



## Primary thyroid tuberculosis: a rare hypothyroidism etiology

Tuberculose primária da tireoide: uma etiologia rara de hipotireoidismo

Tuberculosis primaria de la tiroides: una rara etiología del hipotireoidismo

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### ABSTRACT

**Objective:** To present a clinical case of primary thyroid tuberculosis associated with hypothyroidism. **Case details:** Primary thyroid tuberculosis with associated hypothyroidism is an unusual manifestation of tuberculous infection. We present the case of a 31-year-old female patient who reported a loss of appetite, hair loss, and the development of cervical nodules without fever or secretions. Her thyroid ultrasound revealed only an atypical cervical lymph node on the right side, with no other abnormalities. Laboratory tests indicated hypothyroidism, and she was started on levothyroxine sodium 25 mcg/day. Despite the treatment, the patient remained symptomatic. Fine-needle aspiration cytology of the thyroid suggested a hyperplastic follicular nodule or papillary cancer, leading to a decision for total thyroidectomy. Anatomopathological examination of the thyroidectomy specimen revealed chronic granulomatous thyroiditis with necrosis and granulomatous lymphadenitis. Given the strong response to the tuberculin test, a six-month course of antitubercular treatment was initiated. **Final considerations:** This case punctuates the importance of considering thyroid tuberculosis in the differential diagnosis of cervical masses and the necessity of biopsy and histopathological examination to accurately diagnose the disease and initiate timely treatment.

**Keywords:** Tuberculosis, Endocrine tuberculosis, Thyroid, Hypothyroidism.

### RESUMO

**Objetivo:** Apresentar um caso clínico de tuberculose primária da tireoide associada a hipotireoidismo em uma paciente de 31 anos. **Detalhamento do caso:** A tuberculose primária da tireoide com hipotireoidismo associado é uma manifestação incomum da infecção tuberculosa. Apresentamos o caso de uma paciente de 31 anos que relatou perda de apetite, queda de cabelo e desenvolvimento de nódulos cervicais sem febre ou secreções. Sua ultrassonografia da tireoide revelou apenas um linfonodo cervical atípico no lado direito, sem outras anormalidades. Os exames laboratoriais indicaram hipotireoidismo, e ela iniciou o tratamento com

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levotiroxina sódica 25 mcg/dia. Apesar do tratamento, a paciente continuou sintomática. A citologia de aspiração por agulha fina (FNAC) da tireoide sugeriu um nódulo folicular hiperplásico ou câncer papilífero, levando à decisão de tireoidectomia total. O exame anatomopatológico da peça de tireoidectomia revelou tireoidite granulomatosa crônica com necrose e linfadenite granulomatosa. Dada a forte resposta ao teste tuberculínico, foi iniciado um tratamento antituberculoso de seis meses. **Considerações finais:** Este caso destaca a importância de considerar a tuberculose da tireoide no diagnóstico diferencial de massas cervicais e sublinha a necessidade de biópsia e exame histopatológico para diagnosticar com precisão a doença e iniciar o tratamento oportuno.

**Palavras-chave:** Tuberculose, Tuberculose endócrina, Tireoide, Hipotiroidismo.

## RESUMEN

**Objetivo:** Presentar un caso clínico de tuberculosis primaria de la tiroides asociada con hipotiroidismo. **Detalles del caso:** La tuberculosis primaria de la tiroides con hipotiroidismo asociado es una manifestación inusual de la infección tuberculosa. Presentamos el caso de una paciente de 31 años que reportó pérdida de apetito, caída de cabello y desarrollo de nódulos cervicales sin fiebre ni secreciones. Su ecografía tiroidea reveló solo un ganglio cervical atípico en el lado derecho, sin otras anomalías. Las pruebas de laboratorio indicaron hipotiroidismo, y se inició tratamiento con levotiroxina sódica 25 mcg/día. A pesar del tratamiento, la paciente siguió sintomática. La citología por aspiración con aguja fina de la tiroides sugirió un nódulo folicular hiperplásico o cáncer papilar, lo que llevó a la decisión de una tiroidectomía total. El examen anatomopatológico de la muestra de tiroidectomía reveló tiroiditis granulomatosa crónica con necrosis y linfadenitis granulomatosa. Dada la fuerte respuesta a la prueba de tuberculina, se inició un tratamiento antituberculoso de seis meses. **Consideraciones finales:** Este caso destaca la importancia de considerar la tuberculosis de la tiroides en el diagnóstico diferencial de masas cervicales y subraya la necesidad de biopsia y examen histopatológico para diagnosticar con precisión la enfermedad e iniciar el tratamiento oportuno.

