

Late Presentation of Multidrug-Resistant Pulmonary Tuberculosis 27 Years after Treated Intracranial Tuberculoma: A Case Report

Srinivasa Reddy Kesari^{1*}, Padma Priya Ankathi¹, Hansika Polepaka¹, Praveen Devanandan¹

¹ Department of Pharmacy Practice, St Peter's Institute of Pharmaceutical Sciences, Hanamkonda, Telangana, India

* Corresponding author: Srinivasa Reddy Kesari, Department of Pharmacy Practice, St Peter's Institute of Pharmaceutical Sciences, Hanamkonda, Telangana, India, 506001. Email: kesarisrinivasreddy2@gmail.com. Telephone: 7730841712

ORCID: Srinivasa Reddy Kesari, 0009-0005-7174-0174; Padma Priya Ankathi, 0009-0003-1344-2158; Hansika Polepaka, 0009-0001-0869-4102; Praveen Devanandan, 0000-0002-1139-9075.

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ABSTRACT

Introduction: Reactivation of tuberculosis after decades of apparent cure is not unheard of, but multidrug-resistant disease appearing this late particularly after a central nervous system infection is rarely documented.

Case Presentation We describe a 58-year-old woman who developed fever, weight loss, and a persistent cough twenty-seven years after successful treatment of an intracranial tuberculoma. A cavitary lesion in the right upper lobe led to a diagnosis of multidrug-resistant tuberculosis, with resistance to both rifampicin and isoniazid confirmed on molecular and phenotypic testing. She began a bedaquiline-based regimen in line with current WHO guidance and went on to achieve early culture conversion along with steady clinical and radiological recovery.

Conclusions: This case is a reminder of how unpredictable tuberculosis latency can be, reinforces the diagnostic value of molecular testing, and confirms the effectiveness of contemporary MDR-TB regimens while making clear that clinical vigilance should not lapse even decades after apparent cure.

Keywords: Multidrug-resistant tuberculosis, late recurrence, intracranial tuberculoma, pulmonary tuberculosis, bedaquiline

Introduction

Tuberculosis is notorious for lying dormant for years, sometimes decades, before re-emerging as active disease. Central nervous system tuberculomas illustrate this particularly well: because the site is relatively shielded from both immune surveillance and systemic drug penetration, viable bacilli can persist there long after treatment is considered complete [1,2]. When reactivation does occur, drug resistance adds a further layer of difficulty, and multidrug-resistant tuberculosis (MDR-TB) defined as resistance to at least rifampicin and isoniazid emerging many years after apparently curative treatment is only rarely reported [1]. We describe a case of pulmonary MDR-TB diagnosed twenty-seven years after treatment for an intracranial tuberculoma, a presentation that speaks to both the diagnostic power of molecular testing and the effectiveness of contemporary bedaquiline-based regimens.

Case Presentation

Patient Information

A 58-year-old woman presented with a two-week history of dry cough, discomfort in the right side of her chest, low-grade evening fevers, poor appetite, and an unintentional weight loss of roughly 4 kg. Twenty-seven years earlier she had been treated for an intracranial tuberculoma, undergoing surgical excision followed by a complete course of antitubercular therapy, after which she had remained entirely well. She had no chronic illness, no immunosuppression, and no known tuberculosis contact.

Clinical Findings

On examination she was mildly febrile (37.4°C, with evening spikes to 38°C) and maintained an oxygen saturation of 96% on room air. Her body mass index had fallen slightly, to 21.3 kg/m² from a baseline of 22.8 kg/m². Chest auscultation revealed diminished breath sounds with fine crepitations over the right upper zone; neurological examination was unremarkable.

Timeline

Table 1 summarises the chronological course of this episode, from her original tuberculoma treatment through to her current status on MDR-TB therapy.

