

Paradoxical Reaction during Tuberculosis Treatment in a Non-HIV but Severely Malnourished Patient

Sarah-Marceline Kabamba^{1,2,3}, Prosper Iragi Kulimushi^{1,2}, Pascaline Dunia Muleke^{1,2}, Tony Akilimali Shindano^{1,2,3} 

¹Université Catholique de Bukavu, Bukavu, Democratic Republic of the Congo

²Hospital Provincial Général de Référence de Bukavu, Bukavu, Democratic Republic of the Congo

³Center for Tropical Diseases and Global Health, Bukavu, Democratic Republic of the Congo

Email: shindano.akilimali@ucbukavu.ac.cd

How to cite this paper: Kabamba, S.-M., Kulimushi, P.I., Muleke, P.D. and Shindano, T.A. (2026) Paradoxical Reaction during Tuberculosis Treatment in a Non-HIV but Severely Malnourished Patient. *Case Reports in Clinical Medicine*, 15, 26-32.

<https://doi.org/10.4236/crcm.2026.152004>

Received: December 30, 2025

Accepted: February 6, 2026

Published: February 9, 2026

Copyright © 2026 by author(s) and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Paradoxical Reaction (PR) refers to clinical and/or radiological worsening of tuberculosis in a patient already receiving effective treatment, without alternative explanations such as drug resistance, intercurrent infection, or drug toxicity. PR is frequently reported in HIV-positive patients but can also occur under other conditions of immunosuppression, such as malnutrition. We present the case of a severely malnourished young woman with pulmonary tuberculosis who developed PR during antituberculosis therapy. The outcome was favorable following corticosteroid treatment and nutritional support. This case highlights the importance of recognizing PR as a potential therapeutic complication in immunosuppressed patients.

Keywords

Miliary Tuberculosis, Paradoxical Reaction, HIV Negative, Malnutrition

1. Introduction

Tuberculosis remains a major global public health challenge. According to the World Health Organization (WHO) in 2024, approximately 10.7 million people contracted the disease, resulting in 1.23 million deaths [1].

Despite ongoing eradication efforts, incidence remains high, although mortality has declined due to the demonstrated effectiveness of current first-line therapies [2].

The principal challenges today lie in expanding therapeutic coverage in de-

veloping countries and in detecting and managing resistant forms of tuberculosis [3].

Paradoxical Reaction (PR) is defined as the worsening of clinical signs or the appearance of new lesions despite Appropriate Antituberculosis Treatment (ATT), in the absence of other explanations such as resistance, intercurrent infection, or drug toxicity. It is therefore considered a diagnosis of exclusion [4] [5]. It is more frequently observed and better understood in patients co-infected with Human Immunodeficiency Virus (HIV), particularly following the initiation of Antiretroviral Therapy (ART) [6] [7]. Its incidence in HIV-positive patients with tuberculosis ranges from 3% to 25%, typically occurring 2 - 8 weeks after ART initiation. These reactions are most often seen in extrapulmonary and miliary forms of the disease [4]. Risk factors include high mycobacterial load, extrapulmonary involvement, and immunosuppression such as malnutrition [9]. Although less common, PR has also been reported in HIV-negative patients. The pathophysiological mechanism appears similar, attributed to the release of bacterial antigens following treatment-induced macrophage lysis [10] [11].

Such cases can create diagnostic uncertainty and complicate management, particularly when the patient is initially immunocompetent.

Here, we report a case of miliary tuberculosis presenting as a paradoxical reaction in a severely malnourished patient initially treated for pulmonary tuberculosis.

2. Case Description

The patient was a 31-year-old Congolese housewife, mother of six, with no prior history of tuberculosis exposure but severely malnourished (BMI 14 kg/m²). She was transferred to the Bukavu Provincial General Referential Hospital (HPGRB) for suspected pulmonary tuberculosis. On admission, her complaints included chronic cough, evening and nighttime fever, and progressive deterioration of health.

The illness had begun approximately four months earlier, characterized by a productive cough with yellowish sputum (without hemoptysis), chest pain without dyspnea, evening and nighttime fever, night sweats without chills, anorexia, and unintentional weight loss.

