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A difficult diagnosis: a case report of combined Riedel's disease and fibrosing Hashimoto's thyroiditis

Diagnostyka różnicowa: opis przypadku wola Riedla z cechami choroby Hashimoto

Roman Junik[1], Olga Juraniec[1], Jacek Pypkowski[3], Andrzej Krymer[4], Andrzej Marszałek[2]

[1]*Department of Endocrinology and Diabetology,* Collegium Medicum *in Bydgoszcz, Poland*
[2]*Department of Clinical Pathomorphology,* Collegium Medicum *in Bydgoszcz, Poland*
[3]*Department of General and Endocrine Surgery,* Collegium Medicum *in Bydgoszcz, Poland*
[4]*Outpatient Clinic of Endocrinology, 10 Military Hospital, Bydgoszcz, Poland*

Abstract

Riedel's disease (RD) is a rare form of chronic thyroiditis, predominantly characterised by fibrosis which may involve neighbouring tissues and organs. Hashimoto's disease (HD), on the other hand, is fairly common. Clinical differentiation between these diseases is often difficult, and the results of diagnostic imaging, laboratory tests and cytology studies are often similar. We report the case of a female patient with Riedel's thyroiditis displaying clinical, laboratory and radiological traits of both diseases.

A 44 year-old Caucasian female was diagnosed with hypothyroidism. A fine-needle aspiration biopsy was performed; the findings were suggestive of an exacerbated chronic inflammatory process. However, a small lymphocyte-derived malignancy could not be ruled out with certainty, and so the patient was referred for elective thyroidectomy. The microscopic features of both specimens did not meet the criteria of Hashimoto's thyroiditis. The immunohistochemical studies revealed few scattered B lymphocytes (CD20 positive) and numerous scattered T lymphocytes (CD3 positive). Finally, Riedel's thyroiditis with an intense inflammatory infiltrate composed of lymphocytes was diagnosed. Reaching a diagnosis was particularly difficult in this patient, since Riedel's thyroiditis, the fibrosing form of Hashimoto's disease and malignant tumours of the thyroid can show similar traits upon physical and histopathological examination. As the clinical data was indicative of Hashimoto's thyroiditis and there were partial histological criteria of two forms of thyroiditis, namely Hashimoto's and Riedel's, the very rare diagnosis of a combined disease was made. Dense B and T lymphocytes and some plasma cell infiltrates, as well as the destruction of thyroid follicles by fibrosis extending into surrounding tissues, were supportive of the eventual diagnosis.

Differentiating between the histopathological and clinical presentation of both diseases in one patient is difficult, primarily due to the partial overlapping of their histopathological traits. In order to avoid a diagnostic error, close cooperation between the endocrinologist and pathologist is mandatory. It is our opinion that in our patient the two diseases existed separately, and their coexistence was most likely coincidental. **(Pol J Endocrinol 2011; 62 (4): 351–356)**

Key words: *Riedel's disease, Hashimoto's thyroiditis, differential diagnosis, case report*

Streszczenie

Wole Riedla jest rzadką postacią przewlekłego zapalenia tarczycy, w której dominuje włóknienie mogące obejmować sąsiednie tkanki. Choroba Hashimoto jest stosunkowo częstym schorzeniem. Różnicowanie tych schorzeń bywa trudne, gdyż wyniki badań laboratoryjnych, obrazowych i cytologicznych bywają podobne. Autorzy przedstawiają przypadek pacjentki z wolem Riedla prezentującym kliniczne, laboratoryjne i obrazowe cechy obu tych chorób. U 44-letniej kobiety rozpoznano niedoczynność tarczycy. W preparatach z wykonanej biopsji aspiracyjnej cienkoigłowej rozpoznano zaostrzony przewlekły proces zapalny, ale jednocześnie nie można było wykluczyć chłoniaka. Pacjentkę poddano tyreoidektomii. W badaniu histopatologicznym nie potwierdzono jednoznacznie choroby Hashimoto. Badanie immunohistochemiczne wykazało nieliczne limfocyty B (CD20) i liczne limfocyty T (CD3). Ostatecznie rozpoznano wole Riedla z naciekiem limfocytarnym.

