Transmissibility and clinical significance of Mycobacterium abscessus in patients with cystic fibrosis

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Background. M. abscessus (MA) is a species frequently isolated from cystic fibrosis (CF) patients. Three Subspecies (subsp.) of MA exist and their identification is crucial for epidemiology and optimal patient's management. Although the environment is considered the source of MA infections, its transmission between CF patients has been hypothesized.

Objectives. We aimed to investigate a large collection of MA isolates obtained from CF patients to increase present knowledge about the prevalence of the 3 subsp., their antimicrobial susceptibility, the presence of MA genotypes characterized by increased virulence and responsible for severe clinical manifestations, the transmissibility between patients of the infection.

Methods. Three hundred six MA isolated from 62 FC patients of 4 Italian centers have been identified at level of subsp. by genetic sequencing of rpoB gene. Erm, 16S rRNA and 23S rRNA genes have been sequenced to detect mutations responsible for resistance to macrolides and amikacin. For each patient, the isolates belonging to the same subsp. have been genotyped, determining their VNTR profile and/or resorting to whole genome sequencing, to discriminate chronic infections from subsequent infections by different strains. The susceptibility to 9 antimicrobials by MIC determination in liquid medium has been evaluated on 184 isolates. Clinical data from patients infected by MA have been collected and statistically analyzed.

Results. One hundred ninety nine isolates were identified as belonging to the subsp. MA abscessus; 41 as MA massiliense and 66 as MA bolletii. A single subsp. was invariably isolated from 58 patients while in 3 others were isolated, in different times, 2 different MA subsp. In the large majority of patients persistently infected by the same MA subsp. the VNTR genotype remained unchanged or differed for no more than a single locus. Whole genome sequencing revealed that in patients with persistent isolation of the same subspecies characterized by the same VNTR genotype, the same strain was invariably responsible for the infection. In contrast the isolates from different patients belonged to different strains, even when the same VNTR genotype was shared. WGS analysis revealed in nine strains shared by a couple of patients for which the patient to patient transmission cannot be excluded. The epidemiological investigation we will undertake will help to make clear this hypothesis. The antimicrobial susceptibility testing confirmed that, with the exception of MA massiliense, all the strains were characterized by inducible resistance to macrolides.

Spin-off for research & clinical purposes. The confirmation, or the exclusion, of patient to patient transmission will heavily impact on cross-infections measures.

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