She had previously undergone several consultations where nonspecific antibiotic therapy was prescribed, but without improvement.

On admission, clinical examination revealed fever (38.9°C), severe asthenia, pallor of the skin and mucous membranes, polypnea, and diminished breath sounds throughout the left lung field and the lower third of the right lung.

Laboratory investigations showed leukocytosis (12,310 cells/ μ L) with neutrophilia (11,079 cells/ μ L) and lymphopenia (923 cells/ μ L). C-reactive protein was markedly elevated (>300 mg/L). Additional findings included compensated normocytic hypochromic anemia (hemoglobin 9.7 g/dL; MCV 85 fL; MCHC 34 g/dL), electrolyte disturbances (hyponatremia 132 mmol/L, hypocalcemia 1.09 mmol/L,

hypomagnesemia 1.09 mmol/L), mild hypoalbuminemia (3.3 g/dL), and total protein of 6.3 g/dL. Liver function tests (AST, ALT) were within normal limits. Ziehl-Neelsen staining of sputum was negative, as was the polymerase chain reaction for *Mycobacterium tuberculosis* testing (GeneXpert®). The limited technical facilities did not allow for the mycobacterial culture to be carried out. The diagnosis was therefore strictly clinical and radiological.

Chest X-ray (**Figure 1**) showed bilateral diffuse interstitial pneumonia, presumed bacterial.

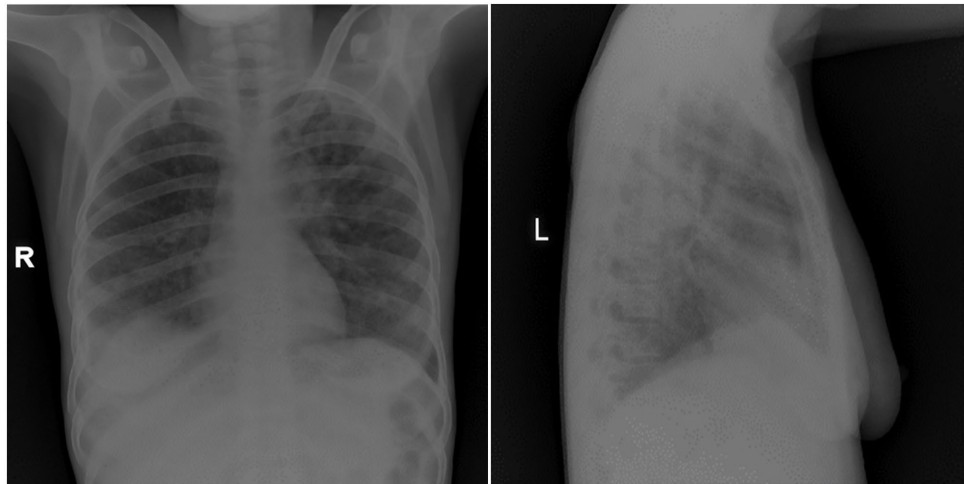


Figure 1. Initial chest X-ray showing bilateral infiltrative reticular opacities.

Given the chronic nature of her condition and lack of improvement after several courses of nonspecific antibiotics (Amikacin, Augmentin®), a standard weight-based antituberculosis regimen was initiated: isoniazid 300 mg daily, rifampicin 600 mg, ethambutol 800 mg, and pyrazinamide 1000 mg. Electrolyte correction and nutritional support were also provided. The clinical picture was consistent with smear-negative pulmonary tuberculosis.

Initial evolution was favorable, with resolution of fever, regression of pulmonary symptoms, and weight gain of 3 kg.

On day 13, however, the patient became febrile again. CRP rose above 300 mg/L, whereas it had decreased to 24 mg/L at day 6 follow-up. The clinical context initially suggested nosocomial infection.

Examination revealed no signs of secondary infection; blood cultures were negative, and empiric antimalarial therapy provided no improvement. Persistent fevers (38.5°C - 40°C) were unresponsive to antipyretics and broad-spectrum antibiotics (Levofloxacin, Ceftriaxone).

After ruling out drug resistance and concurrent illness, the most likely diagnosis was a paradoxical reaction to antituberculosis treatment.

