Atypical Presentation of Riedel’s Thyroiditis: Multifocal Nodular Fibrosis and Resolution with Levothyroxine

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What Is Known about This Topic

- Riedel’s thyroiditis is a rare condition of unknown aetiology, characterised by chronic inflammatory invasive fibrosclerosis of the thyroid gland and surrounding structures. Riedel’s thyroiditis is also associated with a variable degree of systemic fibrosis, including retroperitoneal fibrosis, apical lung fibrosis, and fibrosing mediastinitis. Treatment is directed at reducing the inflammatory response with anti-inflammatory agents, with surgery limited to relief of constrictive pressure when present.

What This Case Report Adds

- The current case of Riedel’s thyroiditis unusually presented with a classical hard thyroid with tracheal compression; however, it also showed nodular lesions within the lungs and liver highly suggestive of metastatic disease, and not previously described in Riedel’s thyroiditis. These lesions turned out to be hyalinised fibrous tissue. Following institution of levothyroxine replacement therapy, significant improvement in the thyroid and lung fibrosis occurred. Whether this resolution represents an immunomodulatory effect of levothyroxine, or was coincidental and the changes represented a subset of the natural history of this entity is unclear.

Key Words
Riedel’s thyroiditis · Nodular extrathyroidal fibrosis · Hypothyroidism · Thyroid peroxidase antibodies · Levothyroxine

Abstract

\textbf{Background:} Riedel’s thyroiditis is characterised by chronic inflammatory invasive fibrosclerosis of the thyroid gland, surrounding structures, and extrathyroidal fibrosis. We present a case of Riedel’s thyroiditis associated with nodular fibrosis of the lungs and liver. \textbf{Case:} A 40-year-old woman presented with a 3-month history of neck swelling, difficulty swallowing and breathlessness on exertion. Core biopsy of the goitre revealed dense fibrous tissue with mixed chronic inflammatory cells. A staging computed tomography scan revealed a large thyroid mass encasing the oesophagus and compressing the trachea, multiple bilateral pulmonary nodules with no evidence of lymphadenopathy, and multiple suspicious nodular lesions in the liver. A thorascopic biopsy...
of a lung lesion in its entirety revealed a haematinising lung lesion with no evidence of malignancy. Following the introduction of levothyroxine replacement, symptomatic improvement occurred in parallel with improvements in imaging. **Conclusion:** To our knowledge, this is the first description of Riedel’s thyroiditis presenting with nodular extrathyroidal fibrosis, and which showed resolution following institution of levothyroxine. Copyright © 2012 European Thyroid Association Published by S. Karger AG, Basel

**Introduction**

In patients presenting with a diffusely enlarged hard thyroid gland, the differential diagnosis lies between anaplastic carcinoma, paucicellular carcinoma, thyroid lymphoma, and Riedel’s thyroiditis. Riedel’s thyroiditis is a rare condition of unknown aetiology, characterised by chronic inflammatory invasive fibrosclerosis of the thyroid gland and surrounding structures [1, 2]. There is associated extrathyroidal fibrosis in around a third of cases [2, 3]. In contrast, Hashimoto’s thyroiditis is a chronic inflammatory condition characterised by lymphoplasmocytic infiltration, where the inflammatory process is limited to the thyroid gland. A fibrosing variant of Hashimoto’s thyroiditis has been described, but local extrathyroidal fibrosis is not described [4].

Where the diagnosis of Riedel’s thyroiditis is raised on clinical examination, histological confirmation is essential to rule out malignancy. In contrast, the diagnosis of Hashimoto’s thyroiditis is usually made on clinical grounds, and is almost certain if a patient has a diffusely enlarged firm, but not hard, goitre with hypothyroidism and high titres of thyroid microsomal antibodies [3].

