

## CASE REPORT

# Case Report of False Rifampin Resistance with Xpert<sup>®</sup> MTB/RIF from an HIV Infected Patient

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### SUMMARY

**Background:** Tuberculosis is one of the main infectious diseases threatening human health, especially in HIV co-infected patients. Xpert<sup>®</sup> MTB/RIF assay amplifies the *rpoB* gene of MTB was recommended by the World Health Organization as the initial diagnostic test in cases of suspected infections with Mycobacterium tuberculosis (MTB) or HIV-coinfected TB.

**Methods:** A 44-year-old male HIV-positive patient co-infected with MTB presented with low-grade fever for 3 months. Rifampicin (RIF) resistance was detected in the celiac pus but not in the pleural effusion using Xpert<sup>®</sup> MTB/RIF assay. The same samples were then sequenced by next-generation sequencing (NGS) and in-house PCR for *rpoB* gene.

**Results:** The results of NGS and in-house PCR, however, were paradoxical in the same samples with low or no mutation sequences of RIF resistance. The patient's tuberculosis (TB) therapy was optimized based on first-line anti-TB drugs and antiretroviral treatment. The patient improved with this therapy.

**Conclusions:** Even with high specificity, false positive results remain possible and RIF resistance detection by Xpert must be considered for clinical interpretation.

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## Supplementary Tables and Figures

Table S1. Xpert MTB-RIF assay G4, version 5 results with the celiac pus.

Analyte name	Ct	EndPt	Analyte result	Probe check result
SPC	27.4	240	NA	PASS
Probe A	0.0	- 172	NEG	PASS
Probe B	9.6	- 61	POS	PASS
Probe C	8.9	54	POS	PASS
Probe D	8.4	109	POS	PASS
Probe E	0.0	- 166	NEG	PASS
Qc-1	0.0	0	NEG	PASS
Qc-2	0.0	0	NEG	PASS

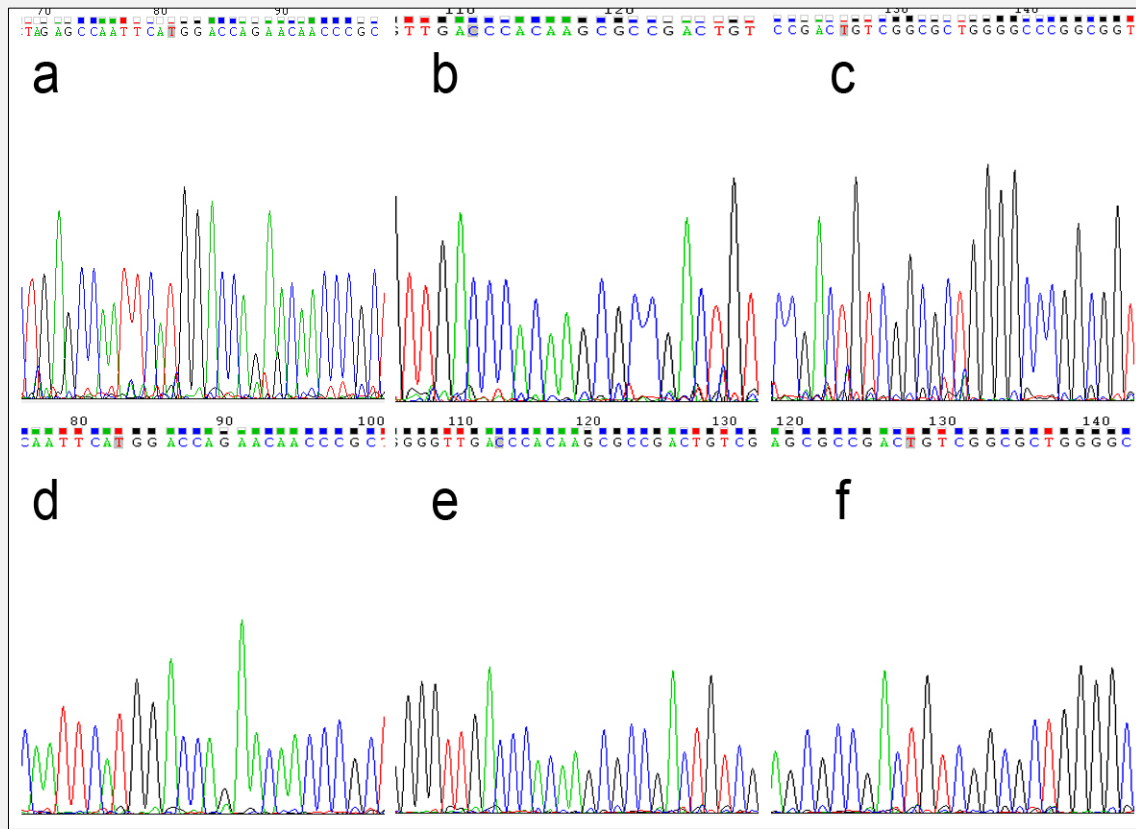
Table S2. Xpert MTB-RIF assay G4, version 5 results with the pleural effusion.

Analyte name	Ct	EndPt	Analyte result	Probe check result
SPC	22.8	318	NA	PASS
Probe A	17.8	131	POS	PASS
Probe B	18.9	126	POS	PASS
Probe C	18.1	242	POS	PASS
Probe D	18.7	260	POS	PASS
Probe E	19.6	121	NEG	PASS
Qc-1	0.0	0	NEG	PASS
Qc-2	0.0	0	NEG	PASS

Table S3. Rifampin resistance-conferring signatures in *rpoB* genes from the samples of celiac pus and pleural effusion deduced by NGS<sup>a</sup>.

Sample ID	Nucleotide substitution(s) in the <i>rpoB</i> gene <sup>b</sup> (81 bp)	Numbers of total reads	Reads of wild-type	Frequency of wild-type (%)	Reads of mutation-type	Frequency of mutation-type (%)
celiac pus	A-1833-G	940,227	935,591	99.51	4,103	0.44
celiac pus	C-1834-T	940,227	939,116	99.88	1,005	0.11
celiac pus	C-1862-T	940,223	939,099	99.88	975	0.10
celiac pus	A-1863-G	940,227	935,952	99.55	2,853	0.30
celiac pus	T-1877-C	940,227	936,020	99.55	3,166	0.34
celiac pus	C-1878-T	940,227	938,320	99.80	1,672	0.18
celiac pus	G-1879-A	940,227	938,159	99.78	1,800	0.19
pleural effusion	A-1833-G	1,250,173	1,244,469	99.54	5,116	0.41
pleural effusion	C-1834-T	1,250,173	1,248,673	99.88	1,377	0.11
pleural effusion	C-1862-T	1,250,173	1,248,531	99.87	1,450	0.12
pleural effusion	A-1863-G	1,250,173	1,245,608	99.63	2,911	0.23
pleural effusion	T-1877-C	1,250,173	1,243,713	99.48	4,668	0.37
pleural effusion	C-1878-T	1,250,173	1,248,137	99.84	1,765	0.14
pleural effusion	G-1879-A	1,250,173	1,245,436	99.62	4,399	0.35

<sup>a</sup> - NGS, next-generation sequencing, <sup>b</sup> - Compared with *M. tuberculosis* H37Rv strain.



**Figure S1. The results of rifampin resistance in *rpoB* gene at positions 516, 526, and 531 with in-house PCR.**

**a) The results of celiac pus at position 516, b) The results of celiac pus at position 526, c) The results of celiac pus at position 531, d) The results of pleural effusion at position 516, e) The results of pleural effusion at position 526, f) The results of pleural effusion at position 531.**