**Palabras clave:** Tuberculosis, Tuberculosis endocrina, Tiroides, Hipotiroidismo.

## INTRODUCTION

Tuberculosis (TB) remains a significant global public health issue, affecting approximately 10.6 million people in 2022, with 1.3 million deaths reported that same year, according to the World Health Organization (WHO) (WORLD HEALTH ORGANIZATION, 2023). In Brazil, the Ministério da Saúde recorded 84,858 new TB cases and approximately 5,500 deaths in 2023. Typical signs of TB include fever, excessive night sweats, and unintended weight loss, often accompanied by symptoms specific to the affected organs (MINISTÉRIO DA SAÚDE, 2023).

TB is a disease caused by *Mycobacterium tuberculosis* (*M. tuberculosis*), a facultative intracellular pathogen which infection in humans can persist for many years even with a fully operational immune system (KALSCHEUER R, et al., 2019). *M. tuberculosis* is generally transmitted through aerosol droplets and firstly invades the alveolar passages of humans. If the infection is not effectively controlled by the immune system, it can spread to other parts of the body, leading to various forms of extrapulmonary TB (EPTB), although Pulmonary TB is the most frequent manifestation of the disease (SMITH I, 2003).

EPTB is frequently associated with lymph nodes and pleura infection and its rates have been increasing year by year since a few decades ago. In Europe in 2020, 21,5% of TB infections were extrapulmonary whereas 73,1% were Pulmonary TB (ROLO M, et al., 2023). The thyroid is a very uncommon region for TB because it offers some resistance to *M. tuberculosis*, but yet, in rare occasions, thyroid has been documented as the primary or secondary site of the infection.

The incidence of thyroid TB (TTB) remains low, ranging from 0.1% to 0.4%, even in countries with a high prevalence of Pulmonary TB (BANSAL LK, et al., 2021). TTB is difficult to diagnose because symptoms may vary between a large variety of clinic manifestations such as dysphagia, presence of abscess, thyroiditis hyperthyroidism and hypothyroidism (BULBULOGLU E, et al., 2006).

There is no laboratory test to TTB, but some tools are known to be helpful. Fine Needle Aspiration Cytology (FNAC) may diagnose TTB in 73% of cases and Polymerase Chain Reaction (PCR) is also a strong method to detect fragments of *M. tuberculosis* DNA in the thyroid, while an imaging approach is frequently non-specific and non-dianostic, nevertheless, helps to identify abnormalities in the thyroid gland (CHAUDHARY P, et al., 2023). Therefore, this study aimed to report a case of a 31-year old female patient who presented a primary TTB with hypothyroidism.