Table 1. Timeline of clinical events

Time Point	Event
27 years before presentation	Diagnosed with an intracranial tuberculoma treated with surgical excision and a complete course of antitubercular therapy, remained well thereafter
2 weeks before presentation	Onset of dry cough, right-sided chest discomfort, low-grade evening fever, anorexia, and unintentional weight loss (~4 kg)
Day 0 (presentation)	Clinical examination, baseline laboratory work-up, chest radiograph, HRCT chest, sputum smear microscopy, GeneXpert MTB/RIF, line-probe assay, and baseline ECG (QTc 423 ms)
Day 14	Mycobacterial culture (set up on presentation) returned positive, with susceptibility to moxifloxacin and bedaquiline and borderline ethionamide resistance
Day 0 (treatment initiation)	Started on bedaquiline, high-dose moxifloxacin, PAS, cycloserine, and low-dose linezolid with pyridoxine, counselling and psychosocial support begun alongside treatment
1 month	Clinical improvement with weight gain, inflammatory markers falling (ESR 38 mm/h, CRP 9 mg/L)
6 weeks	Repeat sputum culture negative, confirming early culture conversion
8 weeks	Repeat QTc 438 ms, within acceptable limits
3 months	HRCT chest showed cavity regression and resolution of nodularity, mild gastrointestinal discomfort and transient paraesthesias managed conservatively
Ongoing	Continues on treatment with sustained clinical, microbiological, and radiological improvement under regular monitoring

Diagnostic Assessment

Laboratory investigations (Table 2) showed mild anaemia (haemoglobin 11.2 g/dL) together with a markedly raised erythrocyte sedimentation rate of 82 mm/h and C-reactive protein of 23 mg/L; renal and hepatic function were normal, as were glycaemic indices, and HIV serology was negative. A chest radiograph showed opacities in the right upper lobe, and high-resolution CT delineated a thick-walled cavity measuring 2.1 cm with surrounding centrilobular nodules

and a tree-in-bud pattern. Sputum smear microscopy was positive for acid-fast bacilli (2+). GeneXpert MTB/RIF identified *Mycobacterium tuberculosis* with rifampicin resistance, and a line-probe assay confirmed additional isoniazid resistance, establishing the diagnosis of MDR-TB. Mycobacterial culture, positive at 14 days, showed susceptibility to moxifloxacin and bedaquiline, with borderline resistance to ethionamide.

Table 2. Baseline laboratory investigations at presentation

Sl. No.	Parameter	Patient Value	Normal Reference Range	Interpretation
1	Haemoglobin (Hb)	11.2 g/dL	Female: 12-16 g/dL	Mild anaemia
2	Total leukocyte count (TLC)	$8.4 \times 10^9/L$	$4.0-11.0 \times 10^9/L$	Within normal limits
3	Neutrophils	71%	40-70%	Mild neutrophil predominance, suggestive of ongoing inflammation/infection
4	Platelet count	$318 \times 10^9/L$	$150-450 \times 10^9/L$	Within normal limits
5	Erythrocyte sedimentation rate (ESR)	82 mm/h	Female: <20 mm/h	Markedly elevated, indicating significant inflammation

Sl. No.	Parameter	Patient Value	Normal Reference Range	Interpretation
6	C-reactive protein (CRP)	23 mg/L	<5 mg/L	Elevated, consistent with active inflammatory process
7	Serum creatinine	0.8 mg/dL	0.6-1.1 mg/dL	Normal renal function
8	Aspartate aminotransferase (AST)	24 U/L	10-40 U/L	Within normal limits
9	Alanine aminotransferase (ALT)	19 U/L	7-35 U/L	Within normal limits
10	Alkaline phosphatase (ALP)	86 U/L	44-147 U/L	Within normal limits
11	Fasting blood glucose (FBG)	93 mg/dL	70-99 mg/dL	Normal glycaemic status
12	HbA1c	5.4%	<5.7%	Non-diabetic range
13	HIV ELISA	Negative	Negative	No evidence of HIV infection

Therapeutic Intervention

Baseline corrected QT interval (QTc) measured 423 ms, and serum electrolytes were within acceptable limits for bedaquiline use. She was started on a regimen combining bedaquiline, high-dose moxifloxacin, para-aminosalicylic acid (PAS), cycloserine, and low-dose linezolid with pyridoxine, consistent with current World Health Organization (WHO) recommendations for MDR-TB. Given the distress of confronting a tuberculosis recurrence after nearly three decades, counselling and psychosocial support were built into her care from the outset.

Follow-up and Outcomes

Within a month she was clinically improved, having gained weight, with inflammatory markers falling (ESR 38 mm/h, CRP 9 mg/L); a repeat sputum culture at six weeks was negative, confirming early culture conversion. QTc remained within acceptable limits (438 ms) at eight weeks, and HRCT at three months showed the cavity regressing with resolution of nodularity. She experienced mild gastrointestinal discomfort and transient paraesthesias, both managed conservatively without interrupting treatment. She remains on therapy, with sustained clinical, microbiological, and radiological improvement under regular monitoring.

Patient Perspective

The patient described considerable emotional distress on learning that her tuberculosis had returned after nearly three decades of presumed cure. She valued the counselling and psychosocial support incorporated into her treatment plan and expressed firm intent to complete the full course of therapy.

