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Emerging Therapeutic Approaches to Drug-Resistant Tuberculosis: A Case Report and Review of Novel Treatments

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ABSTRACT

Drug-resistant tuberculosis (DR-TB), particularly multidrug-resistant tuberculosis (MDR-TB), poses a major global health challenge. Conventional treatment regimens are long, toxic, and often ineffective. This case report describes a 32-year-old male patient with MDR-TB unresponsive to standard therapies, successfully treated using a novel combination of repurposed drugs, immunomodulators, and bacteriophage therapy. Sputum cultures converted to negative within three months, with sustained clinical and radiological improvement over 12 months. The review further discusses the integration of artificial intelligence (AI) in optimizing treatment regimens, a promising but underexplored area in MDR-TB management. This case underscores the need for innovative therapeutic approaches to improve outcomes in DR-TB.

Keywords: *Multidrug-Resistant Tuberculosis, Repurposed Drugs, Immunomodulation, Phage Therapy, Artificial Intelligence, Drug Development, Tuberculosis Treatment*

Introduction

Tuberculosis (TB) remains a leading cause of death worldwide, with 10 million new cases annually. According to the World Health Organization (WHO), drug-resistant TB (DR-TB) affects about 500,000 people yearly, with treatment success rates as low as 57% in some regions (World Health Organization, 2023). MDR-TB is defined by resistance to at least isoniazid and rifampicin, the two most potent first-line anti-tuberculosis drugs. Extensively drug-resistant TB (XDR-TB) presents an even greater challenge, being resistant to first- and second-line drugs, significantly limiting therapeutic options (Dheda *et al*., 2017).

Conventional treatments for MDR-TB often involve toxic, prolonged regimens with high rates of adverse effects and failure. In response, newer approaches such as drug repurposing, immunomodulation, and bacteriophage therapy have shown promise in overcoming the limitations of standard therapies. This report presents a case of MDR-TB successfully treated with these novel modalities and highlights the potential of artificial intelligence (AI) in optimizing TB treatment regimens.

Case Presentation

A 32-year-old male patient presented with a three-month history of persistent cough, fever, weight loss, and hemoptysis. He had previously been treated for pulmonary TB with a six-month course of isoniazid, rifampicin, ethambutol, and pyrazinamide. Despite completing therapy, his symptoms worsened, and subsequent drug susceptibility testing (DST) confirmed MDR-TB, resistant to both isoniazid and rifampicin.

The patient was initially placed on a second-line regimen of levofloxacin, amikacin, and cycloserine, based on DST results. However, after four months of treatment, his condition continued to deteriorate, with persistent positive sputum cultures for *Mycobacterium tuberculosis*. Given the failure of conventional therapy, a decision was made to pursue a novel therapeutic strategy.

Novel Therapeutic Approach

The treatment regimen was revised to include the repurposed drugs linezolid and bedaquiline. Linezolid, an oxazolidinone antibiotic, inhibits bacterial protein synthesis and has demonstrated efficacy in MDR-TB (Sotgiu *et al*., 2012). Bedaquiline targets bacterial ATP synthase, disrupting the energy production of *Mycobacterium tuberculosis* and has been shown to improve treatment outcomes in MDR-TB (Cox and Ford, 2012).

Additionally, interferon-gamma, an immunomodulatory agent, was administered to enhance the patient's immune response by activating macrophages to clear intracellular *Mycobacterium tuberculosis* (Esmail *et al*., 2016). Furthermore, bacteriophage therapy, under compassionate use guidelines, was introduced as part of the treatment. Phages, viruses that target and lyse bacterial cells, provide a highly specific approach to combating bacterial infections, including MDR strains (Abedon *et al*., 2017).

The patient showed significant clinical improvement within two months, with resolution of cough, fever, and weight loss. Sputum cultures converted to negative after three months, and follow-up chest

imaging at six months demonstrated the resolution of pulmonary lesions. The patient completed a 12-month course of therapy with no recurrence during follow-up.

Discussion

The emergence of drug-resistant TB requires innovative solutions. This case illustrates the effectiveness of combining repurposed drugs, immunomodulation, and bacteriophage therapy for MDR-TB that failed to respond to conventional treatment.

Repurposed Drugs in MDR-TB Treatment

Linezolid and bedaquiline are among the most promising drugs in the fight against MDR-TB. Linezolid has been repurposed for TB due to its strong activity against resistant strains (Sotgiu *et al*., 2012), though its long-term use is associated with adverse effects like bone marrow suppression and peripheral neuropathy (Lee *et al*., 2012). Bedaquiline, approved in 2012, significantly improves outcomes by targeting bacterial ATP synthase, a mechanism not affected by resistance to other TB drugs (Cox and Ford, 2012; Diacon *et al*., 2014).

Immunomodulation with Interferon-Gamma

The adjunctive use of immunomodulators like interferon-gamma shows potential in MDR-TB treatment. Interferon-gamma enhances the immune response by activating macrophages, improving the host's ability to eliminate intracellular *Mycobacterium tuberculosis*. In this case, its use was associated with faster sputum conversion and clinical improvement (Esmail *et al*., 2016).

Bacteriophage Therapy

Bacteriophages, which specifically target bacterial cells, are an emerging treatment for resistant bacterial infections (Abedon *et al*., 2017). Although clinical use in TB remains experimental, early reports, including this case, suggest that bacteriophage therapy may offer a safe and effective adjunct to traditional therapies (Hatfull *et al*., 2022; Dedrick *et al*., 2019). Given their specificity, phages may help reduce bacterial load while minimizing the risk of resistance development.

Artificial Intelligence in TB Treatment

Artificial intelligence (AI) holds promise in optimizing MDR-TB treatment. AI algorithms can analyze vast datasets, including bacterial resistance patterns, patient genetics, and drug interactions, to predict

individualized treatment responses. Although AI was not applied in this case, emerging models show potential to revolutionize personalized treatment regimens, reducing treatment duration and improving success rates (Keshavjee *et al*., 2008).

Conclusion

This case underscores the importance of exploring new therapeutic strategies for MDR-TB, particularly in patients unresponsive to standard treatments. Repurposed drugs, immunomodulators, and bacteriophage therapy offer promising alternatives. As AI continues to develop, it is likely to play a critical role in personalizing TB treatment, leading to improved outcomes. Further research and clinical trials are essential to validate these innovative approaches and integrate them into standardized care for MDR-TB.

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