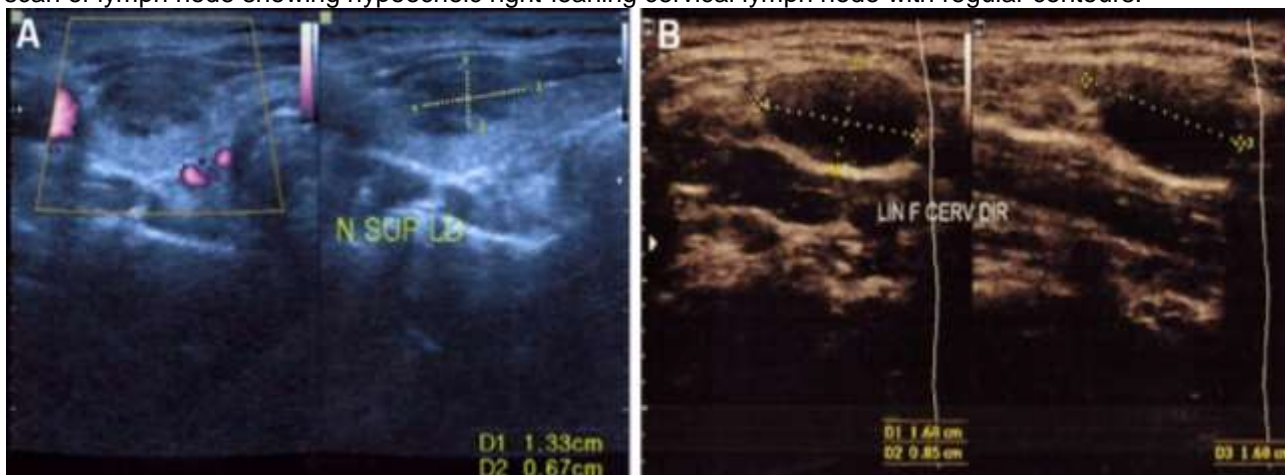
### CASE DETAILS

The Brazilian Ethics Committee for Human Research (CEP/CONEP) approved the present work under the number 67806217.4.0000.5141 and 2.049.722, in compliance with the Declaration of Helsinki and national and patient anonymity and the patient signed the free and informed consent. A 31-year-old female patient, born, raised, and currently residing in Montes Claros, Minas Gerais, Brazil, presented with a ten-month history of a right-sided cervical lump with progressive growth associated with cervical pain but without discharge of secretions.

Her medical history included systemic arterial hypertension for the past three years, treated with hydrochlorothiazide 25 mg/day, and no reported allergies or significant family history. A physical examination revealed an overall good condition, no fever, and eutrophic and standard color. Vital signs within the normal range, with particular attention to the convergent arterial blood pressure (110/100mmHg), assessed in 2 different moments. On cervical palpation, a nodule was noted on the right, in the V region. It was about 2 cm wide, painless, adherent, fibroelastic, and showed no local phlogosis.

Thyroid gland was normal on palpation. Respiratory, cardiovascular, abdominal and neurological examinations were unremarkable. Thyroid and cervical ultrasonography were requested and showed a gland without abnormalities and an atypical cervical lymph node on the right in the Vb region (posterior to the sternocleidomastoid muscle, from the base of the skull to the clavicle, between the thyroid isthmus and the clavicle), measuring 1.68 cm, hypoechoic, with regular contours (**Fig.1B**).

**Figure 1** - Thyroid and Lymph Node Ultrasound Scan. **(A)** Doppler Ultrasound scan of the Thyroid gland – Hypoechoic Right lobe node, non-circumscription margin 1.33 x 0.67 cm. Level 1 Chammas. **(B)** Ultrasound scan of lymph node showing hypoechoic right-leaning cervical lymph node with regular contours.



Source: Oliveira Filho EA, et al., 2025.

