Endogenous Reactivation of MDR Mycobacterium tuberculosis after 28 Years of Latent Infection ? Historical epidemiological data

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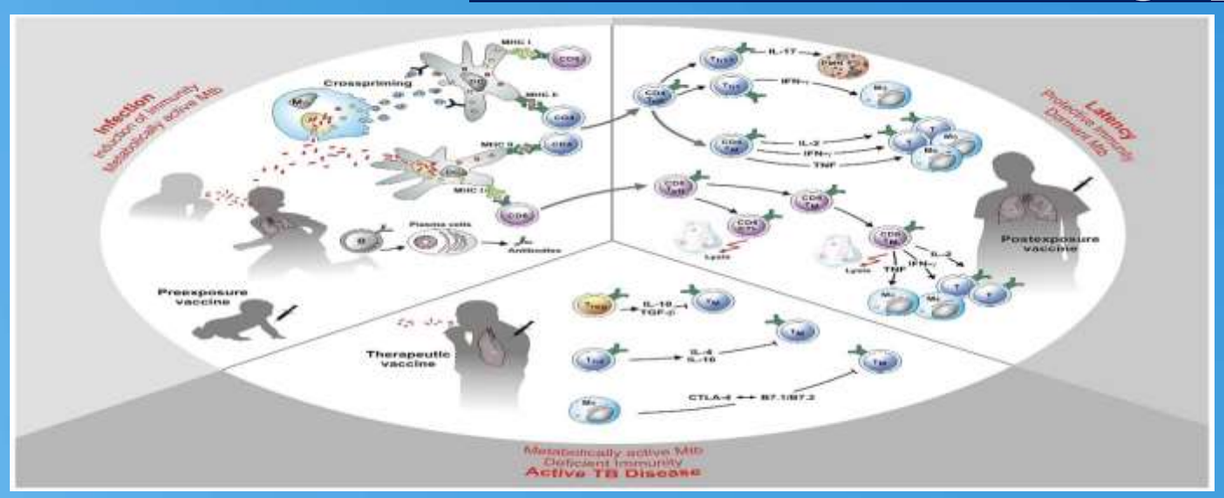
1-Introduction

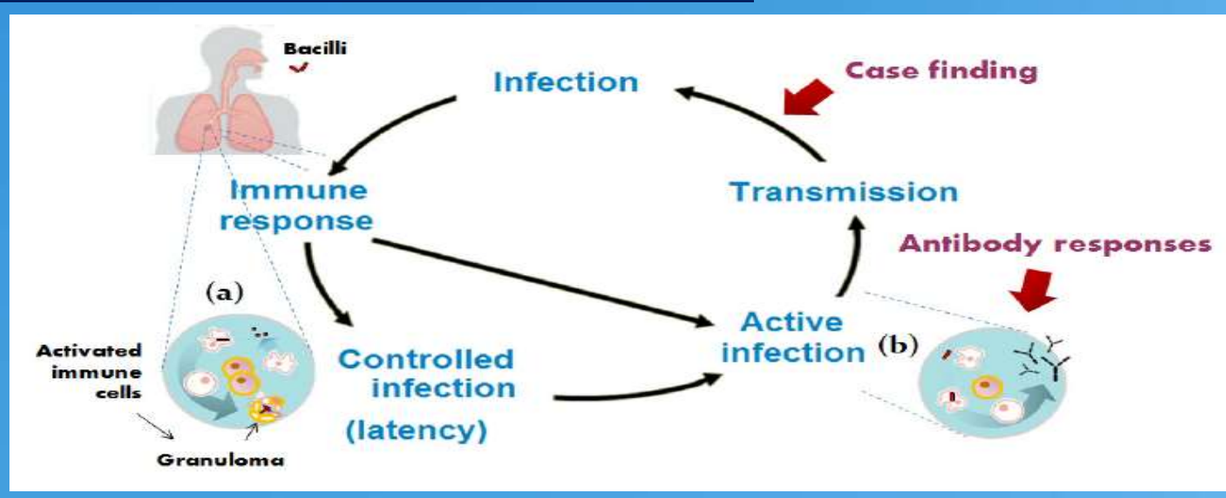
Primary infection with Mycobacterium tuberculosis leads to clinical disease in only 10% of cases. Most infected individuals are able to mount an effective immune response, which limits proliferation of the bacilli and produces a long-lasting partial immunity, both to new infections (often referred to as "exogenous reinfections") and to the reactivation of latent bacilli (often referred to as "endogenous reactivation"). Approximately one-half of infected individuals who develop clinical disease experience "early" progressive disease that occurs within 5 years of infection, and the rest have "late" disease, which is caused by reactivation as long as several decades after infection. The relative contributions of reactivation and reinfection, and even whether each occurs, have been the subject of considerable controversy. Therefore, the potential exists for determining whether disease in a particular patient is caused by a new infection with a strain in current circulation or by reactivation of infection with a previously prevalent strain. Although the possibility of reactivation after longer periods of time is a generally accepted dogma, so far it has been rarely described [1].