Comparison of chest X-rays showed new diffuse micronodular opacities with cavitation (**Figure 2**), consistent with miliary tuberculosis as part of a paradoxical reaction.

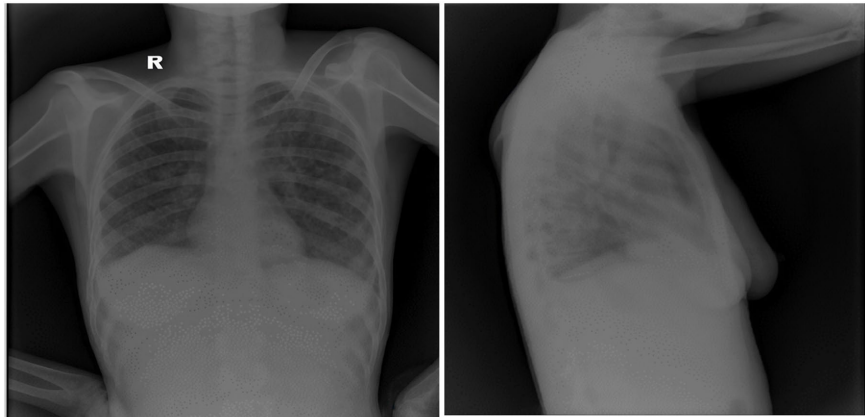


Figure 2. X-ray results showing a worsening of initial infiltrative pulmonary lesions.

Corticosteroid therapy with prednisolone 40 mg (1 mg/kg/day) was initiated, resulting in marked improvement: resolution of fever, weight gain, and radiological improvement (**Figure 3**).

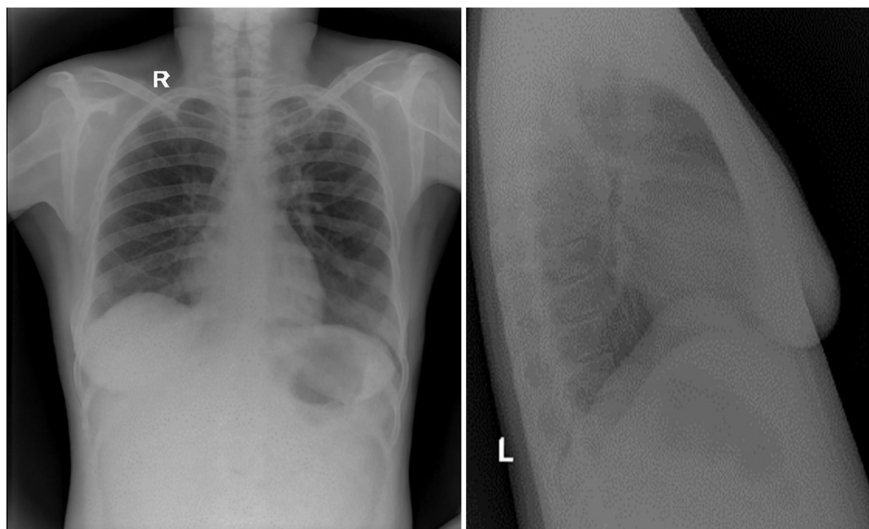


Figure 3. X-ray of the same patient showing a marked improvement in the initial lesions.

Throughout treatment, nutritional support was maintained with a high-protein diet.

3. Discussion

This case illustrates the occurrence of a PR in the form of worsening radiological lesions during antituberculosis treatment in an HIV-negative patient with pulmonary tuberculosis. In our patient, onset occurred at 13 days, which aligns with reports in the literature indicating a range of 2 - 8 weeks [4] [12]. The initial improvement followed by recurrence of fever and radiological deterioration (appearance of diffuse miliary opacities in a patient with initially limited pulmonary disease), together with the absence of evidence of drug resistance or intercurrent in-

fection, supports this diagnosis [13] [14].

Several studies have identified immunological abnormalities such as anemia, lymphopenia, and hypoalbuminemia as well as malnutrition, as predictive or aggravating factors [15] [16]. This is consistent with the biological profile observed in our patient.

It should be noted that paradoxical manifestations are heterogeneous and not yet fully defined. Pulmonary aggravation, characterized by new micronodular opacities or cavitary lesions, is described in 15% - 25% of paradoxical pulmonary reactions, as seen in our case [16] [17].

