Primary Pre-Extensively Drug-Resistant Tuberculosis (Pre XDR-TB) Pulmonary Tuberculosis with Diabetes Mellitus: A Case Report

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Abstract. Drug-resistant tuberculosis remains a major challenge in tuberculosis control, and the occurrence of resistance in patients without any prior treatment history raises concern about the transmission of resistant strains within the community. We report the case of a 63-year-old woman presenting with cough for more than two months, marked weight loss, and intermittent fever, without any previous tuberculosis treatment or known contact with a tuberculosis patient. She had a history of diabetes mellitus. Physical examination revealed bronchial breath sounds with rhonchi, and chest radiography revealed infiltration at the right upper lung apex. Rapid molecular testing detected *Mycobacterium tuberculosis* with resistance to rifampicin, and second-line drug susceptibility testing further revealed additional resistance to isoniazid, fluoroquinolone, and ethionamide, leading to a diagnosis of primary pre-extensively drug-resistant tuberculosis. Random blood glucose was elevated and was managed with insulin, while mild hypochromic anaemia was managed with iron supplementation. The patient received bedaquiline, pretomanid, and linezolid, and remained clinically stable without significant adverse effects after one week of therapy. This case highlights the importance of vigilance for primary drug-resistant tuberculosis and the role of rapid molecular testing in early diagnosis and appropriate treatment selection.

Keywords: Drug-resistant tuberculosis, pre-extensively drug-resistant tuberculosis, diabetes mellitus.

1 Introduction

Tuberculosis remains one of the leading causes of death from infectious diseases worldwide, and the emergence of Mycobacterium tuberculosis strains resistant to first- and second-line drugs further complicates control efforts. The World Health Organization estimates that approximately 470,000 cases of rifampicin-resistant or multidrug-resistant tuberculosis occur globally each year, resulting in approximately 180,000 deaths [1].

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Since 2021, the World Health Organization has revised the definition of pre-extensively drug-resistant (pre-XDR) tuberculosis as rifampicin-resistant or multidrug-resistant tuberculosis with additional resistance to fluoroquinolones, while extensively drug-resistant (XDR) tuberculosis is defined as pre-XDR with additional resistance to bedaquiline or linezolid [1]. Xpert MTB/RIF Ultra enables rapid detection of Mycobacterium tuberculosis together with rifampicin resistance within hours, with high sensitivity and specificity, making it an important first-line screening tool in the diagnostic algorithm for drug-resistant tuberculosis [3].

Diabetes mellitus is also recognised as a risk factor that increases susceptibility to active tuberculosis through impairment of the cellular immune response [6]. The combination of drug-resistant tuberculosis and diabetes mellitus requires an integrated management strategy. This case report aims to describe the clinical course, diagnostic process, and management of a patient with primary pre-XDR tuberculosis accompanied by diabetes mellitus to raise clinical awareness of the possibility of primary drug resistance in new tuberculosis patients.

2 Case presentation

A 63-year-old woman presented with a cough lasting > 2 months, accompanied by marked weight loss and intermittent fever. She had no prior history of tuberculosis treatment or known direct contact with a patient with pulmonary tuberculosis. She had a history of diabetes mellitus with no other significant comorbidities. Detailed occupational, smoking, and other social or behavioural risk factors for tuberculosis exposure were not systematically documented in this report.

2.1 Physical Examination and Laboratory

A physical examination revealed bronchial breath sounds with rhonchi on lung auscultation. Complete blood count on July 27, 2026, showed decreased haemoglobin (11.5 g/dL), MCH (24.4 pg), and MCHC (28.6 g/dL), with increased RDW-CV (15.4%), consistent with mild hypochromic anaemia with anisocytosis; the mean corpuscular volume (85.6 fL) remained within the normal range, so a microcytic pattern was not confirmed. Leukocyte and platelet counts were within normal limits. Random blood glucose on the same examination was 217 mg/dL.

Table 1. Complete blood count and random blood glucose results.

