Case Report

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Thyroid tuberculosis associated with papillary microcarcinoma: case report and review of literature

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Introduction: Thyroid tuberculosis (TB) is extremely rare. Infection may first occur in the thyroid gland or may be secondary to TB in other parts of the body. The diagnosis is rarely made clinically because the disease's variable presentation often resembles that of a malignancy or an euthyroid nodular goiter.

Case report: We present the case of a 40-year-old woman, who presented multiple thyroid nodules in both lobes. Two of these nodules were classified as EU-TIRADS V (European Thyroid Imaging and Reporting Data System). The ultrasound also found an adenopathy of the inferior part of the jugular lymphatic chain, in favor of malignancy. The histopathological examination after total thyroidectomy showed thyroid TB, associated to a papillary microcarcinoma of the right thyroid lobe, and the final examination of the adenopathy showed similar granulomas with caseous necrosis, and no signs of metastasis.

Clinical discussion: Thyroid TB is very rare. Its diagnosis is difficult due to a lack of specific signs and symptoms, which is why the diagnosis is most commonly made on pathological examination after thyroid surgery. It is well known that mycobacterial infection creates an environment of chronic and persistent inflammation, with possible DNA damage. This can create a microenvironment that is highly conductive to carcinogenesis, which could explain the discovery of papillary microcarcinoma in addition to thyroid TB in our patient.

Conclusion: This report presents a rare case of malicious growth development of thyroid nodules and thyroid TB. Therefore, physicians must always be vigilant when managing thyroid nodules, as there is always the possibility of malignant lesions associated to an inflammatory or infectious cause.

Keywords: case report, multifocal tuberculosis, papillary microcarcinoma, thyroid tuberculosis

Introduction

The thyroid is an uncommon site of tuberculosis (TB), even in endemic countries[1]. The disease occurs in ~0.1–0.4% of all TB lesions[2]. The association between thyroid TB and papillary carcinoma is even more unusual[3]. We report the case of a 40-year-old patient who presented with a multinodular thyroid and a cervical lymph node, with the final diagnosis being multifocal thyroid and lymph node TB associated with a thyroid papillary microcarcinoma, and discuss the diagnosis and treatment of each disease, as well as the particularities of this association.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article

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HIGHLIGHTS

- Thyroid tuberculosis (TB) is extremely rare.
- It can present as solitary thyroid nodules or a diffuse multinodular goiter.
- The association between thyroid TB and papillary carcinoma is even more unusual.
- The differential diagnosis is very difficult before surgery, and a positive diagnosis can only be made with pathological analysis.
- The chronic inflammation secondary to TB is suggested to create a microenvironment that is highly conducive to tumorigenesis.

This case has been reported in line with the SCARE (Surgical CAse REport) criteria[4].

Case report

We report the case of a 40-year-old female patient who was admitted to our department of ENT and Head and Neck surgery due to the presence of several thyroid nodules found fortuitously on an ultrasound, as part of a regular check-up. The patient had a family history of thyroid disease, as both her mother and her sister had been treated for thyroid nodules, which revealed a

papillary carcinoma in the case of the sister. She had no history of pulmonary or extra-pulmonary TB, and no contact with any known people with TB.

Clinical examination found a grade one goiter, mobile, soft, and painless. Additionally, there was a palpable, mobile lymph node in the right inferior cervical region, measuring ~2 cm in its biggest diameter. According to the patient, this adenopathy had appeared 3 months prior to her consultation, and had been slowly but steadily growing in volume. No signs of dysthyroid or of a compression to the upper airway and digestive tracts were reported.

An ultrasound of the neck region had been realized, which objectified the presence of multiple thyroid nodules in both lobes. Two of these nodules showed signs of possible malignancy, as they both had micro-calcifications in their midst and were classified as EU-TIRADS V (European Thyroid Imaging and Reporting Data System). These two nodules were both located in the right thyroid lobe, and measured respectively 25×13 millimeters (mm) and 18×5 mm. The ultrasound also found an adenopathy of the inferior part of the jugular lymphatic chain, measuring $23 \times 14 \times 15$ mm, with an altered internal architecture in favor of malignancy. The thyrotropin-stimulating hormone (TSH) dosage was normal at 2.15 mIU/l, showing normal thyroid function.

The patient underwent surgery on both the adenopathy and the thyroid gland, performed by ENT and head and neck surgery residents in their fourth and fifth year of training. We first performed a selective neck dissection of the right side, level IV. The adenopathy was immediately sent to the frozen section laboratory for an extemporaneous examination. A total thyroidectomy was then performed, and the thyroid gland was also sent to the laboratory. The intraoperative histopathological examination showed inflammation in the lymph nodes and diffuse thyroiditis, without any sign of malignancy in the thyroid or in the lymph nodes.