Management relies on continued Antituberculosis Therapy (ATT) and, in severe cases, the use of corticosteroids to modulate the excessive inflammatory response [18]. Corticosteroids have demonstrated clinical benefit, particularly in life-threatening or functionally disabling disease [19]. Withdrawal should be gradual to prevent relapse. Nutritional support is also essential for a favorable outcome.

The favorable evolution of our patient following corticosteroid therapy strongly supports the diagnosis of PR. Our observation underscores the importance of recognizing this phenomenon promptly to avoid unjustified discontinuation of treatment or premature modification of the therapeutic regimen.

4. Conclusion

Paradoxical reaction is a possible immunological complication of antituberculosis treatment, even in HIV-negative patients. It should be considered in any case of clinical and radiological worsening after initial improvement under ATT, but only after other causes have been excluded. This case highlights the importance of screening for risk factors such as malnutrition, hypoalbuminemia, or other causes of immunosuppression at the start of treatment and addressing them during management. Identifying these factors enables continued vigilance regarding the possibility of PR during therapy.

Ethical Statement

Written informed consent was obtained from the patient for publication of this case and associated radiological images. This report respects patient anonymity and adheres to the ethical principles of the Declaration of Helsinki.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] WHO (2024) Global Tuberculosis (TB). 8 p. <https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2024>
- [2] Ferreira, I.B.B., Menezes, R.C., Araújo-Pereira, M., Rolla, V.C., Kritski, A.L., Cordeiro-

- Santos, M., *et al.* (2025) Effects of Missed Anti-Tuberculosis Therapy Doses on Treatment Outcome: A Multi-Center Cohort Study. *The Lancet Regional Health*, **48**, Article ID: 101162.
- [3] Korotych, O., Achar, J., Gurbanova, E., Hovhannesian, A., Lomtadze, N., Ciobanu, A., *et al.* (2024) Effectiveness and Safety of Modified Fully Oral 9-Month Treatment Regimens for Rifampicin-Resistant Tuberculosis: A Prospective Cohort Study. *The Lancet Infectious Diseases*, **24**, 1151-1161. [https://doi.org/10.1016/s1473-3099\(24\)00228-7](https://doi.org/10.1016/s1473-3099(24)00228-7)
- [4] Narita, M., Ashkin, D., Hollender, E.S. and Pitchenik, A.E. (1998) Paradoxical Worsening of Tuberculosis Following Antiretroviral Therapy in Patients with Aids. *American Journal of Respiratory and Critical Care Medicine*, **158**, 157-161. <https://doi.org/10.1164/ajrccm.158.1.9712001>
- [5] Alharbi, A., Aljahdali, A., Ahamed, M.F. and Almarhabi, H. (2024) Left Hand Abscess as a Paradoxical Reaction during Treatment of Disseminated Tuberculosis in Immunocompetent Patient: Case Report and Review of Literature. *BMC Infectious Diseases*, **24**, Article No. 1186. <https://doi.org/10.1186/s12879-024-10077-w>
- [6] Cheng, V., Ho, P., Lee, R., Chan, K., Chan, K., Woo, P., *et al.* (2002) Clinical Spectrum of Paradoxical Deterioration during Antituberculosis Therapy in Non-HIV-Infected Patients. *European Journal of Clinical Microbiology & Infectious Diseases*, **21**, 803-809. <https://doi.org/10.1007/s10096-002-0821-2>
- [7] Church, L.W.P., Chopra, A. and Judson, M.A. (2017) Paradoxical Reactions and the Immune Reconstitution Inflammatory Syndrome. *Microbiology Spectrum*, **5**. <https://doi.org/10.1128/microbiolspec.tnmi7-0033-2016>
- [8] Sharma, J. and Dorairajan, G. (2024) Atypical Progress of Tuberculosis in the Peripartum Period: Report of a Paradoxical Reaction. *Annals of the National Academy of Medical Sciences (India)*, **60**, 228-230. [https://doi.org/10.25259/anams-2023-5-3-\(921\)](https://doi.org/10.25259/anams-2023-5-3-(921))
- [9] Guo, T., Guo, W., Song, M., Ni, S., Luo, M., Chen, P., *et al.* (2019) Paradoxical Reaction in the Form of New Pulmonary Mass during Anti-Tuberculosis Treatment: A Case Series and Literature Review. *Infection and Drug Resistance*, **12**, 3677-3685. <https://doi.org/10.2147/idr.s211556>
- [10] Gooding, M.S., Hammoud, D.A., Epling, B., Rocco, J., Laidlaw, E., Kuriakose, S., *et al.* (2024) Perplexing Paradoxical Reactions: Navigating the Complexity of Protracted Tuberculosis Meningitis—A Case Report. *Frontiers in Immunology*, **15**, Article 1441945. <https://doi.org/10.3389/fimmu.2024.1441945>
- [11] Hermans, S.M., Akkerman, O.W., Meintjes, G. and Grobusch, M.P. (2024) Post-Tuberculosis treatment paradoxical reactions. *Infection*, **52**, 2083-2095. <https://doi.org/10.1007/s15010-024-02310-0>
- [12] Kocak, I.F., Makki, I., Valdes Bracamontes, M.D.C., Derevenskikh, G., Gupta, K. and Krishnan, P. (2024) Paradoxical Reaction during Active Pulmonary Tuberculosis Treatment in a HIV Negative Patient. *Chest*, **166**, A1515-A1516. <https://doi.org/10.1016/j.chest.2024.06.964>
- [13] Brown, C.S., Smith, C.J., Breen, R.A.M., Ormerod, L.P., Mittal, R., Fisk, M., *et al.* (2016) Determinants of Treatment-Related Paradoxical Reactions during Anti-Tuberculosis Therapy: A Case Control Study. *BMC Infectious Diseases*, **16**, Article No. 479. <https://doi.org/10.1186/s12879-016-1816-4>
- [14] Kassegne, L., Bourgarit, A. and Fraisse, P. (2020) Les réactions paradoxales au cours du traitement de la tuberculose (Hors infection par le VIH). *Revue des Maladies Respiratoires*, **37**, 399-411. <https://doi.org/10.1016/j.rmr.2020.03.006>