**Case Report**

A 40-year-old previously healthy woman presented with a 3-month history of neck swelling, difficulty swallowing and breathlessness on exertion. There was no previous history of thyroid disease or neck irradiation. Examination revealed a hard, fixed, diffuse goitre with no tenderness. There was no associated lymphadenopathy. Thyroid function test revealed hypothyroidism with a free T₄ <5.2 (9.0–24.0) pmol/l, TSH 62.3 (0.20–4.0) mIU/l, thyroid peroxidase antibodies >1,300 IU/ml and CRP 52 (<5) mg/l. Repeat thyroid function tests confirmed biochemical hypothyroidism. Levothyroxine was commenced, and the dose titrated to normalise her thyroid function tests. The maintenance dose was 150 μg. Neck ultrasonography showed a large nodular goitre suspicious of malignancy. A staging computed tomography (CT) scan of the neck and thorax revealed a large thyroid mass, encasing the oesophagus and trachea (fig. 1a). There was compression of the trachea and infiltration of the carotid sheath. The minimum diameter of the trachea was 9 mm. Additionally, there were multiple bilateral pulmonary nodules, the largest being 2.3 cm with no evidence of cervical, hilar or mediastinal lymphadenopathy (fig. 2a). There were, however, multiple suspicious nodular lesions in the liver and a complex 4.9-cm cyst on the left and 3.8-cm cyst on the right kidney with enlargement of the para-aortic lymph nodes.

Core biopsy of the goitre revealed dense fibrous tissue with mixed chronic inflammatory cells focally infiltrating muscle and walls of trapped veins (fig. 3a). Notably, there was no evidence of giant cells, lymph follicles, oncocyes or granulomas that would be suggestive of Hashimoto’s thyroiditis. Immunohistochemistry showed absence of an epithelial component that would be suggestive of paucicellular anaplastic carcinoma. Histological features were consistent with a fibrotic process, and suggestive of Riedel’s thyroiditis. Because of the imaging appearances suggesting metastatic disease, the patient was referred for ultrasound-guided biopsy of the liver which was not performed as the lesions seen on CT were not clearly demonstrable on ultrasound. Instead, a CT-guided biopsy of one of the larger lung nodules was performed. The latter showed small fragments of fibrous tissue with no evidence of malignancy. Concerns over a potential occult malignancy remained and a thorascopic biopsy of the lung lesion was performed. Histology revealed a haematinising lung lesion with no evidence of malignancy or granulomatous tissue (fig. 3b). Autoantibody screening including ANCA, rheumatoid factor, ANA, ENA’s were negative. Repeat inflammatory markers (CRP and plasma viscosity) 2 months following the initially elevated CRP were normal.

On review at 4 months, the dysphagia and exertional breathlessness had significantly improved without specific intervention other than levothyroxine. Clinically, the size of the goitre decreased and was less hard in consistency. Repeat CT scan of the neck and thorax 6 months after the initial scan revealed a significant decrease in size of the goitre, and no significant narrowing of the trachea, which now had a minimum diameter of 12 mm (fig. 1b). The lung nodules had significantly reduced in size and no new abnormality was identified (fig. 2b).

**Discussion**

This interesting case describes a woman who presented with a history and imaging consistent with a diagnosis of disseminated thyroid carcinoma. Repeated attempts to obtain confirmatory histology showed only fibrous tissue necessitating thorascopic biopsy of a lung nodule in its entirety. The results of the latter biopsy confirmed the wholly fibrous nature of these lesions. Furthermore, resolution of the inflammatory process occurred temporally after institution of thyroxine replacement therapy. To our knowledge, this is the first description of Riedel’s thyroiditis presenting with widespread nodular fibrosis, which improved following initiation of levothyroxine therapy.
Initial imaging was suggestive of metastatic carcinoma. Where there is any suspicion of thyroid malignancy, it is essential to obtain histological confirmation. Paucicellular variant of anaplastic carcinoma can mimic Riedel’s thyroiditis because of low cellularity, absence of nuclear anaplasia and presence of spindle cells which resemble fibroblasts. The presence of local lymphadenopathy, spindle cell plugging of large vessels, coagulative necrosis and foci of cellular areas with mitosis at the peripheries favour a diagnosis of paucicellular variant of anaplastic thyroid carcinoma [5]. Our patient did not exhibit any of these features, and immunohistochemistry for epithelial content, a diagnostic marker of paucicellular carcinoma, was absent. Despite negative immunohistochemistry for epithelial content, the concurrent appearance of nodular lesions suggestive of metastatic disease warranted further investigation that proved these lesions to be fibrotic, effectively excluding malignancy.

