

Tamoxifen Treatment for Riedel's Thyroiditis: A Case Report

CASE REPORT
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ABSTRACT

Riedel's thyroiditis is a rare variant of thyroiditis, and treatment recommendations are based on case reports. This thyroiditis form is considered among immunoglobulin G4-related diseases. Intense fibrosis of the thyroid gland can cause compression of the surrounding tissues and hypothyroidism. Glucocorticoids are recommended as first-line therapy, and tamoxifen is second-line therapy. Other immunosuppressive agents have also been used in some resistant cases. Our case was presented with a palpable firm mass in the neck, shortness of breath, and hypothyroidism. The exact diagnosis of Riedel's thyroiditis was made after a pathological examination of a true-cut biopsy. We present the successful management of this case with glucocorticoid and tamoxifen combination treatment.

Keywords: Riedel's thyroiditis, tamoxifen, hypothyroidism, immunoglobulin G4-related disease

Introduction

Riedel's thyroiditis (RT) is a rare disease characterized by chronic inflammation and fibrosis of the thyroid gland.¹ It is an extremely rare thyroid disorder with an outpatient incidence of 1 in 100 000. Women are 4 times more likely to be affected than men, and the disease usually occurs in the third to fifth decades.² The exact etiology is unknown; however, it is suggested to be a localized form of the systemic fibrotic process.

The disease may affect only the thyroid gland or be associated with systemic fibrotic disorders such as retroperitoneal fibrosis, sclerosing cholangitis, autoimmune pancreatitis, and lacrimal fibrosis.³

In chronic thyroiditis, the thyroid and surrounding structures are replaced by dense fibrous tissue. These changes lead to the destruction of the thyroid follicular cells, and hypothyroidism may occur in 25%-80% of individuals as the fibrosis progresses.² Classically, it presents as a painless goiter, "hard as stone, hard as wood," and hypothyroidism.¹

Treatment approaches are generally case-based due to their rarity. We present a case of RT treated with tamoxifen (TMX) and glucocorticoid (GC).


Written informed consent was taken from the patient to publish this case report.

Case Presentation

A 30-year-old male with a palpable, painless, firm mass in the lower neck that had been growing for several months presented with shortness of breath for a few weeks, and it was getting worse, especially when he was lying on his back. On physical examination, it was found that there was a wood-hard mass reaching approximately 5 cm on the left side of the thyroid lobe. In laboratory tests, thyroid stimulating hormone (TSH)=17.0 uIU/mL [normal range (NR): 0.4-4.2], free thyroxine (T4)=1.2 ng/dL (NR: 0.9-1.7), free triiodothyronine (T3)=2.1 pg/mL (NR: 2-4.4), anti-thyroid peroxidase =>600 IU/mL (NR: 0-34), and anti-thyroglobulin antibody=3614 IU/mL (NR: 0-115) were found. Levothyroxine replacement therapy was started. Thyroid ultrasonography (US) revealed a hypoechoic mass covering the entire left lobe of the thyroid [Anterior-Posterior (AP) × Transverse (T), 35 × 40 mm] surrounding the left carotid artery and with no clear separation of the thyroid from the surrounding muscle tissues (Figure 1A).

Neck computed tomography (CT) showed a mass covering the left lobe reaching 46 mm, pushing the trachea to the right-side thyroid (Figure 2A). Thyroid fine-needle aspiration

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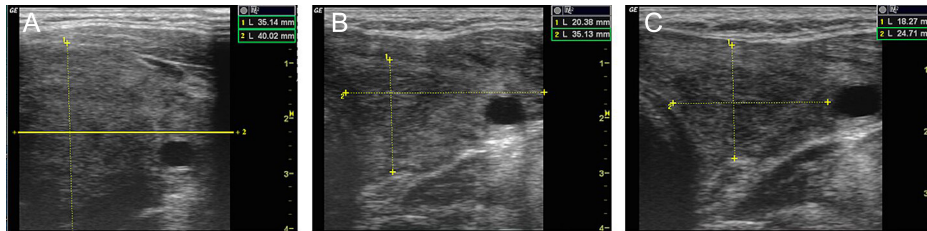


Figure 1. (A) Thyroid ultrasonography (US) image at the time of diagnosis, mass covering the entire left lobe of the thyroid [Anterior-Posterior (AP) × Transverse (T), 35 × 40 mm] surrounding the left carotid artery and with no clear separation of the thyroid from the surrounding muscle tissues. (B) Thyroid US image after the third month of tamoxifen (TMX) treatment, there was an evident reduction in mass size (AP × T, 20 × 35 mm). (C) Thyroid US image at the sixth month of the TMX treatment, the mass had almost completely regressed (AP × T, 18 × 24 mm).

