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Original Research Article

Rifampicin-Induced Hypothyroidism: A Case Report and Review of Clinial Management

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Abstract:

Introduction: Tuberculosis (TB), caused by Mycobacterium tuberculosis, primarily affects the lungs but can spread to other body parts. Drug-resistant TB strains complicate treatment efforts, highlighting the need for new drugs. Rifampicin is crucial for TB treatment but can cause side effects, hypothyroidism being a rare one.

Case Report: A 35-year-old female with pulmonary TB developed fatigue, weight gain, constipation, and dry skin 8 weeks after starting a Rifampicin-based regimen. Elevated TSH (10.5 µIU/mL) and low free T4 (0.7 ng/dL) indicated hypothyroidism. After temporarily discontinuing Rifampicin, her thyroid function normalized, and she was treated with levothyroxine. Symptoms improved, and thyroid function stabilized.

Discussion: Rifampicin can induce hypothyroidism by increasing thyroid hormone metabolism and disrupting thyroid function. Monitoring thyroid function in patients on Rifampicin, especially those at risk, is essential to manage potential hypothyroidism.

Conclusion: Rifampicin can induce hypothyroidism, necessitating vigilant thyroid function monitoring during treatment. Early detection and management with levothyroxine ensure better patient outcomes and adherence to TB therapy.

Keywords: Tuberculosis, Rifampicin, Hypothyroidism, Levothyroxine, Thyroid Function Monitoring.

Introduction

Tuberculosis (TB), caused by the bacterium *Mycobacterium tuberculosis*, primarily targets the lungs but can also disseminate to other areas of the body, resulting in symptoms like coughing, fever, and weight loss[1].The increasing prevalence of drug-resistant tuberculosis strains presents a significant hurdle in global efforts to combat this ongoing public health threat[2,3]. Addressing this issue requires the urgent development of new drugs and an integrative approach [4].

While current chemotherapy has led to better outcomes, the persistent and latent nature of the bacterium, along with the advent of drug-resistant TB, underscores the need for continuous research into novel anti-TB targets and drug candidates [5]. The World Health Organization's DOTS strategy, which utilizes a specific regimen of anti-TB drugs, is a crucial component of TB management [6].

Rifampicin is essential in TB treatment due to its strong bactericidal action against Mycobacterium tuberculosis when used with other anti-TB drugs. It has significantly improved treatment outcomes and shortened therapy duration, solidifying its role in managing the disease[7–9]. Rifampicin is associated with several side effects such as liver damage, rash, gastrointestinal problems, and immune modulation, all of which can affect treatment outcomes and patient adherence[7,10,11]. In this case report, we aim to present a distinctive instance of Hypothyroidism induced by Rifampicin in an adult female.

Case Report

A 35-year-old female with a history of pulmonary tuberculosis, previously not noted for hypothyroidism, presented to the outpatient department of ENT, VIMSAR, Burla, Sambalpur with fatigue, weight gain, constipation, and dry skin 8 weeks after initiating anti-tuberculosis therapy consisting of rifampicin (600 mg daily), isoniazid (300 mg daily), pyrazinamide (1500 mg daily), and ethambutol (1200 mg daily). Physical examination revealed a four-kilogram weight gain

over two months, dry and coarse skin, and slowed relaxation phase reflexes, with no palpable goiter or nodules on thyroid examination. Diagnostic workup revealed elevated thyroid-stimulating hormone (TSH) levels at 10.5 μIU/mL (normal range: 0.4-4.0 μIU/mL) and low free thyroxine (T4) levels at 0.7 ng/dL (normal range: 0.9-2.3 ng/dL). Thyroid peroxidase antibodies (TPOAb) and thyroglobulin antibodies (TgAb) were negative, and thyroid ultrasound showed normal echotexture without nodules or enlargement. Patient was not hypothyroid nor any relevant history was present at the start of ATT. In pre-existing literature, several cases of Rifampicin-induced hypothyroidism were reported. Hence Rifampicin was withdrawn from the treatment regimen temporarily. Regular monitoring showed improvement in symptoms and normalization of TSH levels to 3.2 μIU/mL and maintenance of free T4 levels at 1.5 ng/dL eight weeks post-withdrawal of Rifampicin. A causality assessment of this case was done using WHO UMC criteria and found to be "Probable". Hence the patient was diagnosed with primary hypothyroidism likely induced by Rifampicin, known to increase thyroid hormone metabolism by inducing hepatic enzymes, resulting in lowered T4 and triiodothyronine (T3) levels. Treatment involved the continuation of rifampicin for effective tuberculosis management and initiation of levothyroxine at 25 μg daily with dose titration based on follow-up thyroid function tests. Four weeks after the initiation of levothyroxine treatment, the patient underwent another follow-up assessment. The thyroid function tests showed normalization of TSH levels to 2.8 μIU/mL and maintenance of free T4 levels at 1.4 ng/dL. The patient reported further improvement in symptoms, indicating effective management of the hypothyroidism. Regular monitoring and appropriate dose adjustments of levothyroxine were continued to ensure sustained thyroid function stability.

Discussion

Rifampicin, an essential drug for tuberculosis treatment, has been linked to inducing hypothyroidism in certain patients. This side effect arises because Rifampicin enhances the metabolism and clearance of thyroid hormones by activating cytochrome P-450 enzymes. Additionally, it disrupts iodine uptake, thyroid hormone synthesis, hormone receptor activity, and intracellular signal transduction[12]. It has also been found that ethionamide, prothionamide, and para-aminosalicylic acid are some other antitubercular drugs responsible for the development of hypothyroidism[13].