Diagnostyka u tej pacjentki była utrudniona, gdyż wole Riedla, włókniejąca forma choroby Hashimoto oraz guz złośliwy mają podobne cechy w badaniu fizykalnym i histopatologicznym. Jeżeli występują kliniczne cechy choroby Hashimoto oraz histologiczne cechy obu form zapalenia, można rozpoznać rzadką kombinację choroby Hashimoto i wola Riedla. Naciek limfocytów B i T oraz komórek plazmatycznych, jak również niszczenie pęcherzyków tarczycy przez włóknienie, które przechodzi na sąsiednie tkanki, może pomóc w postawieniu ostatecznego rozpoznania. Różnicowanie pomiędzy histopatologicznym i klinicznym obrazem obu chorób bywa trudne szczególnie z powodu nakładania się cech histopatologicznych. Konieczna jest ścisła współpraca patologa i klinicysty w celu uniknięcia pomyłki diagnostycznej. Zdaniem autorów u badanej pacjentki występowały obie te choroby, ale związek pomiędzy nimi był jedynie przypadkowy.
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Słowa kluczowe: *wole Riedla, choroba Hashimoto, diagnostyka różnicowa, opis przypadku*

Roman Junik, Department of Endocrinology and Diabetology, *Collegium Medicum* in Bydgoszcz, ul. Skłodowskiej-Curie 9, 85–094 Bydgoszcz, Poland, e-mail: junik@cm.umk.pl

Introduction

Riedel's disease (RD) is a rare form of chronic thyroiditis, predominantly characterised by fibrosis which may involve neighbouring tissues and organs [1]. There is a theory stating that RD is a local representation of a generalised process, described as the 'invasive fibrosis syndrome', since the pathological growth of connective tissue may also involve the orbits, mediastinum, biliary tract or retroperitoneal space. The clinical representation of the disease may be variable enough to suggest a malignant lesion in many cases. Riedel's thyroiditis has been reportedly found in 0.05% of 42,000 thyroid surgeries [2]. Hashimoto's disease (HD), on the other hand, is fairly common (1–2% of the population) and may have a fibrosing form in 10–13% of cases [3]. Clinical differentiation between these diseases is often difficult, and the results of diagnostic imaging, laboratory tests and cytology studies are often similar.

We report the case of a female patient with Riedel's thyroiditis displaying clinical, laboratory and radiological traits of both of these diseases.

Case presentation

A 44 year-old Caucasian female was diagnosed with hypothyroidism in January 2009. Levothyroxine (L-T4) therapy was initiated. In June 2009, the following laboratory results were observed at a dose of 75 μg L-T4/day: TSH — 103 mU/L; anti-TPO > 1,300 U/ml; CRP — 85.5 mg/L.

Upon ultrasound of the thyroid, the right lobe of the gland was found to measure 59 × 31 × 26 mm, and the left lobe 53 × 29 × 25 mm. The volume of the gland was 45 ccm; the volume of the isthmus was 14 ccm. Above the isthmus, a structure was present, measuring 9 × 6 × 8 mm, which was identified as the pyramid lobe. Overall, the thyroid gland was markedly increased in size, hypoechogenic, and displaying a highly heterogeneous echogenicity with no evidence of nodular lesions. In the lateral regions of the neck, lymph nodes were visible, of a normal echogenicity, measuring 18 × 5 mm on the right side and 18 × 7 mm on the left side. 131-I scintigraphy was performed, revealing a thyroid situated above the jugular notch of the sternum, the lobes approximately 6 cm long, the radiotracer uptake uneven and generally decreased, and a "cold field" present in the superior — medial part of the right lobe. Iodine uptake after 24 hours reached 4%. A fine-needle aspiration biopsy (FNAB) was performed. Lymphoid cells were present in the specimens from ultrasound-guided FNAB of both thyroid lobes and the hypoechogenic focus located superior to the isthmus, predominantly small lymphocytes with some plasma cells and neutrophils. This finding was suggestive of an exacerbated chronic inflammatory process, although a small lymphocyte-derived malignancy could not be ruled out with certainty. The L-T4 dose was increased to125 μg, then to 150 μg/day, and the patient was referred for elective thyroidectomy. On 18 August 2009 a subtotal thyroidectomy was performed.

The operating surgeon's report states that all of the tissues surrounding the thyroid were edematous and brittle. The gland itself was hard, fibrous and closely adherent to the neighbouring tissues, with unclear anatomical borders. Visualisation of recurrent laryngeal nerves and parathyroid glands was impossible.