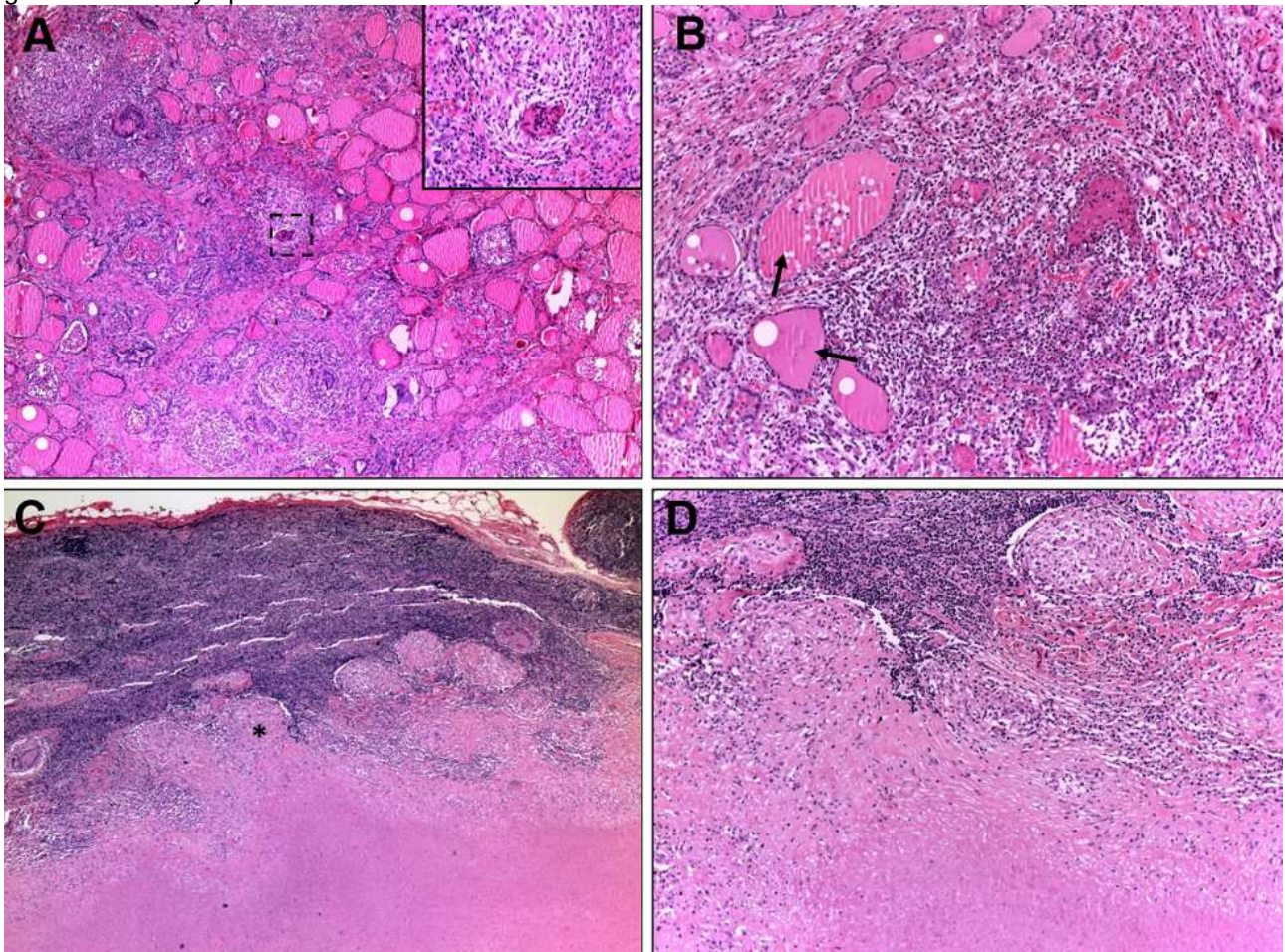
On another visit, she reported that she had had decreased appetite and hair loss for one month, without fever, weight loss, cough, or any other symptoms or signs. Laboratory tests revealed hypothyroidism and she was immediately started on Puran T4 25mcg/day, with further chest radiography and another round of ultrasound (US) of the neck and thyroid. Chest radiography showed no changes, and US revealed a thyroid nodule with reactive lymphadenopathy (**Fig. 1A**). Lymph node fine-needle aspiration cytology (FNAC) with the



hemorrhagic specimen, moderately cellular without atypical cytologic findings, showed cytoarchitectural atypical findings of undetermined significance, Bethesda 3 category.