No postoperative complications were observed. The final histopathological examination showed multiple white nodules of the thyroid gland, presenting with epithelial cell granulomas with caseous necrosis, confirming the diagnosis of thyroid TB, associated to a papillary microcarcinoma of the right thyroid lobe, measuring 5 mm. The final examination of the adenopathy showed similar granulomas with caseous necrosis, and no signs of metastasis. Thus, the diagnosis of multifocal thyroid and lymph node TB coexisting with papillary microcarcinoma of the thyroid was established.

The patient underwent 9 months of medical treatment for her TB, based on isoniazid, rifampicin, pyrazinamide, and ethambutol. She also received a permanent substitution with L-thyroxin. Follow-ups were done every 3 months for the first year, and every 6 months after that, and were based mainly on clinical examination. No sign of a recurrence has been detected to this day.

Discussion

Thyroid TB was first described by Lebert in 1862. It is very rare, accounting for 0.1–1% of reported TB cases[1]. It accounts for 0.6–1.15% of fine-needle aspiration cytology (FNAC) performed on a single thyroid nodule in some endemic areas (India)[5]. All age groups are affected, with a mean age between 30 and 46 years[5] and a predominance of women. The authors emphasize that the relative resistance of the thyroid to *Mycobacterium tuberculosis* explains the rarity of this location due to its good oxygenation (abundant vascularization) and the bacteriostatic properties of thyroid hormones. However, factors such as advanced age, diabetes mellitus, immunosuppression (HIV), and malnutrition can contribute to the development of TB[6].

In general, chronic inflammatory conditions can use multiple mechanisms to create an appropriate microenvironment for malignant development[7]. Mycobacterial infection results in chronic and persistent inflammation. Previous studies have reported that mycobacterial cell wall components are able to induce DNA damage through the production of nitric oxide and reactive oxygen species[8]. This DNA damage has been linked to inflammation and carcinogenesis[9]. *M. tuberculosis* was also found to induce anti-apoptotic activity by upregulating B-cell lymphoma 2 gene expression[10]. In addition, elevated levels of prostaglandins following mycobacterial infection have been observed in some clinical and experimental studies[11]. The combination of direct DNA damage, inhibition of apoptosis, and chronic inflammation can create a microenvironment that is highly conducive to tumorigenesis[8].

Thyroid TB is difficult to diagnose due to lack of specific signs and symptoms. Thyroid TB can present as solitary nodules, diffuse nodules, or multinodular goiter, even presenting as a chronic neck abscess[12]. The presence of another TB lesion or even sequelae can aid in the diagnosis. We can even see signs of compression, such as difficulty swallowing or paralysis of the larynx[1]. General features may not be present. Sometimes, the only clinical sign is an unexplained low-grade fever[6,13]. Early in evolution, hyperthyroidism can occur after parenchymal destruction and massive release of thyroid hormones. Thereafter, hypothyroidism may develop due to the complete destruction of the gland[1]. Lymphadenopathy may be present but is more suggestive of neoplastic disease[3]. Indeed, in our case, who presented a first-grade goiter that was mobile, tender, and painless, with no evidence of hypothyroidism. In addition, a mobile lymph node was palpable in the right lower neck, with a maximum diameter of about 2 cm. The final examination of the adenopathy showed similar granulomas with caseous necrosis, and no signs of metastasis.

Only a few cases of tuberculous thyroiditis associated with thyroid cancer have been described in the literature. Hizawa *et al.*[14] described a case of thyroid and pulmonary miliary TB in a postpartum patient. The diagnosis was made by FNAC of palpable thyroid nodules. Despite anti-TB treatment, subtotal thyroidectomy and unilateral neck dissection were performed due to persistently high thyroglobulin levels and the presence of firm thyroid nodules, which revealed papillary glandular TB cancer.

Allen *et al.*[15] also reported a case of thyroid TB occurring 7 years after total thyroidectomy for medullary thyroid carcinoma. El Kohen *et al.*[3] reported the case of a young patient who was found to have accumulators of papillary microcarcinoma with tuberculous thyroiditis after partial thyroidectomy.

Suri *et al.*[16] described the case of a patient with nodular goiter and cervical lymphadenopathy with papillary carcinoma in FNAC. The pathological examination of the thyroid gland showed the simultaneous presence of thyroid TB.

However Meng *et al.* reported a case with a grade 1 to grade 2 mobile, tender, painless multinodular goiter palpation. There

were no palpable lymph nodes in the neck; in addition, hypothyroidism was revealed[17].

Imaging technology is not very useful in engraving diagnosis[18]. Using FNAC with acid-fast bacilli seems to be the best method for preoperative diagnosis of TB[19]. However, most cases of thyroid TB are diagnosed based entirely on postoperative histopathological examination.

Conclusion

Thyroid TB is a rare disease, and the positive diagnosis remains histological and/or bacteriological. An exception is associated with papillary carcinoma in the same thyroid. The clinical manifestations of this association are variable. Treatment is based on surgery and anti-TB treatment. The prognosis is generally good except in disseminated forms.

Conflicts of interest disclosure

There are no conflicts of interest.

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