Parameter	Result	Reference Range
Hemoglobin	11.5 g/dL	12–16 g/dL
Hematocrit	40.2 %	38–47 %
Leukocytes	8.64 $\times 10^3/\mu L$	4–10 $\times 10^3/\mu L$
Erythrocytes	4.70 $\times 10^6/\mu L$	4–5.5 $\times 10^6/\mu L$

Platelets	287 ×10³/µL	150–350 ×10³/µL
MCV	85.6 fL	80–100 fL
MCH	24.4 pg	26–32 pg
MCHC	28.6 g/dL	32–36 g/dL
RDW-CV	15.4 %	11.5–14.5 %
MPV	6.9 fL	6.5–9.5 fL
Random Blood Glucose	217 mg/dL	110–150 mg/dL

Xpert MTB/RIF Ultra testing of a sputum sample on 20 June 2026 detected Mycobacterium tuberculosis at a high level with Rifampicin resistance. Subsequent second-line Line Probe Assay testing revealed additional resistance to Isoniazid, Fluoroquinolone, and Ethionamide, while resistance to Amikacin, Kanamycin, and Capreomycin was not detected. Sputum smear microscopy grading, mycobacterial culture, and follow-up sputum conversion testing were not performed in this setting and could not be reported.

Table 2. Xpert MTB/RIF Ultra and second-line Line Probe Assay results (June 20, 2026).

Parameter	Result
Xpert MTB/RIF Ultra	MTB detected high; Rifampicin resistance detected
LPA – Isoniazid (H)	Resistance detected
LPA – Isoniazid, low-level	Resistance not detected
LPA – Fluoroquinolone (Fq)	Resistance detected
LPA – Fluoroquinolone, low-level	Resistance not detected
LPA – Amikacin (Amk)	Resistance not detected
LPA – Kanamycin (Km)	Resistance not detected
LPA – Capreomycin (Cm)	Resistance not detected

LPA – Ethionamide (Eto)	Resistance detected

Renal and liver function tests on 28 July 2026 showed urea 19 mg/dL, creatinine 0.8 mg/dL, uric acid 4.3 mg/dL, total bilirubin 0.4 mg/dL, direct bilirubin 0.2 mg/dL, SGOT 20 U/L, and SGPT 19 U/L, all within normal limits, providing a baseline prior to treatment initiation.

Table 3. Renal and liver function test results (July 28, 2026).

Parameter	Result	Reference Range
Urea	19 mg/dL	0–48 mg/dL
Creatinine	0.8 mg/dL	0.6–1.1 mg/dL
Uric Acid	4.3 mg/dL	2.4–5.7 mg/dL
Total Bilirubin	0.4 mg/dL	0–1.3 mg/dL
Direct Bilirubin	0.2 mg/dL	0–0.5 mg/dL
SGOT	20 U/L	0–38 U/L
SGPT	19 U/L	0–35 U/L



Fig. 1. Chest radiograph, PA view, showing infiltrate in the right upper lung apex.

2.2 Diagnosis and Management

Based on the history, physical examination, and investigation results, the patient was diagnosed with primary pre-extensively drug-resistant pulmonary tuberculosis with diabetes mellitus. Specifically, the confirmed resistance to rifampicin, isoniazid, and fluoroquinolones fulfils the current World Health Organization definition of pre-XDR-TB (MDR/RR-TB with additional fluoroquinolone resistance); because resistance to bedaquiline and linezolid was not tested or detected, the case does not meet the additional criterion required for a diagnosis of XDR-TB.

The patient received bedaquiline, pretomanid, and linezolid (BPaL) for the management of pre-XDR tuberculosis following the World Health Organization-recommended dosing schedule of bedaquiline 400 mg once daily for two weeks followed by 200 mg three times weekly, pretomanid 200 mg once daily, and linezolid 600 mg once daily for a planned total duration of 26 weeks (six months). The patient had no prior history of antituberculosis treatment and therefore no previous exposure to bedaquiline, linezolid, pretomanid, or delamanid, an important eligibility consideration for BPaL-based regimens. Baseline safety assessment prior to treatment initiation included a complete blood count (Table 1), renal and hepatic function tests (Table 3), both within normal limits, aside from the anaemia noted above; baseline electrocardiography with corrected QT interval and formal assessment for peripheral neuropathy were not performed and could not be reported. Blood glucose was managed with 10 units of insulin and mild anaemia was empirically managed with intravenous iron supplementation; ferritin, serum iron, and transferrin saturation were not obtained, so an iron-deficiency aetiology could not be objectively confirmed. After one week of therapy, the patient remained clinically stable without any significant adverse effects.