- [15] Bhargava, A., Chatterjee, M., Jain, Y., Chatterjee, B., Kataria, A., Bhargava, M., *et al.* (2013) Nutritional Status of Adult Patients with Pulmonary Tuberculosis in Rural Central India and Its Association with Mortality. *PLOS ONE*, **8**, e77979. <https://doi.org/10.1371/journal.pone.0077979>
- [16] Dash, N., Jain, L., Malik, M., Pradhan, P., Choudhary, M., Mandula, P.P., *et al.* (2024) Paradoxical Reaction to Tuberculosis Therapy among HIV-Negative Children: A Systematic Review and Meta-Analysis. *The American Journal of Tropical Medicine and Hygiene*, **111**, 1273-1279. <https://doi.org/10.4269/ajtmh.24-0174>
- [17] Cheng, V.C.C., Yam, W.C., Woo, P.C.Y., Lau, S.K.P., Hung, I.F.N., Wong, S.P.Y., *et al.* (2003) Risk Factors for Development of Paradoxical Response during Antituberculosis Therapy in HIV-Negative Patients. *European Journal of Clinical Microbiology & Infectious Diseases*, **22**, 597-602. <https://doi.org/10.1007/s10096-003-0998-z>
- [18] Samad, M., Dallevet, C.A., Tandjaoui-Lambiotte, Y., Bourgarit, A. and Jaquet, P. (2023) Spectacular Improvement of Paradoxical Reaction in Tuberculosis after Tumor Necrosis Factor-Alpha Antagonist Therapy. *Cureus*, **15**, e50596. <https://doi.org/10.7759/cureus.50596>
- [19] Marais, S., Meintjes, G., Pepper, D.J., Dodd, L.E., Schutz, C., Ismail, Z., *et al.* (2012) Frequency, Severity, and Prediction of Tuberculous Meningitis Immune Reconstitution Inflammatory Syndrome. *Clinical Infectious Diseases*, **56**, 450-460. <https://doi.org/10.1093/cid/cis899>