Curative high-dose rifampin-based regimen in a case with borderline-resistance rpoB mutation

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Introduction: Rifampin (RIF) is the most crucial anti-tuberculosis (TB) drug. RIF-resistant TB (RR-TB) is refractory to treatment, and requires long-term multidrug-(MDR)/RR-TB regimens. An rpoB mutation of Mycobacterium tuberculosis confers resistance in nearly all RR-TB cases. The degree of RIF resistance varies by the rpoB mutation type, with common types conferring high-level resistance, requiring long-term high-dose treatment, while other types inducing low-level resistance to RIF ("borderline resistance"). Although high-dose RIF (HD-RIF; 20 mg/kg) is suggested to effectively overcome borderline resistance, reports of such HD-RIF-based regimens are limited.

Case: A 52-year-old man with persistent cough (for 3 weeks) was examined clinically; radiography revealed multiple nodules with cavitary lesion in a right upper-lobe suggestive of pulmonary tuberculosis (Figures 1 and 2A), which was confirmed by a sputum culture that was positive for M. tuberculosis. As a BD MaxTM MDR-TB assay indicated isoniazid and RIF resistance, MDR-TB was diagnosed and an MDR/RR-TB regimen including bedaquiline was initiated. The total treatment period was scheduled to be at least 18 months, according to the current treatment guideline of MDR/RR-TB. However, a subsequent phenotypic drug-susceptibility test showed only isoniazid resistance and RIF susceptibility. Due to the discordant results in RIF susceptibility between the two tests, we accordingly conducted rpoB gene sequencing and identified a GAC516TAC mutation, which is a representative mutation that confers borderline resistance. Thus, the treatment regimen was changed to the HD-RIF-based regimen (HD-RIF, moxifloxacin, clofazimine, and pyrazinamide), which resulted in achievement of sputum culture negative results. After a 9-month treatment with HD-RIF-based regimen, the treatment was completed. Chest X-ray at treatment completion showed marked improvement (Figure 2-B), and the treatment success was confirmed based on persistent sputum culture negativity.

Conclusion: A short-term HD-RIF-based regimen can successfully treat patients with rpoB mutations that confer borderline RIF resistance.

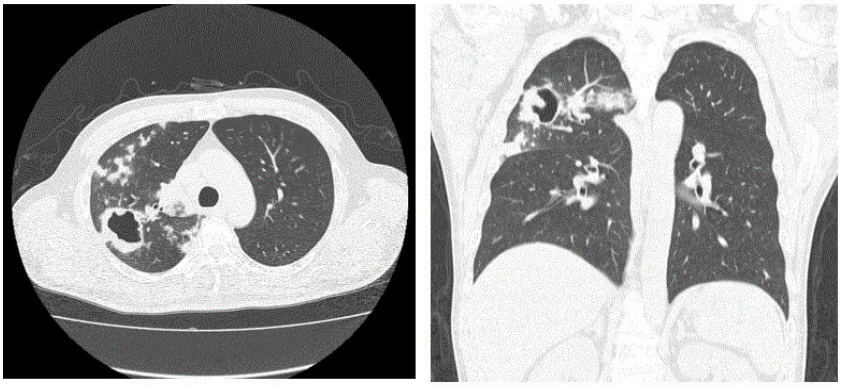

Figure 1. Initial chest computed tomography showed multiple nodules with a tree-in-bud appearance in the right upper lobe, as well as a thick-walled cavity.

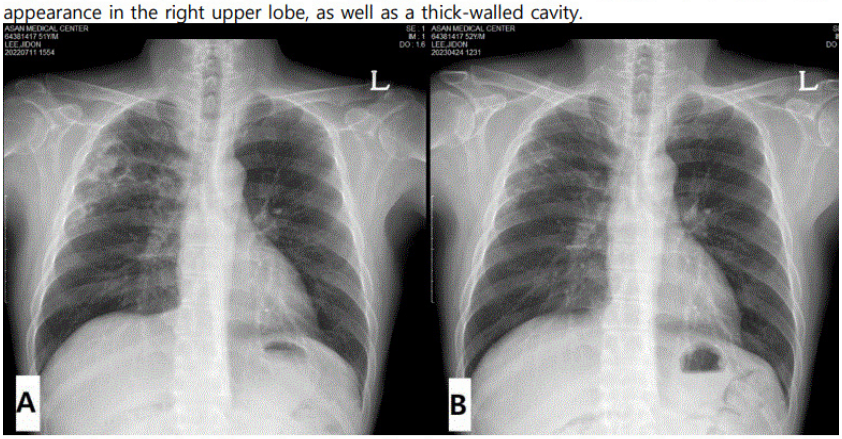

Figure 2. A. Initial chest X-ray showed a cavitary lesion surrounded by nodular infiltration in the right upper lobe. **B.** Chest X-ray taken 9 months after treatment initiation revealed near-total regression of the cavitary lesion.