The surgery was complicated by a mediastino-tracheal fistula. On 3 October 2009 the patient was admitted to the Department of Endocrinology and Diabetology of the Ludwik Rydygier College of Medicine, Nicolaus Copernicus University. Upon admission, the patient complained of pressure on the neck, difficulty in breathing and orbital pain on extreme gaze. Physical examination revealed an increased neck circumference with a hard, painful infiltration of the soft tissues of the neck, and periorbital oedema with limited eye movement.

The consulting ophthalmologist discovered: a periorbital oedema, reddening of the eyelids, and oedema of the bulbar conjunctiva, especially in the lateral angles. The cornea and irises were normal. Laboratory findings were as follows: anti-TG — 1,378 U/ml, anti-TPO — 441 U/ml, TSH — 0.39 mU/L, FT4 — 1.73 ng/dl.

A computed tomography (CT) of the chest was performed, revealing a thickening of the soft tissues surrounding the larynx and trachea from the superior margins of the thyroid cartilage to the base of the neck, with air and a fluid level present in the pretracheal area. Upon CT, the jugular vessels were spread apart, and no contrast could be observed in the right jugular vein. The abovementioned lesions filled the retrocricoid, perioesophageal and paraspinal spaces; at the level of the lesion, the trachea was somewhat narrowed and slightly shifted to the left. MRI of the orbits was performed. In T1-W1, eight quite well-defined hypointensive lesions could be observed bilaterally in the supero-lateral part of the orbit, corresponding to the location of the lacrimal glands. In T2-W1 and STIR, heterogeneously hyperintensive lesions were seen. These lesions were adjacent to the ocular globe and neighboured the insertions of the superior and medial rectus muscles; the lesion in the right orbit measured 24 × 14.5 mm in cross-section and 21 mm in the vertical plane; the lesion of the left orbit measured 25 × 11.5 × 20 mm, respectively. After contrast, the lesions showed an intense, somewhat heterogeneous, enhancement. Due to the suspicion of Riedel's disease, 800 mg/day of ibuprofen was introduced. After

this approach proved ineffective, corticosteroid therapy was initiated: 1 g of methylprednisolone i.v. for three days, followed by prednisone, initially at 60 mg/day, followed by 40 mg/day. A gradual reduction of neck circumference was observed, along with the withdrawal of soft tissue infiltration within the neck and orbits; eyeball mobility also improved. Presently, the patient remains on 150 μg L-T4 combined with 30 mg/day of prednisone and is feeling well.

Pathologic case study

During the treatment of the patient for a thyroid condition, the following specimens were referred for histopathological studies:

— specimen 6110/09 (Figure 1) Sample received for rapid intraoperative diagnosis. The tissue specimen consisted of six partially firm tissue samples. The greatest diameter of the specimens was 2.5 × 1.5 cm. Histological examination during surgery revealed fragments of fibrous tissue with foci of inflammatory infiltrate. No structure of thyroid gland folliculi could be observed. Upon microscopic examination, Riedel's thyroiditis was suggested. As the diagnosis was temporary, later routine paraffin blocks containing embedded tissue samples were prepared, as well as haematoxyllin-eosin stained slides. Additionally, as an intense inflammatory infiltrate was recorded, immunohistochemical studies were performed, which revealed the presence of a mixed lymphocytic infiltrate with B cells (CD20 positive, CD79a positive) and T cells (CD3 positive, CD5 positive). Procedures for Bcl-2, cyclinD1, and CD23 were negative. According to the microscopic picture and immunostain results, the second pathologist's diagnosis was consistent with Hashimoto's thyroiditis;

— specimen 6178/09 (Figures 2–4) — consisted of the left and right lobe of the thyroid gland. The left lobe was delivered to the lab as three formalin-fixed fragments of tissue of the following sizes: one irregular fragment, measuring 3.5 × 0.5 × 1.5 cm, and two round fragments 2.0 cm and 1.5 cm in diameter. Microscopic examination revealed the predominance of connective tissue with numerous foci of dense inflammatory infiltrate, composed mainly of mononuclear cells (e.g. lymphocytes) and an increased amount of collagen fibres. The formalin-fixed right lobe of the gland measured 3.5 × 2.0 × 2.0 cm upon arrival at the lab. Microscopic examination demonstrated areas of fibrous tissue and inflammatory infiltrate composed of mononuclear cells. The microscopic features of both specimens did not meet the criteria of Hashimoto's thyroiditis. The immunohistochemical studies revealed few scattered B lymphocytes (CD20 positive) and numerous scattered T lymphocytes (CD3 positive). Additionally, reactive CD15 positive cells were observed. There were no CD30 positive cells. As there was a clinical suggestion of a lymphoproliferative disease, after obtaining additional clinical data and pathological second-look microscopic examination, the diagnosis of lymphoma was excluded. Finally, Riedel's thyroiditis with an intense inflammatory infiltrate composed of lymphocytes was diagnosed;