One year after the first symptoms on FNAC, papillary carcinoma was suspected, which led to a complete thyroidectomy with right-sided selective cervical leakage. The material was sent for anatomopathologic examination, which revealed necrotizing chronic granulomatous thyroiditis (Figure 2A and B) and granulomatous lymphadenitis (Figure 2C and D). Despite negative tests for alcohol-acid-resistant bacilli, the histologic findings were suggestive of TB.

**Figure 2** - H&E stained thyroid and lymph node histopathology. **(A)** Thyroid parenchyma at 10X showing cohesive epithelioid granulomas and foreign body type multinucleated giant cells at 100X. **(B)** Thyroid tissue section showing chronic granulomatous inflammatory process and focal necrosis (100X). Normal thyroid follicles (arrow). **(C)** Histologic section of lymph node (40X) showing chronic granulomatous inflammatory process with caseous necrosis in central areas (\*). **(D)** 100X lymph node section showing "chronic caseating granulomatous lymphadenitis" with extensive area of necrosis.



**Source:** Oliveira Filho EA, et al., 2025.

After highly reactive tuberculosis test results, the patient was referred to the Center for Infectious Diseases and started a 6-month TB treatment. After one month, the patient was asymptomatic with an excellent response to pharmacological treatment. The patient's status evolved to permanent regression of symptoms without further changes after five months of anti-tuberculosis drug therapy.

## DISCUSSION

The most common EPTB is the tuberculous lymphadenitis; it affects local lymph nodes and can occur either through hematogenous spread following primary tuberculosis or as a direct extension from a tuberculous

infection in the tonsils or adenoids. The clinical presentation varies depending on the affected lymph nodes, with cervical node involvement being the most common. Lymphadenitis in the cervical, axillary, and inguinal regions often manifests as painless swelling without notable systemic symptoms (CATAÑO JC e ROBLEDÓ J, 2017). In some cases, the swelling may become noticeable due to the gradual increase in size, leading to cosmetic concerns and discomfort. Additionally, in more severe instances, the swelling may progress to form abscesses, further complicating the clinical picture.

Another form of EPTB that is found to occur in up to 5% of TB patients in developed countries is pleural TB. Pleural TB involves the pleural space. Patients commonly present with symptoms such as fever, sharp chest pain, and a dry cough. Physical examination may reveal signs of pleural effusion, including reduced breath sounds and dullness to percussion over the affected area. In some cases, patients may also experience difficulty in breathing and general malaise, which can contribute to reduced physical activity and overall quality of life.

Diagnosis typically involves imaging techniques such as chest X-rays or CT scans, which can detect pleural effusion. Confirmation is achieved through pleural fluid analysis, where findings may include elevated levels of adenosine deaminase (ADA), a predominance of lymphocytes, and the presence of *M. tuberculosis* identified via culture or molecular tests (SHAW JA et al., 2018). Early and accurate diagnosis is crucial to prevent the progression of the disease and potential complications like pleural thickening or fibrothorax.

Skeletal TB, also known as bone TB, is also an extrapulmonary manifestation of TB where *M. tuberculosis* infects the bones and joints. The spine is frequently affected, a condition referred to as Pott's disease. This form of tuberculosis typically presents with chronic back pain, fever, and weight loss, and can lead to significant spinal deformities and bone damage if not treated promptly. In advanced cases, the spinal deformities can severely impact mobility and quality of life, necessitating ongoing physical therapy and rehabilitation.

Diagnosis is generally made using imaging techniques such as X-rays or magnetic resonance imaging (MRI) to evaluate the extent of bone damage, coupled with microbiological tests to confirm the presence of the TB bacteria. Treatment involves a prolonged course of antitubercular medications similar to those used for pulmonary TB, and in severe cases, surgical intervention may be necessary to correct spinal deformities or to drain abscesses (GOLDEN MP e VIKRAM HR, 2005). The choice of surgical intervention depends on the severity of the deformities and the presence of any neurological deficits. TTB was first reported by Lebert in 1862 in a patient diagnosed with miliary TB.