In a case report of an 85-year-old woman with pulmonary tuberculosis and tuberculous pleurisy, Rifampicin caused hypothyroidism, manifesting as persistent appetite loss, malaise, and edema. Treatment with levothyroxine improved her symptoms without interrupting the tuberculosis regimen, highlighting the need to consider Rifampicin-induced hypothyroidism in similar cases[12].In another study, three euthyroid patients with Hashimoto's thyroiditis developed hypothyroidism after receiving Rifampicin for tuberculosis treatment. A study of 67 tuberculosis patients treated with Rifampicin found that 42 ATA (Anti-thyroid antibodies) negative patients and 22 of 25 ATA-positive patients maintained stable TSH levels. However, three ATA-positive patients developed hypothyroidism, with significant increases in TSH levels, which resolved after discontinuing Rifampicin. These patients (two women and one man) required temporary T4 therapy until the completion of Rifampicin treatment, highlighting the risk of Rifampicin-induced hypothyroidism in at-risk individuals[14].

Conclusion

This case report highlights the potential for Rifampicin, a cornerstone drug in tuberculosis treatment, to induce hypothyroidism. In this instance, a 35-year-old female without prior thyroid issues developed significant hypothyroidism shortly after commencing a Rifampicin-based anti-tuberculosis regimen. The patient's thyroid function normalized following the temporary cessation of Rifampicin and initiation of levothyroxine therapy, underscoring the importance of monitoring thyroid function in patients receiving Rifampicin, particularly those with risk factors for thyroid dysfunction.

This case, along with existing literature, suggests that healthcare providers should remain vigilant for signs of hypothyroidism in patients treated with Rifampicin, ensuring prompt intervention to manage this adverse effect without compromising the efficacy of tuberculosis treatment. Regular thyroid function tests and appropriate levothyroxine dosing adjustments are critical for the effective management of Rifampicin-induced hypothyroidism, promoting better patient outcomes and adherence to the anti-tuberculosis regimen.

References

1. Corleis B, Tzouanas CN, Wadsworth MH, Cho JL, Linder AH, Schiff AE, et al. Tobacco smoke exposure results in recruitment of inflammatory airspace monocytes and accelerated growth of Mycobacterium tuberculosis [Internet]. bioRxiv; 2022; 2022.12.21.521304. Available from: https://www.biorxiv.org/content/10.1101/2022.12.21.521304v1
2. Jena L, Harinath BC. Anti-tuberculosis Therapy: Urgency for New Drugs and Integrative

Approach. Biomed Biotechnol Res J BBRJ. 2018 Mar; 2(1):16.
3. 3. Jones TF, Craig AS, Valway SE, Woodley CL, Schaffner W. Transmission of tuberculosis in a jail. Ann Intern Med. 1999 Oct 19; 131(8):557–63.
4. Sarkar S, Suresh MR. An Overview Of Tuberculosis Chemotherapy – A Literature Review. J Pharm Pharm Sci. 2011 Apr 27; 14(2):148.
5. Chetty S, Ramesh M, Singh-Pillay A, Soliman MES. Recent advancements in the development of anti-tuberculosis drugs. Bioorg Med Chem Lett. 2017 Feb 1; 27(3):370–86.
6. Bansal R, Sharma D, Singh R. Tuberculosis and its Treatment: An Overview. Mini-Rev Med Chem. 18(1):58–71.
7. Decroo T, Maug AKJ, Hossain MA, Uwizeye C, Gumusboga M, Demeulenaere T, et al. Injectables' key role in rifampicin-resistant tuberculosis shorter treatment regimen outcomes. PLoS ONE. 2020 Aug 31; 15(8):e0238016.
8. Dutta NK, Karakousis PC. Can the duration of tuberculosis treatment be shortened with higher dosages of rifampicin? Front Microbiol. 2015 Oct 14; 6:1117.
9. Radtke KK, Svensson EM, van der Laan LE, Hesseling AC, Savic RM, Garcia-Prats AJ. Emerging data on rifampicin pharmacokinetics and approaches to optimal dosing in children with tuberculosis. Expert Rev Clin Pharmacol. 2022 Feb; 15(2):161–74.
10. Bandgar HR. Side Effects of TB Therapy and Recent Therapeutic Approaches for Tuberculosis Management. Asian J Pharm Res. 2023 Mar 22; 13(1):31–3.
11. Odeh A, Altaei T. Impact of Isoniazid and Rifampicin on Chemokines with Clinical Parameters in Tuberculosis Patients. Biomed Pharmacol J. 2023 Mar 21;16(1):611–27.
12. Hamada Y, Sato A, Motojima S. [Pulmonary Tuberculosis and Tuberculous Pleurisy Complicated With Rifampicin-Induced Hypothyroidism: A Case Report]. Kekkaku. 2017 Jan; 92(1):41–5.
13. Hypothyroidism induced by antituberculosis drugs. | Bulletin of the Academy of Sciences of Moldova. Medical Sciences. 2022 Dec 12; Available from: https://bulmed.md/bulmed/article/view/3498
14. Takasu N, Kinjou Y, Kouki T, Takara M, Ohshiro Y, Komiya I. Rifampin-induced hypothyroidism. J Endocrinol Invest. 2006 Jul 1; 29(7):645–9.