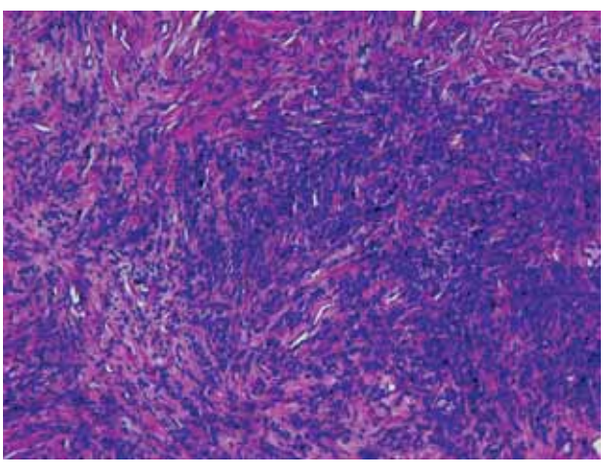

Figure 1. *(6110_09_HE_10×). Easily visible lymphocytic infiltrate within a dense fibrous stroma. Haematoxillin and eosin, primary magnification 10×*

Rycina 1. *Obecny wyraźny intensywny naciek limfocytarny w obrębie włóknistego zrębu. Preparat HE, pierwotne powiększenie obiektywu 10×*

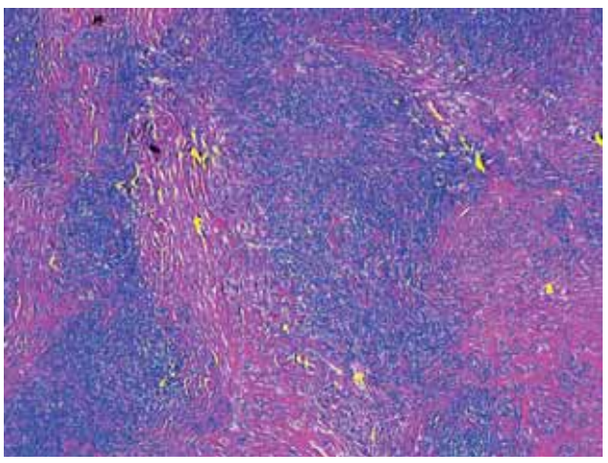

Figure 2. *(6178_09_HE_4×). Dense fibrotic and collagenous tissue is infiltrated by lymphocytes. Haematoxillin and eosin, primary magnification 4×*

Rycina 2. *Silnie zwłókniały zrąb z naciekami limfocytarnymi. Preparat HE, pierwotne powiększenie obiektywu 4×*

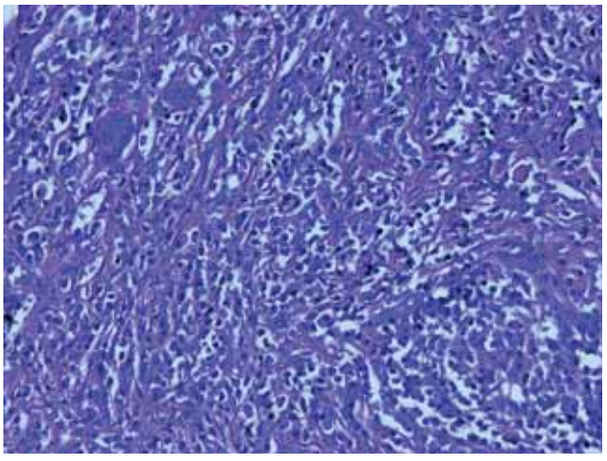

Figure 3. *(6178_09_HE_20×). Tissue is almost completely replaced by fibrous tissue and dense lymphocytic infiltrate. Haematoxillin and eosin, primary magnification 20×*

Rycina 3. *W wycinku tkankowym pierwotne utkanie jest prawie całkowicie zastąpione przez tkankę łączną oraz naciek limfocytarny. Preparat HE, pierwotne powiększenie obiektywu 20×*