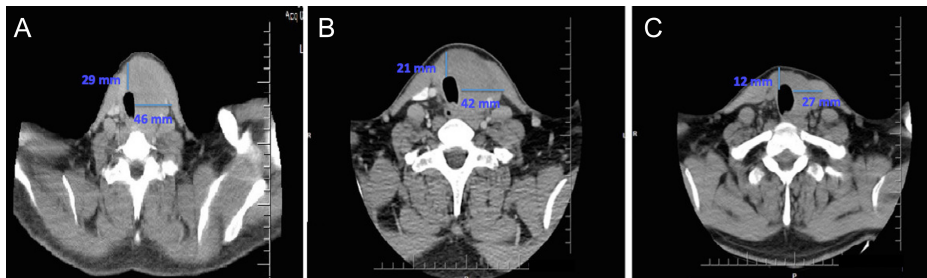


Figure 2. (A) Neck computed tomography (CT) transverse section image at the time of diagnosis showed a mass covering the left lobe reaching 46 mm, pushing the trachea to the right-side thyroid (isthmus: 29 mm, transverse size: 46 mm). (B) Neck CT transverse section image after 3 months of glucocorticoid treatment, minimal reduction in the mass size (isthmus: 21 mm, transverse size: 42 mm). (C) Neck CT transverse section image at the sixth month of the tamoxifen treatment, the mass had almost completely regressed (isthmus: 12 mm, transverse size: 27 mm).

biopsy resulted in non-diagnostic. The true-cut biopsy was performed, and pathological examination revealed extensive fibrosis with no thyroid follicular cells. A diagnosis of RT was made based on clinical and pathological findings. Serum immunoglobulin G4 (IgG4) level was found to be within the NR. There was no evidence of hypoparathyroidism or recurrent laryngeal nerve damage. A thoracoabdominal CT scan ruled out mediastinal or retroperitoneal fibrotic involvement. Treatment was started with methylprednisolone (MP) 32 mg/day.

After the third month of the GC treatment, the patient's dyspnea improved, but there was a minimal reduction in the mass size on CT (Figure 2B). Tamoxifen 20 mg q.d was added, and the MP dose decreased to 24 mg/day. After the third month of TMX treatment, shortness of breath was almost entirely improved, and there was an evident reduction in mass size in the control neck US (AP × T, 20 × 35 mm) (Figure 1B). The TMX dose was increased to 20 mg bid due to an excellent response to TMX, and the MP dose was decreased to

16 mg/day. At the sixth month of the TMX treatment, the mass had almost wholly regressed [Figure 1C (AP × T, 18 × 24 mm); Figure 2C]. No adverse events were observed related to TMX, and it was continued as a 20 mg bid. Methylprednisolone was tapered and then stopped in a few weeks. Although there was an improvement in thyroid volume, there was no significant change in thyroid hormone requirement after 6 months.

Discussion

Riedel's thyroiditis is extremely rare, and no randomized controlled studies on its treatment exist. We present a case of RT in which we successfully treated with TMX and GC combination.

We made the diagnosis with typical clinical and pathological findings consistent with RT. Although RT is considered among IgG4-related diseases, data regarding the use of serum IgG4 levels in the diagnosis are conflicting. Serum IgG4 levels, in our case, were within normal limits. Even though some studies reported that high serum IgG4 levels have a sensitivity of 90%,⁴ many others reported RT cases with normal serum IgG4 levels as in our case.⁵ The thyroid ultrasound findings of our patient were also compatible with RT. The inability to distinguish the thyroid tissue from the surrounding muscles and the encircling of the carotid artery were specific findings for RT.⁶

Fibrosis in the thyroid gland can cause hypothyroidism, which is common in RT.⁷ Our patient also had hypothyroidism at the time of initial diagnosis. Thyroid autoantibody positivity may also be found in some cases, such as in our patients. However, antibody positivity is thought to occur as a reaction to thyroid damage rather than an autoimmune process.¹

MAIN POINTS

- Riedel's thyroiditis should be considered in patients with rapidly developing hard masses in the neck.
- Although there are typically clinical and imaging findings, a pathological examination is necessary to make a definitive diagnosis.
- Glucocorticoids are generally preferred as the first choice in treatment; however, tamoxifen treatment may be safer and more effective.

It may cause life-threatening compression if it is untreated. Medical treatment is the first choice; surgical treatment alone does not provide adequate recovery. However, surgical debulking/isthmectomy may be required to reduce local compression.⁷ It is recommended to use GC as the first treatment, and then TMX may be used in the second step with a GC combination or alone. Tamoxifen was first used in 1996 in treating RT.⁸ Before its use in RT, improvements were also reported in some cases of retroperitoneal fibrosis.⁹ Tamoxifen reduces fibroblast proliferation, collagen production, and fibrosis by decreasing transforming growth factor beta (TGF- β) expression.⁴ Rituximab can also be used in resistant cases.^{10,11}