The cytomorphological features of dense nodular fibrosis with inflammatory infiltrate in distant organs including the lungs, liver and para-aortic lymph nodes in association with a fibrotic thyroid gland suggested a unifying diagnosis of Riedel’s thyroiditis. Previous reports associate Riedel’s thyroiditis with multifocal systemic fibrosclerosis [2] which may include sclerosing cholangitis [6], fibrosing mediastinitis [7] apical lung fibrosis [8, 9], and retroperitoneal fibrosis [10–12]. Although fibrotic lung nodules have not been previously described in Riedel’s thyroiditis, a similar appearance has been reported in IgG4-associated multifocal systemic fibrosclerosis [13], which can include Riedel’s thyroiditis. Extensive extrathyroidal involvement of multiple organs with local fibrosclerosis and infiltration of surrounding structures including the trachea, oesophagus and carotid sheath indicates our patient had an extensive systemic inflammatory process, supported by an elevated CRP. IgG4 levels in our case were not elevated.

It has been hypothesised that Riedel’s thyroiditis and Hashimoto’s thyroiditis/fibrosing Hashimoto’s thyroiditis may represent different ends of the spectrum of the same inflammatory process with a common immunological aetiology. A number of cases with features consistent with both diseases have been described [12], inferring that the sequence of events in Riedel’s thyroiditis might have initiated as Hashimoto’s thyroiditis [10]. Our patient has a number of features consistent with a diagnosis of both Hashimoto’s and Riedel’s thyroiditis. Patients with Riedel’s thyroiditis are euthyroid in the early stages of their disease, although the majority become hypothyroid with progressive destruction of the thyroid parenchyma [2, 14,
When hypothyroid, these patients usually present with either subclinical or mild hypothyroidism, and the corresponding antimicrosomal antibody titre is elevated in most cases [2, 15]. Our patient had a very high antimicrosomal antibody titre with overt hypothyroidism more in keeping with Hashimoto's thyroiditis. The fibrosing variant of Hashimoto's thyroiditis is characterised by destruction of thyroid architecture, follicular atrophy, epithelial metaplasia, and keloid-like fibroblasts [2, 16]. In contrast to Riedel's thyroiditis, this process is limited to the thyroid gland. We observed no histological features within the thyroid biopsy consistent with either Hashimoto's or fibrosing Hashimoto's thyroiditis, and the observed fibrosis of the perithyroidal tissues is not reported to occur in these conditions. Whether areas of concomitant Hashimoto's thyroiditis were present elsewhere within the thyroid, as previously reported [2, 10, 12, 17], is not possible to exclude without histological examination of the complete thyroid.

Symptoms improved with levothyroxine therapy, with a concurrent reduction in goitre size, tracheal diameter, and pulmonary lesion size on repeat CT imaging. In tandem with these findings, the CRP level normalised. Data support a decrease in volume of the thyroid following treatment with levothyroxine in patients with goitrous Hashimoto’s thyroiditis [18, 19]. This effect appears to be due to the immunomodulating effect of levothyroxine [20]. In our case, whether the reduction in goitre size and extrathyroidal fibrosis is an effect of levothyroxine, or in fact represents the natural history of a subset of patients with this entity is unclear. A fibrosing variant of Hashimoto’s thyroiditis has been described [4]; however, the absence of germinal cell centres and Hürthle cells, and presence of local fibrous infiltration make this diagnosis unlikely. Notably, Hashimoto’s thyroiditis has been reported in association with idiopathic retroperitoneal fibrosis in a number of case studies [21–23].

In summary, our case highlights the diagnostic difficulties faced in differentiating benign from malignant conditions. Furthermore, the described case highlights a number of atypical features of Riedel’s thyroiditis including multifocal nodular extrathyroidal fibrosis, resolution following institution of thyroxine therapy, overt hypothyroidism, and high thyroid peroxidase antibody titres.

**Disclosure Statement**

The authors have nothing to declare.
References


