infected patients posttreatment than in M. tuberculosis-infected patients; however, the reason for this remains unclear. Therefore, we hypothesized that these differences could be either due to significant differences in drug resistance between the MTBC lineages or a difference in their content of persisters, as indicated by the percentage of LP-positive bacilli in sputum.

Methods: Sputum isolates collected before treatment from patients with TB were subjected to drug susceptibility testing using the BD BACTEC MGIT 960 SIRE kit. The percentage of acid-fast bacilli (AFB) and LB-positive bacilli in pretreatment sputum was determined by a dual staining procedure using Auramine O and LipidTOX Red neutral lipid stain, respectively, and fluorescence microscopy imaging.

Results: Out of the 77 isolates tested, 9 showed resistance to at least one drug and only 2 showed multidrug (rifampicin and isoniazid) resistance among M. tuberculosis-infected patients. The percentage of AFB-positive smears was similar between the two groups (p = 0.821), whereas that of LP-positive bacilli was significantly higher (p = 0.0059) in M. africanum-infected patients' sputa (n = 24) than in M. tuberculosis-infected patients' sputa.

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(n = 36). In addition, the bacillary lengths were significantly higher in *M. africanum*-infected patients’ sputa than in *M. tuberculosis*-infected patients’ sputa (*p = 0.0007). A high frequency of LP-positive bacilli in pretreatment sputum was associated with a poor body mass index and lung damage on chest X-ray improvement following anti-TB treatment in both the groups (r² = 0.022; *p = 0.017*).

**Conclusion:** The slow clinical recovery of *M. africanum*-infected patients compared with *M. tuberculosis*-infected patients posttreatment may be at least partially associated with the persistence of drug-tolerant “fat and lazy” bacilli.

**Conflicts of interest**

The authors have no conflicts of interest to declare.