Informed Consent

Written informed consent for publication of this case, including clinical and laboratory details, was obtained from the patient; confidentiality was maintained throughout, and the case was managed in accordance with institutional ethical standards and the Declaration of Helsinki (1964, and its later amendments).

Conclusions

This case underlines just how unpredictable the long-term behaviour of *Mycobacterium tuberculosis* can be, resurfacing here twenty-seven years after treatment for an intracranial tuberculoma. Whether this represents late reactivation of the original infection or reinfection with a new, resistant strain cannot be settled with certainty; genotyping would be required for that but several clinical features are informative [1,2].

Mycobacterium tuberculosis is well known to persist for years within granulomas by down-regulating its metabolism and entering a non-replicating state [3,4]. Tuberculomas of the central nervous system are a particularly favourable niche for this kind of persistence, since the site is relatively sheltered from both immune surveillance and drug penetration [5]. Bacilli lodged in such microscopic foci may lie beyond the reach of the immune system and of adequate drug concentrations for years, only to reactivate as immune function shifts subtly with age [6].

Reinfection is at least as plausible an explanation, especially given how endemic tuberculosis remains in this setting, and arguably fits the facts better here: a relapse of her original disease would be expected to reflect the drug-susceptible pattern typical of the era in which she was first treated, yet she instead presented with fully developed MDR-TB [1,7]. An alternative possibility is that bacilli surviving her original at the time adequate treatment already carried low-level resistance, which was then selected for over the following decades [8].

The radiological picture upper-lobe cavitation with tree-in-bud nodularity together with a high bacillary burden, is characteristic of reactivation-pattern tuberculosis, while her constitutional symptoms reflect the cytokine-driven response typical of active disease [2,9]. Non-tuberculous mycobacterial infection, fungal disease, and malignancy were all reasonably excluded given the strength of the microbiological and molecular findings.

Rapid molecular testing proved decisive in this case. Detecting rifampicin resistance by GeneXpert early on meant she was spared continued exposure to first-line drugs that

would not have worked, and this result was subsequently confirmed by phenotypic susceptibility testing [10]. It is a useful reminder that molecular diagnostics retain their value even in patients whose history might otherwise suggest drug-susceptible disease.

The bedaquiline-based regimen achieved early culture conversion with good tolerability, in keeping with the established performance of modern MDR-TB treatment relative to the older injectable-based regimens it has largely replaced [11]. Her prognosis, provided adherence continues, is favourable, though her history of recurrence argues for sustained long-term follow-up.

Two points from this case are worth carrying into practice. First, a remote history of treated tuberculosis even involving the central nervous system does not rule out drug-resistant pulmonary disease decades later, and clinicians should keep their threshold for suspicion low regardless of how long ago the earlier episode occurred. Second, the case shows how rapid molecular diagnostics and contemporary bedaquiline-based therapy can work together to produce a good outcome even in an unusual and high-risk scenario, reinforcing the case for sustained vigilance and modern diagnostic and therapeutic tools in tuberculosis care more broadly.

Declarations

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Conflicts of Interest / Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

As a single-patient case report, formal institutional ethics committee approval was not required under institutional policy; the institutional ethics committee confirmed that no separate approval was needed for retrospective reporting of routine clinical care. The case was managed and reported in accordance with the ethical standards of the responsible institutional review body and with the Declaration of Helsinki (1964) and its later amendments.

Consent to Participate

Informed consent to participate was obtained from the individual participant included in the study.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying clinical details. Patient confidentiality has been strictly maintained throughout, and a copy of the consent form is available for review by the Editor-in-Chief upon request.

Availability of Data and Material

The datasets analysed for this case report are available from the corresponding author on reasonable request, subject to maintaining patient confidentiality.

Code Availability

Not applicable.

Authors' Contributions

All authors contributed to the study conception and clinical management of the patient. Srinivasa Reddy Kesari was primarily responsible for initial patient evaluation, clinical data collection, and day-to-day monitoring of the patient's condition and treatment response. Padma Priya Ankathi and Hansika Polepaka contributed to patient care, assisted in interpretation of diagnostic investigations, and participated in therapeutic decision-making and follow-up assessments. Praveen Devanandan provided overall supervision of the case, confirmed the diagnosis, guided the multidisciplinary management plan including the initiation and monitoring of the bedaquiline-based regimen, and ensured adherence to current clinical guidelines. The first draft of the manuscript was written by Praveen Devanandan and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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