



Case Report

Multi-Drug Resistant Tuberculosis With Extensive Bilateral Lung Involvement Can be Cured With Just Three Drugs for 6 Months

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Multi-drug resistant tuberculosis (MDR-TB), defined as resistance to at least rifampicin and isoniazid, has become one of the major obstacles to global TB control.¹ Until very recently, the MDR-TB treatment required multiple drugs (some of questionable efficacy) for a minimum of 18 months, with multiple adverse reactions and cure rates not exceeding 60%.^{1–5} However, the arrival of new drugs with action against *Mycobacterium tuberculosis*, much more bactericidal and sterilizing^{2–5} has completely changed this landscape. Therefore, the Spanish Society of Pneumology and Thoracic Surgery (SEPAR) already advised, in its 2020 recommendations, that these cases of MDR-TB could be treated with a 6-month regimen of bedaquiline + levofloxacin + linezolid.² However, it wasn't until December 2022 that World Health Organization recommended (these) the shortened 6-month regimens for MDR-TB treatment, though with a combination of 4 drugs (bedaquiline + pretomanid + linezolid + moxifloxacin).³

We present the case of a 37-year-old woman, regular smoker, originally from Russia, who had recently traveled to Italy and stayed there for several months. She reported a 6-month clinic of persistent cough, purulent sputum, minimal exertion dyspnea, hyporexia, and a weight loss of 20 kg. On physical examination, she exhibited only a low-grade fever and severe malnutrition (height 175 cm and 48 kg). Laboratory tests revealed anemia with a hemoglobin level of 9.4 g/dL, leukocytosis of 23,700/mm³ with lymphopenia (1020/mm³, 4.3%), and thrombocytosis of 1,282,000/mm³. Chest radiography showed extensive involvement of the lung parenchyma with bilateral micronodular pattern, cavities in both hemithorax (largest measuring 13 and 7 cm in right lung) and multiple mediastinal lymph nodes. Microbiological testing revealed positive smear (auramine staining) and PCR for *Mycobacterium tuberculosis*, with rifampicin resistance detected by GeneXpert MTB/RIF. Sensitivity molecular and phenotypic testing confirmed resistance to isoniazid (mutations in *katG* and *inhA* genes), ethambutol, and aminoglycosides, but without fluorquinolones resistance.

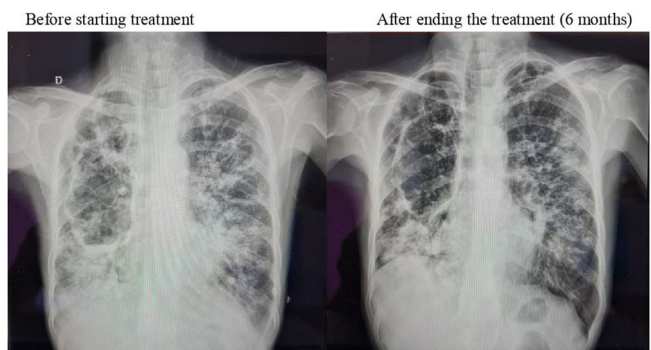


Fig. 1. Chest X-ray film of the patient. (A) Before starting treatment. (B) After ending the treatment (6 months).

With the confirmation of MDR-TB, treatment was initiated with levofloxacin 1000 mg/day, linezolid 600 mg/day, and bedaquiline (400 mg daily for two weeks and followed by 200 mg three days/week for 6 months). The patient received supervised home treatment for the scheduled six months, with good compliance, significant clinical improvement, and negative smear and mycobacterial cultures at the 2nd, 5th, and 6th months of treatment, leading to acceptance of cure of the disease. The patient did not experience relevant side effects during treatment. Fig. 1 shows radiological improvement at the end of treatment compared to the beginning. One year after completing treatment, the patient remained cured with no signs of potential relapse in subsequent visits (clinically asymptomatic and negative mycobacterial culture every two months in the follow-up).

The present case supports that with a shortened 6-month treatment and only 3 drugs, with good bactericidal and sterilizing activity,^{4,5} these forms of MDR-TB can be cured, even in cases with cavitory and bilateral involvement, as recommended by SEPAR in 2020.² This approach could further streamline the treatment of these complex MDR-TB patients compared to the latest recommendations by the WHO.³

We believe it is important that these evidences are known, which can help to greatly simplify the management of these complex MDR-TB cases, especially in Spain and other countries where

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is very difficult to achieve pretomanid. Anyway, we support putting pressure on all levels to make pretomanid easy to obtain, so that it can be used in these MDR/pre-XDR-TB patients.

Conflict of interests

The authors state that they have no conflict of interests.

References

1. World tuberculosis report 2022. Geneva: World Health Organization; 2022.
2. Caminero JA, García-García JM, Caylà JA, García-Pérez FJ, Palacios Gutiérrez JJ, Ruiz-Manzano J. Actualización de la normativa SEPAR «Diagnóstico y tratamiento de la tuberculosis con resistencia a fármacos». Arch Bronconeumol. 2020;56:514–21.
3. WHO operational handbook guidelines on tuberculosis 2022 update. Module 4: treatment drug-resistant tuberculosis treatment 2022 update. World Health Organization; 2022.
4. Caminero Luna JA, Pérez Mendoza G, Rodríguez de Castro F. Multi-drug resistant tuberculosis, ten years later. Med Clin (Barc). 2021;156:393–401, <http://dx.doi.org/10.1016/j.medcli.2020.08.018>. English, Spanish. Epub 2021 Jan 31. PMID: 33531151.
5. Caminero JA, García-Basteiro AL, Rendon A, Piubello A, Pontali E, Migliori GB. The future of drug-resistant tuberculosis treatment: learning from the past and the 2019 World Health Organization consolidated guidelines. Eur Respir J. 2019;54:1901272, <http://dx.doi.org/10.1183/13993003.01272-2019>. PMID: 31601719.