In 1983, Bruns documented a case of primary TTB, marking an important milestone in understanding this uncommon manifestation of the disease. Since then, only a limited number of cases have been reported, primarily through post-mortem studies, underscoring the rarity of TTB in clinical practice. The precise prevalence of this condition remains uncertain, with estimates ranging from 0.1% to 0.6%. Despite the high incidence of TB in certain regions, TTB continues to be a rare finding, with approximately 200 cases reported globally (VARGHESE A, et al., 2015). This low prevalence contributes to the challenges in recognizing and diagnosing TTB early, often leading to delayed treatment and increased risk of complications.

This indicates that while thyroid involvement can occur in the context of TB, it is an infrequent event, warranting further investigation and awareness in both clinical and research settings. Thyroid function is typically preserved in cases of TTB, and alterations in thyroid hormone levels are exceptionally rare. A comprehensive literature review was conducted according to Bulbuloglu et al., and 240 articles published between 1862 and 2024, of which only 19 reported changes in thyroid function associated with TB were identified. The majority of cases are concentrated in Eastern countries, particularly India. TTB affects individuals aged 18 to 79 years, with no specific age group predominance, although there is a higher susceptibility among females.

The presence of TTB in a relatively broad age range suggests that while the condition is rare, it can impact various demographic groups, emphasizing the need for vigilance across different age categories. The presence of comorbidities does not appear to be a significant factor for infection, as many cases occurred in the absence of chronic diseases. Treatment with anti-tuberculosis drugs has demonstrated promising results



in managing the condition and improving patient outcomes. A case of a 45-year-old man in India with TTB presented with a diagnosis of hyperthyroidism, characterized by elevated levels of thyroid hormones and respiratory and constitutional symptoms. This hyperthyroid state was a result of an infection of the thyroid gland by the *M. tuberculosis* bacillus, which can cause increased hormone release.

The initial presentation of hyperthyroidism in TTB cases can be misleading, often complicating the diagnosis as it may mimic other forms of thyroid dysfunction or hyperthyroid conditions. However, as the disease progressed and the infection caused further damage to thyroid tissue, the patient's condition evolved into hypothyroidism. This subsequent hypothyroidism was marked by low levels of thyroid hormones (LUIZ HV, et al., 2013). This transition from hyperthyroidism to hypothyroidism underscores the dynamic nature of thyroid involvement in TB and highlights the need for ongoing monitoring and adjustment of treatment strategies.

Thyroid involvement in TB can be either primary or secondary, with secondary involvement often occurring due to hematogenous spread in miliary TB. It is estimated that the thyroid is the primary site in only 0.003 to 0.1% of all TB cases, making isolated thyroid tuberculosis exceptionally rare and most TB cases originate from other organs, with the thyroid rarely being the primary focus (VARGHESE A, et al., 2015). Secondary thyroid TB can result from widespread dissemination of TB bacteria, highlighting the importance of assessing the thyroid gland in patients with advanced or disseminated TB.

The extrapulmonary location of the thyroid serves as a barrier to infection by TB bacilli. This resistance is attributed to the presence of colloidal and iodine-rich material in the thyroid follicles, both of which exhibit significant bactericidal activity. Additionally, the thyroid's relatively low temperature compared to other organs might also contribute to its reduced susceptibility to infection. Furthermore, the rich vascularization of the thyroid gland further contributes to its defense against bacterial invasion (BULBULOGLU E, et al., 2006).

