

Riedel's Thyroiditis Treated with Tamoxifen

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A 46-year-old woman with clinical diagnosis of Riedel's thyroiditis was admitted to our Department, presenting with dyspnea, dysphagia, fatigue, and hoarseness. Previously, she had been diagnosed with Hashimoto's thyroiditis and hypothyroidism. The disease had a progressive course and had lasted for a year before the definitive diagnosis of Riedel's thyroiditis was confirmed and treated with methylprednisolone, 12 mg daily, without success. We started therapy with tamoxifen, 10 mg twice a day, together with methylprednisolone, 16 mg daily, and L-thyroxin substitution therapy. The follow-up lasted for one year. Treatment with tamoxifen led to a significant subjective improvement and objective changes, confirmed by regular clinical examinations, ultrasonography, and computed tomography of the neck. After 8 months of therapy, the patient had no compression symptoms and goiter decreased in estimated weight from 105 g to 63 g according to ultrasound measurements. The patient underwent partial thyroidectomy at 10 months after diagnosis of Riedel's thyroiditis. Histopathology confirmed the diagnosis of Riedel's thyroiditis. Our report indicates that tamoxifen can be a valuable drug therapy in the treatment of Riedel's thyroiditis.

Key words: *tamoxifen; thyroid gland; thyroiditis*

Riedel's thyroiditis is a rare disease of unknown etiology, characterized by invasive fibrosclerosis of the thyroid gland, which often involves surrounding tissues. It is also known as invasive fibrous thyroiditis. Bernhard Riedel first recognized the condition in 1883 and published the first case report in 1896. Since then, less than 200 cases have been reported (1,2). The disorder predominantly affects middle-aged women (2). Patients usually have dyspnea, dysphagia, and painless goiter. The thyroid is usually enlarged, stony hard, and fixed to the surrounding structures. Histological criteria for the diagnosis of Riedel's thyroiditis include involvement of the thyroid with a fibrotic process consisting of fibroblasts and collagen, and histological evidence of involvement of the surrounding tissues. Thyroid tissue spared by fibrosis retains relatively normal architecture (3).

Many reports of extracervical fibrosclerosis associated with Riedel's thyroiditis suggest a systemic nature of the disease (1,4,5). Affected sites include the retroperitoneum, mediastinum, biliary tract, and orbit. Other authors postulate that Riedel's thyroiditis has autoimmune etiology and relate it to Hashimoto's disease and other autoimmune disorders (6-9). Hypothyroidism occurs in 30-40% of the patients. Perithyroidal fibrosis can involve the parathyroid glands, causing hypoparathyroidism (9,10). It is necessary to perform an open biopsy to establish the diagnosis of Riedel's thyroiditis because it may resemble carcinoma or lymphoma. Surgical treatment is sometimes necessary to relieve symptoms of tracheal compres-

sion, and wedge resection of the isthmus is the treatment of choice. There is no consensus on more extensive resection, because it bears a substantial risk of the injury to adjacent structures. However, surgical treatment is often unsatisfactory and usually combined with the steroid treatment (11,12). There are also some reports indicating that tamoxifen could be an effective treatment option for Riedel's thyroiditis (13,14).

Case Report

A 46-year-old woman was admitted to our Department because of suspected Riedel's struma. She was previously treated in a district hospital with L-thyroxin for hypothyroidism accompanied by high titers of thyroid antibodies. Hashimoto's thyroiditis had been confirmed by fine needle aspiration two years before the diagnosis of Riedel's thyroiditis. A year before admission, the goiter rapidly increased in size and became very hard, causing dyspnea, dysphagia, and pain in the neck. The treatment with methylprednisolone (12 mg daily) failed to improve the condition. The goiter further increased in size, causing more severe dyspnea and dysphagia, with hoarseness and neck-pain. At the time of admission to our Department, the patient was very weak, could only whisper, and movements of the neck were very painful. The thyroid was enlarged, fixed to the surrounding structures, and stony-hard on palpation. Ultrasonography of the neck revealed enlarged goiter (calcu-

lated weight, 105 g), invading the adjacent neck structures. Fine needle aspiration was in accordance with the clinical diagnosis of Riedel's thyroiditis. Computed tomography (CT) of the neck showed diffusely enlarged thyroid gland, with compression of adjacent neck structures, including tracheal stenosis (Fig. 1A). Extracervical fibrosclerosis was excluded on CT of the thorax, mediastinum, and abdomen, and orbital ultrasonographic examination. Tamoxifen 10 mg twice a day was introduced, and previous therapy with L-thyroxine 100 µg and methylprednisolone 16 mg daily was continued. Since the initiation of tamoxifen therapy, the patient has been monitored clinically, by ultrasound examinations and by CT of the neck. After 8 months of therapy, she could normally breathe, eat, speak, and work. Neck pain disappeared. The goiter decreased in estimated weight from 105 g to 63 g according to ultrasonographic measurements. CT of the neck showed a pronounced reduction of the goiter (Fig. 1B).

