

Mycobacterium tuberculosis Beijing family: Analysis of the epidemiological and clinical factors associated with an emerging lineage in the urban area of Milan

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Abstract

The *Mycobacterium tuberculosis* Beijing genotype raises major concern because of global spreading, hyper-virulence and association with multi-drug resistance (MDR). The aims of the study were to evaluate role of Beijing family in the epidemiological setting of Milan and to identify predictors associated with the spreading of this [lineage](#). Overall 3830 TB cases were included. Beijing family accounted for 100 isolates (2.6%). Prevalence grew from 1.7% to 5.4% in the period 1996–2009. Foreign origin increased significantly the risk of having a Beijing strain: the greatest risk was observed among patients coming either from China [AOR = 57.7, 95%CI (26.3–126.8)] or from Former Soviet countries [AOR = 33.9, 95%CI (12.8–99.6)]. Also MDR was independently associated with Beijing family [AOR = 2.7, 95%CI (1.3–5.8)], whereas male gender and younger age only approximated the statistical significance [p 0.051 and p 0.099, respectively].

However, the percentage of cases attributable to MDR strains decreased over time, both in the Beijing group and in the non-Beijing group.

97 isolates were grouped in 37 sub-lineages: MT11, MT33 were predominant. Beijing family is an emerging lineage in Milan. Origin from countries like China and Ukraine and MDR are significantly associated with Beijing. The broad range of the sub-lineages reflects the recent dynamics of the migration flows to our area. This scenario can prelude to a constant increase in the spreading of Beijing strains in the near future.

Introduction

The Beijing family of *Mycobacterium tuberculosis* is widespread worldwide and it seems to be the most prevalent strain of *M. tuberculosis* in specific areas (Parwati et al., 2010). On a global scale, the Beijing lineage accounts for 13% of *M. tuberculosis* strains with a significant geographical variability (Brudey et al., 2006, European Concerted Action on New Generation Genetic Markers and Control of Tuberculosis, 2006): while in Asia more than half of the cases of tuberculosis (TB) are attributable to this genotype, Beijing strains have been identified in less than 1% of the TB patients in Latin America. The uncommon

virulence associated with the ability to elude the immune system may justify the vast distribution and the apparent intrinsic advantage in spreading of the Beijing family of *M. tuberculosis* compared to other genotypes (Parwati et al., 2010). The reported association with epidemic outbreaks (Moss et al., 1997, Narvskaya et al., 2002) and multidrug-resistance makes the Beijing family of *M. tuberculosis* a severe health concern (Kubica et al., 2004, Borgdorff et al., 2003, Alonso et al., 2010, Jagielski et al., 2010). Despite individual reports (Lari et al., 2007), there has not been an extensive evaluation of the epidemiology of the Beijing lineage in Italy. In this observational study we assessed the diffusion of the Beijing genotype in the urban area of Milan from January 1st, 1996 to December 31st, 2009 and we evaluated its association with resistance to anti-TB drugs and other epidemiological and clinical features.

Study population

This retrospective cohort study was based on data within the TB registries maintained at the III Division of Infectious Diseases, Luigi Sacco Hospital (Milan, Italy) and at the Regional TB Reference Center, Villa Marelli Institute, Niguarda Cà Granda Hospital (Milan, Italy). The electronic database of Infectious Diseases Service of the Lombardy Region was used as an additional source of information. The TB registries and the electronic regional database mentioned above contain demographic,

Results

3830 culture-confirmed TB cases were included in the study. Of these, 2362 (61.7%) were male and 1446 (37.8%) female. Data about nationality were available in 3689 patients: 1969 (53.4%) patients were Italian-born, while 1720 (46.6%) were foreigners. Of the non-Italian patients, 617 came from Southern America, 476 from Africa, 349 from Asia (of which 77 were Chinese), 37 from Former Soviet Union countries (mainly Ukraine), and 241 from other European countries (mainly Romania and former

Discussion

The genotypic Beijing family accounted for 2.6% of the 3830 *M. tuberculosis* isolates collected in the period 1996–2009. The prevalence of this lineage increased gradually over the time, from 1.7% in the period 1996–1998 to 5.4% in the period 2008–2009. Our findings are similar to the results of previous international studies: Glynn and co-workers showed that the prevalence of Beijing strains in Western Europe was inferior to 6% and increased over time (Glynn et al., 2002).

Few data are available

Conclusions

In conclusion, the Beijing family of *M. tuberculosis* may be considered an emerging lineage in the metropolitan area of Milan. Since it is not an endogenous strain, the progressive increase in its prevalence may be due to an increasingly intense migration from geographic areas where this genotypic family is endemic. Of note, Beijing strains tended to affect mainly young foreign-born patients. Moreover it was associated with the presence of MDR, while a clear correlation with HIV infection or

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- S. Gagneux

[Fitness cost of drug resistance in *Mycobacterium tuberculosis*](#)

Clin. Microbiol. Infect. (2009)

- C. Garzelli *et al.*

[Impact of immigration in a low-incidence area of Italy: a molecular epidemiology approach](#)

Clin. Microbiol. Infect.

(2010)

- M. Hanekom *et al.*

[Mycobacterium tuberculosis Beijing genotype: a template for success](#)

Tuberculosis (Edinb.)

(2011)

- E. Lasunskaja *et al.*

[Emerging multidrug resistant Mycobacterium tuberculosis strains of the Beijing genotype circulating in Russia express a pattern of biological properties associated with enhanced virulence](#)

Microbes Infect.

(2010)

- I. Mokrousov

[Genetic geography of Mycobacterium tuberculosis Beijing genotype: a multifacet mirror of human history](#)

Infect. Genet. Evol.

(2008)

- I. Parwati *et al.*

[Possible underlying mechanisms for successful emergence of the Mycobacterium tuberculosis Beijing genotype strains](#)

Lancet Infect. Dis.

(2010)

- M. Alonso *et al.*

Characterization of *Mycobacterium tuberculosis* Beijing isolates from the Mediterranean area

BMC Microbiol.

(2010)

- Ia.M. Balabanova *et al.*

Preponderance of *Mycobacterium tuberculosis* strains of the family Beijing and risk factors of their transmission in the Samara Region

Probl. Tuberk. Bolezn. Legk.

(2006)

- M.W. Borgdorff *et al.*

Mycobacterium tuberculosis Beijing genotype, the Netherlands

Emerg. Infect. Dis.

(2003)

- K. Brudey *et al.*

Mycobacterium tuberculosis complex genetic diversity: mining the fourth international spoligotyping database (SpolDB4) for classification, population genetics and epidemiology

BMC Microbiol.

(2006)

- T.N. Buu *et al.*

The Beijing genotype is associated with young age and multidrug-resistant tuberculosis in rural Vietnam

Int. J. Tuberc. Lung Dis.

(2009)

- European Concerted Action on New Generation Genetic Markers and Techniques for the Epidemiology and Control of Tuberculosis

Beijing/W genotype *Mycobacterium tuberculosis* and drug resistance

Emerg. Infect. Dis.
(2006)

- E. Garcia-Pachon *et al.*

Incidence of Beijing genotype of *Mycobacterium tuberculosis* in Elche, Spain: a 13-year surveillance study

Euro. Surveill.
(2007)

- J.R. Glynn *et al.*

Worldwide occurrence of Beijing/W strains of *Mycobacterium tuberculosis*: a systematic review

Emerg. Infect. Dis.
(2002)