Symptoms of TTB can be quite variable, and the condition may sometimes be asymptomatic (KATARIA SP, et al., 2012). The most common clinical finding is a solitary thyroid nodule. However, the disease can also present with other manifestations, including cervical masses or lymph nodes, dysphagia (difficulty swallowing), dysphonia (voice changes), thyroid abscesses, subacute granulomatous thyroiditis, and chronic nonsuppurative thyroiditis. Patients with TTB may also experience symptoms such as fatigue and generalized weakness, which can further complicate the clinical picture. In a review conducted by Bulbuloglu E et al. (2006), which examined 76 patients with thyroid tuberculosis identified between 1905 and 2004, 49 patients presented with solitary nodules or multinodular goiter, ten had thyroid abscesses, and two had cysts.

Imaging plays a crucial role in the diagnosis of TTB, though imaging findings alone are not definitive for diagnosis. Various imaging techniques, including chest X-ray, magnetic resonance imaging (MRI), contrast-enhanced computed tomography (CT), thyroid scintigraphy, and ultrasound (US), can reveal abnormalities associated with thyroiditis and help distinguish TTB from other thyroid conditions (CHAUDHARY P, et al., 2023). US in TTB may show heterogeneous masses, hypoechoic lesions, and atypical lymphadenopathy. However, these findings are nonspecific and can be seen in various other conditions (MAJUD U e ISLAM N, 2011).

For a more accurate diagnosis, a combination of imaging results and clinical findings is essential. In the case presented, the US revealed nonspecific findings such as nonvascular nodules within the thyroid gland, in addition to lymph nodes that were characteristic of an infectious process. FNAC can be valuable for diagnosing TTB, although it may not always differentiate it from other conditions such as papillary carcinoma. Histopathological analysis typically reveals granulomas characterized by epithelioid histiocytes and Langhans giant cells, central caseous necrosis, and peripheral lymphocytic infiltration (AKBULUT S, et al., 2011).

Careful interpretation of FNAC results is necessary to avoid misdiagnosis, particularly in distinguishing TTB from malignancies. A systematic review published in 2022 pointed out that FNAC is an effective diagnostic tool for TTB and provides valuable comprehension for managing the disease (CHAUDHARY P, et al., 2023). In the presented case, the histological findings (**Fig. 2 and 3**), along with strong reactivity to tuberculosis tests, reinforced the diagnosis of tuberculosis. The antimicrobial regimen for treating *M. tuberculosis* is generally effective without requiring surgical intervention, although a definitive diagnosis is often confirmed after lesion

removal (TAN KK, 1993). The effectiveness of the treatment regimen is enhanced by adherence to the prescribed therapy and regular monitoring of patient response. In the case described, the initial treatment included rifampicin, isoniazid, ethambutol, and pyrazinamide for the first two months.

This was followed by a continuation phase with rifampicin and isoniazid for an additional four months. Ongoing follow-up and evaluation are crucial to ensure the resolution of infection and to manage any potential side effects of the medication. The patient demonstrated a positive clinical response to this treatment regimen. There is no evidence suggesting that the standard antituberculosis drugs used for pulmonary TB are ineffective against other forms of TB. Therefore, the same regimen can be employed for TTB.

Rifampicin, a macrocyclic antibiotic, is a cornerstone in TB treatment due to its potent activity against *M. tuberculosis* and other mycobacterial species. It works by inhibiting bacterial DNA-dependent RNA polymerase. Isoniazid, the most widely used TB medication, is highly effective and works by inhibiting the synthesis of lipids and DNA, thus, inhibiting cell wall synthesis. Ethambutol is a bacteriostatic agent that inhibits cell wall synthesis and is always used in combination with rifampicin and isoniazid. Pyrazinamide, another key drug in the regimen, is used in combination with isoniazid or rifampicin.

Although its exact mechanism of action is not fully understood, it exhibits both bactericidal and bacteriostatic properties (NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES, 2012). The reported case describes primary thyroid tuberculosis progressing to hypothyroidism, which is rare in the literature, and opens the possibility of new research aimed at the physiopathologic basis of this involvement. Furthermore, it should be considered in the differential diagnosis of cervical masses.

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