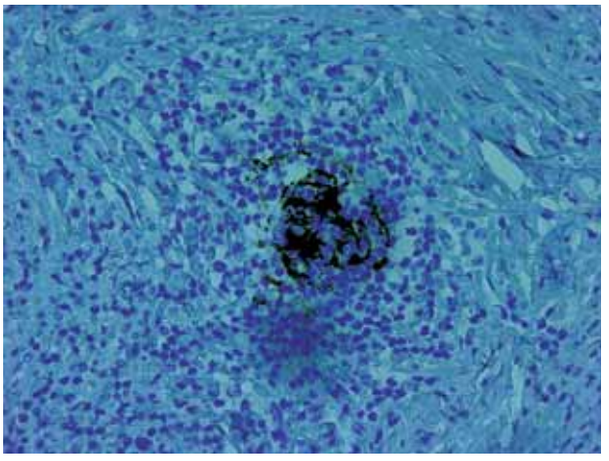

Figure 4. *(6178_09_HE_10×). Within dense collagenous tissue and between lymphocytes, remnants of thyreoglobulin material are visible. Immunohistochemistry for thyreoglobulin, primary magnification 20×*

Rycina 4. *W obrębie zwłókniałej tkanki pomiędzy limfocytami obecne są pozostałości tyreoglobuliny. Badanie immunohistochemiczne na obecność tyreoglobuliny, pierwotne powiększenie obiektywu 20×*

— specimen 7540/09 — included two tissue fragments. The first one constituted a full-thickness fragment of the skin with some subcutaneous tissue. The dimensions of the tissue sample were 1.2 × 0.2 × 0.3 cm. Atrophy of the skin appendages, thinning of the epidermis and an increased concentration of collagen fibres in the dermis were observed upon microscopic examination. The second sample was a muscle fragment, measuring 0.8 × 0.6 × 0.2 cm. Microscopic examination revealed features of myo-fibrill fragmentation and degeneration (hyaline changes).

OPIS PRZYPADKU

Discussion

Reaching a diagnosis was particularly difficult in this patient, since Riedel's thyroiditis, the fibrosing form of Hashimoto's disease, and malignant tumours of the thyroid can all show similar traits upon physical and histopathological examination.

Patients with Riedel's disease are usually euthyreotic. In a study by Schwaegerle, euthyreosis was observed in 64%, hypothyreosis in 32% and hyperthyreosis in 4% of patients [4]. The hypothyreosis is usually mild, resulting from the replacement of the majority of thyroid tissue by fibrous tissue, and is sometimes accompanied by a high anti-thyreoperoxidase antibody count. Our patient presented with clinical and laboratory hypothyreosis, associated with a high TSH level and a high anti-TPO antibody count since the start of the follow-up. Hay reported elevated anti-thyroid antibody counts in 45% of patients with RD referred to the Mayo Clinic [5]. Thyroid ultrasound is of limited relevance for the diagnosis. Hypoechogenicity is a common trait of inflammatory diseases of the thyroid gland and results from the presence of lymphocytes [6]. Scintigraphy reveals low radiotracer uptake, when either radioactive iodine or technetium is used [7, 8].

The classical morphological description of Hashimoto's thyroiditis includes a diffuse infiltration of the thyroid parenchyma by mononuclear cells (T and B lymphocytes at a 1:1 ratio, and plasma cells). The formation of lymphoid follicles with germinal centres, scattered histocytes and even giant multinucleated cells is a possible finding. Sometimes follicular atrophy with Hürthle cells metaplasia is recorded. Finally, a decrease of colloid may be observed [9–11]. Some authors have reported the presence of a fibrous variant of Hashimoto's thyroiditis which may be seen in as many as 10% of cases of autoimmune thyroiditis. However, where such a diagnosis is made, the presence of atrophic colloid follicles with Hürthle cell metaplasia should be recorded in histological slides. This was not the case in our patient. The main factor used to differentiate between the fibrous variant of Hashimoto's thyroiditis and other fibrous or fibrosclerotic entities in this area is the presence of fibroblastic proliferation limited to the thyroid gland. Differential diagnosis includes Riedel's disease, which is currently viewed as a rare thyroid problem. In Riedel's thyroiditis, an important morphologic factor is the replacement of thyroid follicles by dense and often hyalinised

collagen bands. Moreover, the fibrosis and inflammatory infiltrate extend beyond the gland and involve the surrounding tissues. The inflammatory infiltrate may present as a wide spectrum of patterns, mostly with lymphocytes, plasma cells, eosinophils and neutrophils.