2-Objective

Late onset of tuberculosis after infection has been attributed to the endogenous reactivation of dormant bacteria. However, this has been rarely documented for latencies of more than a few years. **Here we present historical epidemiological and microbiological data** of reactivation of **Multi-Drug-Resistant (MDR)** Mycobacterium tuberculosis (M.t) infection after **28 years** of latency in HIV patient.

3-Bibliographic reminder





4-Methods

Data collection:

all microbiological tests for mycobacteria have been carried out at the International Reference Laboratory for tuberculosis at the institut pasteur of Algeria. This is the only laboratory that performs culture-based proportion method drug susceptibility testing (DST) for TB in Algeria. Patients informations were collected from medical sheets as well as patient files following contact with treating doctors.

Specimen processing:

Patients's sputums were decontaminated following modified Petroff method, then launched for culture on Lowenstein-Jensen (LJ) medium. Bacteria were harvested after 28 days of incubation and underwent a drug susceptibility test (DST), using the proportion method for Rifampicin (RIF), Isoniazid (INH), Streptomycin (STP), Ethambutol, Ofloxacin and kanamycin.

5-Results and discussion

Index case: Big brother.

He was given a diagnosis of pulmonary tuberculous (TB) infection in 1994 and the DST revealed a Multi-Drug-Resistant (MDR) strain (Resistance to RIF, INH, STP). He received his treatment properly and went abroad (France) in 1998.

Secondary case: Little brother.

He was given a diagnosis of multifocal lymph node TB in 2022. This led to the suspicion and diagnosis of HIV infection. Few months after, and despite having received first-line anti-tuberculosis treatment, he developed symptoms and was diagnosed of pulmonary TB. DST revealed an MDR strain with the same resistance pattern as his big brother.

we wanted to ensure that it was the same strain transmitted from the big brother to the little one (reactivated following HIV immunodeficiency), using molecular typing means, however the strain of the first was not preserved in 1994. Despite this, we have quite convincing historical epidemiological and microbiological data :

-The brothers lived together (in the same house) until 1998, after that the big one moved abroad (France).
-The little one never developed symptoms until he was diagnosed simultaneously for extrapulmonary TB and HIV in 2022 (probable reactivation).
-No notion of contagion was recorded all these years for the little one.
-The two strains have exactly the same resistance pattern (Resistance to RIF, INH, STP).

This observation has rarely been described in the scientific literature. We only found one work of Troels Lillebaek et al in which he gave molecular evidence (using RFLP) of reactivation after 33 years of latency [2].

6-Conclusion and perspective

Primary infection with M.t is associated with a substantial early risk of developing TB, but even if the primary infection does not lead to progressive disease within the first few years after transmission, we can say that the M.t bacilli may remain dormant for decades and thereby constitute a persistent, although probably small, risk of reactivation.

Molecular subtyping methods introduced and Culture-DNA-collections Developped in the NRL will permit characterization of specific strains of M. tuberculosis and determination of whether isolates from different patients might have a common origin.

7-References

1-Hernandez-Pando R, et al. Persistence of DNA from Mycobacterium tuberculosis in superficially normal lung tissue during latent infection.
2-Troels Lillebaek et al. Molecular Evidence of Endogenous Reactivation of Mycobacterium tuberculosis after 33 Years of Latent Infection.