

Characterization of Extensively Drug-Resistant Tuberculosis Cases from Valle del Cauca, Colombia

Extensively drug-resistant tuberculosis (XDR-TB), which is TB resistant to isoniazid and rifampin plus one fluoroquinolone and a second-line injectable drug, represents an obstacle for the treatment and control of TB. Previously, we reported four XDR-TB cases and a high proportion of the Beijing genotype among multidrug-resistant TB (MDR-TB) isolates in the state of Valle del Cauca, Colombia (3), where a MDR-TB hot spot had been identified (7). According to the information of the local TB program, to date 21 XDR-TB cases have been diagnosed in the country, 14 of which were from this state.

With the approval of the Centro Internacional de Entrenamiento e Investigaciones Médicas (CIDEIM) Review Board, we characterized the XDR-TB cases detected in Valle del Cauca in the period 2001 to 2009, including their clinical and epidemiological features.

Resistance profiles were identified using the proportion method on 7H10 agar (6) and confirmed by a supranational laboratory. Molecular characterization of the isolates was performed by spoligotyping (5) and 24-locus variable-number tandem-repeat (VNTR) typing (8). GenoType MTBDR*plus* and *-sl* assays (Hain Lifescience GmbH) were applied to identify mutations associated with resistance to first- and second-line anti-TB drugs. Shared types and lineages of *Mycobacterium tuberculosis* complex were identified.

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TABLE 1 Phylogenetic and epidemiological data of XDR-TB isolates from Valle del Cauca, Colombia^m

UPGMA Tree	ID	Spoligotype Lineage (SIT) ^a	MIRU-VNTR pattern (MIT) ^b	Year	Sex/Age	Initial condition	BCG	HIV	Clinical outcome	Mutations			
										<i>katG</i>	<i>inhA</i>	<i>rpoB</i>	<i>gyrA</i>
	01	77777774020731 H1 (SIT62)	225325153323333554234423 (MIT101)	2001 ^e	M/36	R	Yes	Neg	Died	S315T1 ^f	WT ^h	526-529 ⁱ	D94N or D94Y
	02	77777774020731 H1 (SIT62)	225325153323333374234423 (Orphan)	2007	F/22	F	Yes	Neg	OT	S315T1 ^f	WT	526-529 ⁱ	D94N or D94Y and D94G
	03	77637777740731 S (SIT3010)	232325153324424352314234 (Orphan) ^c	2007	M/30	R	Yes	Neg	Died	WT	WT	S531L	D94G
	04	77637777000731 Unk (SIT881)	232325153322424352314234 (Orphan) ^c	2009	F/43	F	Yes	Neg	OT	S315T1 ^f	WT	510-517 ^j	D94G and D94A
	05	675737607760771 LAM2 (SIT545)	224226153321224382334133 (Orphan)	2009	M/46	F	Yes	Neg	OT	S315T2 ^g	WT ^h	S531L	D94G
	06	00000000003731 Beijing (SIT190)	223325171431524992264433 (MIT46) ^d	2009	M/44	R	Yes	Neg	OT	S315T1 ^f	WT	S531L	A90V and D94G ^k
	07	00000000003731 Beijing (190)	223325171431524992264433 (MIT45) ^d	2009	M/30	N	Yes	Pos	Died	S315T1 ^f	WT	S531L	D94G
	08	00000000003731 Beijing (190)	223325171431524992264433 (MIT45) ^d	2007	F/24	N	NA	NA	Died	S315T1 ^f	WT	S531L	D94G
	09	00000000003731 Beijing (190)	223325171431524992264433 (MIT45) ^d	2007	F/16	N	NA	NA	Died	S315T1 ^f	WT	S531L	D94G
	10	00000000003731 Beijing (190)	223325171431524992264433 (Orphan) ^d	2009	M/29	F	Yes	Neg	Died	S315T1 ^f	WT	S531L	D94G

^a Spoligotypes are shown in octal format; lineages are designated according to the SITVIT2 database.

^b MIT numbers represent mycobacterial interspersed repetitive unit (MIRU) international types determined using 24 loci. The 8 unique profiles are defined as MIT101, -45, and -46 and five different orphan patterns.

^c Strains 03 and 04, which differ at a single MIRU locus (4 and 2 copies for MIRU-40, respectively), showed related spoligotype binary patterns SIT3010 and SIT881; hence, it is possible that SIT881 evolved by loss of a single block of spacers 25 to 31 either directly from SIT3010 or from a linked ancestor.

^d All the Beijing SIT190 strains (ID 06, 07, 08, 09, and 10) are highly related, since they represent a single locus variant in the 24-locus typing scheme (4, 3, 3, 3, and 2 copies for MIRU-39, respectively).

^e Diagnosed in 2001 but classified as an XDR-TB case until 2007 according to the WHO definition.

^f S315T1: base exchange at codon 315, AGC to ACC.

^g S315T2: base exchange at codon 315, AGC to ACA.

^h For this isolate, there was no hybridization either in the WT2 probe which analyzed nucleic acid in the position 8 or in either of the two mutations described.

ⁱ This gene region is defined by the absence of WT7 probe which could represent any of these mutations: H526R, H526P, H526Q, H526N, H526L, H526S, and H526C.

^j Isolate with an absence in the hybridization probes WT2 and WT2/WT3 that could have represented any of these mutations: Q513L, Q513P, and del514–516.

^k Heteroresistant strain.

^l Epidemiologically linked cases.

^m Abbreviations: BCG, *Mycobacterium bovis*; bacillus Calmette-Guérin vaccination SIT, spoligotype international type; ID, identification number; Unk, unknown; NA, data not available; M, male; F (in column 6), female; R, relapse; F (in column 7), failure of treatment with first-line drugs; N, new case; OT, on treatment; Neg, negative; Pos, positive; WT, wild type. Numbers in column 6 represent age in years.

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We declare no potential conflict of interest relevant to this article.

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