Additionally vasculitis, especially in the form of phlebitis with occlusion of small and larger vessels, should be observed [11]. In our case, we observed lymphocytes but the eosinophils and neutrophils were not seen. Neither was the phlebitis phenomenon seen. The aforementioned features are enough to exclude a diagnosis of Riedel's thyroiditis. Recently, one author proposed a theory that Riedel's thyroiditis is an expression of inflammatory fibrosclerosis which might coexist with fibrosclerotic lesions or pseudoinflammatory tumours found in other locations [11]. The fibrotic variant of Hashimoto's thyroiditis could be excluded using the criteria reviewed by Papi and LiVolsi [1]. These criteria consist of a fibroinflammatory process involving the thyroid gland, at least partially, with evidence of expansion into the surrounding tissues, a lymphocytic infiltrate without giant cells and a lack of occlusive phlebitis or a tumour.

Finally, as the clinical data was indicative of Hashimoto's thyroiditis, and there were partial histological criteria of two forms of thyroiditis, namely Hashimoto's and Riedel's, the very rare diagnosis of combined disease was made [4]. Dense B and T lymphocytes and some plasma cell infiltrates, as well as the destruction of thyroid follicles by fibrosis extending into surrounding tissues were supportive of the final diagnosis. Additionally, in classical Riedel's disease, the inflammatory infiltrate is usually scattered, which was not the case in our patient. Such cases are rare but they have been reported [3, 12, 13].

Cytological evaluation, while being the basic diagnostic tool for diseases of the thyroid gland, is of limited use in Riedel's thyroiditis. The specimens are often oligocellular or acellular and thus non-diagnostic [14]. If a diagnostic sample is obtained, the cells are often polymorphic, a small inflammatory component is observed and intracellular intrusions are present, which can easily lead to diagnostic errors [15–17].

A definite diagnosis of RD is usually based on the histopathological evaluation of a post-surgery specimen. The following diagnostic criteria have been proposed by Woolner and later corrected by Meijer, Hausman and Schwaegerle:

— the presence of a fibrosing inflammatory process, involving the thyroid gland in its entirety or a part of it;
— evidence of the process spreading to the neighbouring tissues, including muscles;
— the presence of inflammatory cell infiltrates, yet without the presence of giant cells, oncocytes, lymph follicles or granulomas;
— evidence of obliterating phlebitis;
— absence of a neoplasm [2, 9, 18].

Outside the areas of fibrosis, areas of normal thyroid parenchyma are usually observed. In Hashimoto's thyroiditis, the inflammatory process is limited to the thyroid gland and does not exceed its capsule, the inflammatory cells (lymphocytes) form germinal centres, and oncocytes are present [19]. No areas of normal thyroid parenchyma are observed.

As we can see, apart from the histopathological criteria, all other elements contributing to a diagnosis of RD and HD are either similar or non-diagnostic. In a few reported cases, the authors diagnosed the coexistence of the two diseases. Taubenberger et al. reported the case of a 36 year-old female, who had started therapy for hypothyroidism nine years prior to a diagnosis of RD.

High counts of antimicrosomal antibodies were observed. FNAB was non–diagnostic. A surgical biopsy of the thyroid and neighbouring tissues was performed. A histopathological analysis revealed an inflamed thyroid tissue, divided by strands of fibrous tissue. The inflammatory infiltrate contained lymphocytes and plasmatic cells forming germinal centres; oxyphilic metaplasia was also observed. In the neighbouring tissue samples, a fibrosing process with a lymphocyte inflammatory infiltrate, without germinal centres, was observed [3]. A similar case was reported by Baloch et al. [12]. Pirola reported a case of simultaneous RD, HD and purulent thyroiditis [13].

Considering the clinical course and histopathological presentation, a decision was made to diagnose Riedel's goitre with coexistent Hashimoto's thyroiditis. The coexistence of these diseases is a very rare occurrence, which makes reaching the correct diagnosis much more difficult.

Only a handful of such cases have been reported in the literature.

Conclusions

Differentiating between the histopathological and clinical presentation of both diseases in one patient is difficult, primarily due to the partial overlapping of their histopathological traits; this is a potential pitfall. In order to avoid a diagnostic error, close cooperation between the endocrinologist and pathologist is mandatory. It is the authors' opinion that in our patient the two diseases existed separately, and their coexistence was most likely coincidental.

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