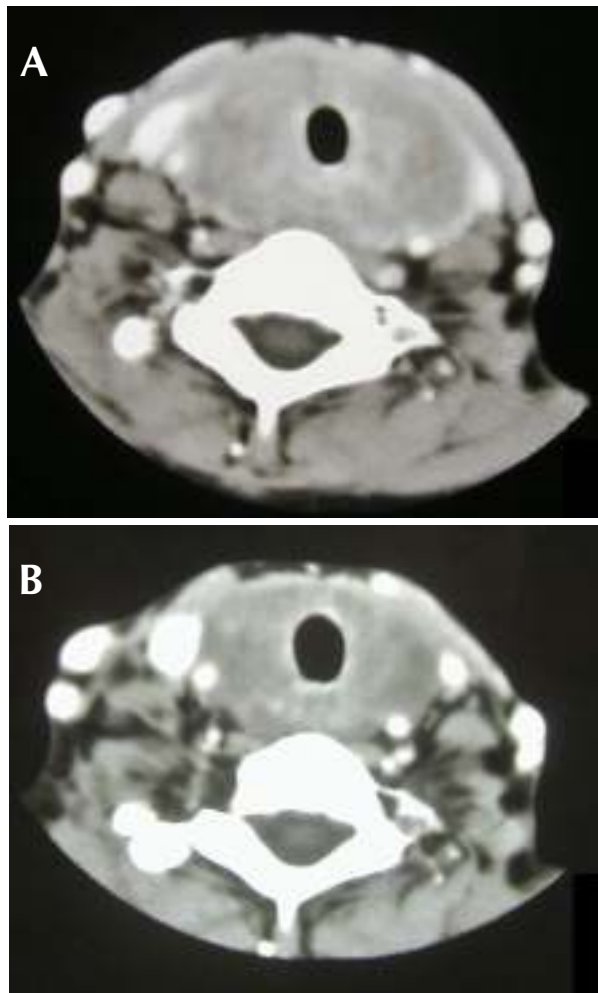


Figure 1. Contrast-enhanced computed tomography of thyroid gland affected by Riedel's thyroiditis. (A) Scan before the treatment with tamoxifen, showing diffusely enlarged hypodense thyroid gland with the compression and infiltration of adjacent neck structures, tracheal stenosis, and displacement of vascular structures. (B) Scan after 8 months of tamoxifen therapy shows pronounced reduction of the goiter and increased diameter of the trachea.

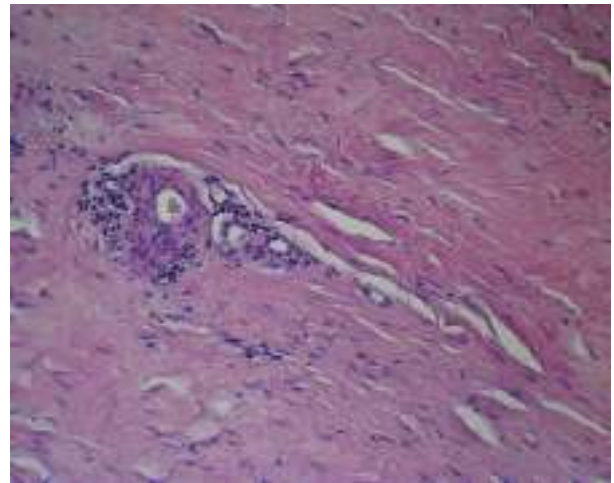


Figure 2. Microscopic section of thyroid gland affected by Riedel's thyroiditis (hematoxylin eosin, magnification $\times 200$). Extensive fibrosis and chronic inflammatory cells are visible.

After 10 months of follow-up, the patient underwent thyroid surgery. Partial thyroidectomy was performed, including the resection of the isthmus and parts of the right and left lobe. Histopathology was consistent with the diagnosis of Riedel's thyroiditis (Fig. 2). At present, the patient is relieved from all her symptoms. She is still followed-up.

Discussion

The patient had previously diagnosed Hashimoto's thyroiditis accompanied by high titers of anti-microsomal and antithyroglobulin antibodies and hypothyroidism. Cases of Riedel's thyroiditis associated with Hashimoto's thyroiditis have already been described (8,9,15,16). The possible relationship of the two conditions is still unknown. About two-thirds of the patients with invasive fibrous thyroiditis may have high serum thyroid antibody concentrations (2). Riedel's thyroiditis and the fibrosing variant of Hashimoto's thyroiditis were once considered morphologic variants of the same disease, but since the 1970s, they have been recognized as distinct clinico-pathologic entities (2).

There are no clinical trials on the efficacy of therapy for Riedel's thyroiditis. The condition is extremely rare and the therapy is based on empiric data. Surgical treatment commonly consists of isthmus wedge resection and is usually combined with steroid treatment. After the successful treatment of retroperitoneal fibrosis with tamoxifen (17), Few et al (13) were the first who administered tamoxifen in the treatment of Riedel's thyroiditis. All four patients in their study responded dramatically to the treatment with tamoxifen. The second report of Riedel's thyroiditis treated with tamoxifen was published only recently (14). The patient initially responded to the treatment with steroids and subsequently to tamoxifen. Recently published data from investigations of other fibroproliferative disorders, such as keloid and Dupuytren's contracture, demonstrated that tamoxifen could decrease transforming growth factor (TGF)- β expression,

as well as fibroblast function (18,19). TGF- β is a growth factor known to promote extracellular matrix production and fibrosis. The authors proposed that one of the mechanisms by which tamoxifen decreased fibroblast collagen production could be the inhibition of TGF- activity (18).

Our report confirms tamoxifen as a valuable drug in the treatment of Riedel's thyroiditis.

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