3 Discussion

This case illustrates apparent primary pre-extensively drug-resistant tuberculosis in a patient who reported no prior tuberculosis treatment and no known contact with a tuberculosis patient. The designation of primary resistance in this report relied on the patient's self-reported history; the absence of a known contact does not exclude previous unrecognised exposure or establish community transmission with certainty, and a fully comprehensive assessment of prior antituberculosis or other antimicrobial treatment, household and close-contact history, occupational exposure, and other social risk factors was not obtained. With this caveat, the case remains consistent with the global concern that Mycobacterium tuberculosis strains resistant to rifampicin and second-line drugs can be transmitted directly between individuals in the community rather than arising solely from inadequate treatment [1].

Xpert MTB/RIF Ultra, used in this patient, enabled rapid and accurate detection of Mycobacterium tuberculosis together with Rifampicin resistance, as demonstrated in a multicentre diagnostic study and a more recent Cochrane systematic review update, both reporting high sensitivity and specificity for Rifampicin resistance detection compared with conventional phenotypic drug susceptibility testing [3,10]. Further confir-

mation with second-line Line Probe Assay was then required to identify additional resistance to Fluoroquinolones and second-line injectable agents, allowing the patient to be accurately classified as pre-XDR tuberculosis according to the updated World Health Organization definition [1].

Based on the resistance pattern identified, the bedaquiline, pretomanid, and linezolid (BPaL) regimen was selected for treatment, in line with the World Health Organization recommendation establishing this short oral regimen as the preferred option for rifampicin-resistant tuberculosis with additional fluoroquinolone resistance [2]. The efficacy of this regimen is supported by the Nix-TB and ZeNix trials, which reported high treatment success rates in patients with pre-XDR and XDR tuberculosis with an acceptable safety profile [4,5]. Because bedaquiline is associated with QT prolongation and linezolid with haematological and neurological toxicity that may emerge only after several weeks of therapy, structured baseline and ongoing monitoring is recommended throughout treatment [9]. In this patient, no early adverse events were observed during the first week of therapy; this short observation period should not be interpreted as evidence of overall regimen tolerability, and continued clinical and laboratory monitoring remains necessary given the potential for later haematologic and neurologic toxicity of linezolid. Sustained surveillance and infection control also remain important given emerging evidence that resistance to the newer BPaL/M-regimen drugs can itself be transmitted between patients, as recently documented by whole-genome sequencing studies in several countries [8].

Diabetes mellitus was also an important consideration, as diabetes mellitus has been shown to increase the risk of active tuberculosis and multidrug resistance through impairment of cellular immune function and altered drug pharmacokinetics [6,7]. Insulin therapy was initiated to lower the elevated random blood glucose; however, in the absence of HbA1c and serial inpatient glucose measurements, this reflects glucose-lowering treatment rather than confirmed longer-term glycaemic control, and adequate glycaemic control should continue to be assessed alongside drug-resistant tuberculosis treatment to support an optimal therapeutic response.

This report has several limitations. The follow-up duration was still short, so long-term treatment success and any subsequently emerging adverse effects could not be assessed. The classification of this case as primary resistance relies on the patient's self-reported treatment and contact history; occupational exposure, detailed household and close-contact history, smoking history, and other social or behavioural risk factors were not systematically documented, so previous unrecognised exposure to a resistant source case cannot be excluded. Baseline data such as HbA1c, serial glucose measurements, the specific insulin regimen, iron studies (ferritin, serum iron, transferrin saturation), HIV status, baseline electrocardiography with corrected QT interval, and formal peripheral neuropathy assessment were also unavailable, as were sputum smear grading, mycobacterial culture, and follow-up sputum conversion testing, and a detailed radiological description of disease extent and the presence or absence of cavitation. Together, these gaps limit a complete picture of all contributing risk factors and constrain confidence in the treatment-monitoring narrative, and should be addressed in future prospective reporting of similar cases.

4 Conclusion

This case illustrates that pre-extensively drug-resistant tuberculosis can occur primarily, even without any prior tuberculosis treatment or known contact with a tuberculosis patient. Rapid molecular testing with Xpert MTB/RIF Ultra, confirmed by line probe assay, plays an important role in establishing an early diagnosis and determining the appropriate treatment regimen. No early adverse events were observed during the first week of bedaquiline, pretomanid, and linezolid therapy, while concurrent management of diabetes mellitus was pursued alongside tuberculosis treatment; continued monitoring is needed to assess longer-term tolerability and treatment success. Clinical vigilance for the possibility of primary drug-resistant tuberculosis should be heightened in every new tuberculosis patient, supported by adequate access to rapid molecular testing.

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Disclosure of Interests. The author declares no conflict of interest.

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