Initial GC doses varied from 15 to 100 mg of prednisone daily across the reports. We had a limited response in the first 3 months of 32 mg MP treatment. Glucocorticoid use is usually limited to 6-12 months due to the side effects.¹ Prednisone was the most commonly used GC in a meta-analysis, usually at 40 mg orally once daily, and the most prevalent duration of prednisolone therapies was 3 months. Methylprednisolone was the second most commonly used GC. Treatment duration was between 3 days and 24 months, with a median of 2 months.¹²

Adding TMX to GC treatment seems entirely adequate, and it is a safe maintenance treatment that reduces the longest-term side effects of GC.¹³ Tamoxifen is usually started at a dose of 20-40 mg/day, and it was reported that it could be used safely up to 60 mg/day.¹³ There has yet to be a definite consensus on the duration of its use. After 3 months of TMX treatment, the shrinkage of the thyroid gland was more evident, and we did not observe any side effects. After that, we increased the TMX dose to 40 mg to increase the effectiveness and to be able to discontinue the GC treatment. After 6 months of TMX treatment, the response was quite good, and GC was terminated without any problems. In a meta-analysis, a median dose of 20 mg once daily of TMX was taken in 14% of RT cases (range, 10-40 mg), and it lasted for 8 months (range, 1-48 months).¹²

Tamoxifen is quite effective in improving the fibrotic process in RT, perhaps even better than GC, which is used as the first-line therapy. Although it is generally a safe drug, care should be taken in cases with risk factors of deep vein thrombosis and endometrial cancer.¹⁴

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Declaration of Interests: The authors have no conflict of interest to declare.

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References

- Gosi SKY, Nguyen M, Garla VV. *Riedel Thyroiditis*. 2021 Jun 29. StatPearls Treasure Island (FL): StatPearls Publishing; 2021. (PMID: [\[CrossRef\]](#))
- Fatourechi MM, Hay ID, McIver B, Sebo TJ, Fatourechi V. Invasive fibrous thyroiditis (Riedel thyroiditis): the mayo clinic experience, 1976-2008. *Thyroid*. 2011;21(7):765-772. [\[CrossRef\]](#)
- Katz G, Stone JH. Clinical perspectives on IgG4-related disease and its classification. *Annu Rev Med*. 2022;73:545-562. [\[CrossRef\]](#)
- Er-Rahali Y, Massine El Hammoumi M, Issouani J, et al. Riedel's thyroiditis, a diagnostic and management challenge: a case report and review of literature. *Case Rep Endocrinol*. 2021 12;2021:5185259. [\[CrossRef\]](#)
- Carruthers MN, Khosroshahi A, Augustin T, Deshpande V, Stone JH. The diagnostic utility of serum IgG4 concentrations in IgG4-related disease. *Ann Rheum Dis*. 2015;74(1):14-18. [\[CrossRef\]](#)
- Gökçay Canpolat A, Cinel M, Dizbay Sak S, et al. Long-term outcomes of tamoxifen citrate therapy and histo- and immunopathological properties in Riedel thyroiditis. *Eur Thyroid J*. 2021;10(3):248-256. [\[CrossRef\]](#)
- Hennessey JV. Clinical review: Riedel's thyroiditis: a clinical review. *J Clin Endocrinol Metab*. 2011;96(10):3031-3041. [\[CrossRef\]](#)
- Few J, Thompson NW, Angelos P, Simeone D, Giordano T, Reeve T. Riedel's thyroiditis: treatment with tamoxifen. *Surgery*. 1996;120(6):993-8; discussion 998. [\[CrossRef\]](#)
- Clark CP, Vanderpool D, Preskitt JT. The response of retroperitoneal fibrosis to tamoxifen. *Surgery*. 1991;109(4):502-506.
- Hunt L, Harrison B, Bull M, Stephenson T, Allahabadia A. Rituximab: a novel treatment for refractory Riedel's thyroiditis. *Endocrinol Diabetes Metab Case Rep*. 2018;2018(1):17-0132. [\[CrossRef\]](#)
- Mammen SV, Gordon MB. Successful use of rituximab in a case of Riedel thyroiditis resistant to treatment with prednisone and tamoxifen. *AACE Clin Case Rep*. 2019;5(3):e218-e221. [\[CrossRef\]](#)
- Zala A, Berhane T, Juhlin CC, Calissendorff J, Falhammar H. Riedel thyroiditis. *J Clin Endocrinol Metab*. 2020;105(9):dgaa468. [\[CrossRef\]](#)
- Falhammar H, Juhlin CC, Barner C, Catrina SB, Karefylakis C, Calissendorff J. Riedel's thyroiditis: clinical presentation, treatment, and outcomes. *Endocrine*. 2018;60(1):185-192. [\[CrossRef\]](#)
- Meier CR, Jick H. Tamoxifen and risk of idiopathic venous thromboembolism. *Br J Clin Pharmacol*. 1998;45(6):608-612. [\[CrossRef\]](#)