Riedel’s thyroiditis in a black African: A case report and review of literature

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Abstract

Riedel’s thyroiditis is a rare cause of the enlargement of the thyroid gland. The etiology is not fully known. There has been no report of Riedel thyroiditis in our country. We report a case of a 61-year-old man with the disease as well as review the literature. We present the case of 61-year-old carpenter seen in our clinic with 2½ years history of painless anterior neck swelling associated with hoarseness of voice. He had multiple hard nodules on the left lobe of the thyroid gland with multiple cervical lymph nodes enlargement. No feature of hypothyroidism or thyroiditis. Clinical diagnosis of malignant goiter was made although Fine-needle aspiration for cytology did not suggest malignancy. He had surgery, findings included nonresectable hard multinodular left thyroid lobe from which a wedge biopsy was taken, Histology of the specimen revealed Riedel’s thyroiditis. He was managed with oral Prednisolone and Tamoxifen with remarkable improvement in his clinical symptoms. Riedel’s thyroiditis is a rare disease. It can easily mimic malignant goiter hence proper histological diagnosis will be necessary to differentiate. Review of medical literature showed that Riedel thyroiditis has not been reported in a black African patient inhabiting the sub-Sahara Africa. This was a report of Riedel thyroiditis in a black Nigerian patient that was successfully managed on oral glucocorticoid, tamoxifen and L-thyroxine.

Key words: Malignant goiter, Nigerian patient, prednisolone, Riedel’s, tamoxifen, thyroiditis

Date of Acceptance: 17-Feb-2015

Introduction

Riedel’s thyroiditis is a fibrosclerotic condition of the thyroid gland that results in destruction of the gland and its replacement with dense fibrotic tissues. There is also infiltration of the fibrotic tissues into the surrounding structures such as the skeletal strap muscle, vessels, the trachea, esophagus and sometimes the upper mediastinum.¹

More than 100 years ago, Riedel described 3 cases of a peculiarly hard, infiltrative lesion of the thyroid gland.²⁻⁴ Based on physical examinations and intraoperative findings, all 3 patients were believed to have thyroid malignancies. However, histological examination revealed a chronic inflammatory process in each case. Riedel commented on “collections of round cells interspersed among normal thyroid tissue, whereby the latter becomes destroyed”⁵ This unusual and poorly understood thyroid disorder became known as Riedel’s thyroiditis.

It is a rare entity with etiology that is largely unknown.⁶⁻⁷ Early medical literature postulated that it is an autoimmune disorder⁸ while others see it as a local manifestation of systemic fibrotic process.⁹⁻¹⁰ Because of its rarity, only few cases have been recorded in medical literatures. The estimated incidence is 1.06 per 100,000 populations accounting for 0.06% and 0.05% of thyroidectomies in two separate series at the Mayo Clinic, London tertiary healthcare level.¹⁰,¹¹ Like most thyroid
diseases, females are more affected than males with a ratio of 4:1. People aged 30-50 years are predominantly affected. Riedel’s thyroiditis was first described by Bernhard Riedel in 1884, who described two patients with iron-hard, fixed and painless enlargement of the thyroid gland. Since then, owing to its rarity, few cases of Riedel’s thyroiditis has been reported worldwide. The pattern of clinical presentation may be easily mistaken for thyroid cancer. Although no pathognomonic clinical feature defines this disease, compressive symptoms and signs as well as endocrine abnormalities may be present. The compressive symptoms in addition to the occasional presence of lymph nodes and hoarseness of voice make it to be easily misdiagnosed as thyroid cancer, a disease, which has seen recent increase in iodine sufficiency place like Nigeria.

Our search of medical literatures revealed that only one case has been reported in a black patient in sub-Saharan Africa, the diagnosis of which was made at postmortem examination. In view of its rarity in black Africans and the fact that no report of Riedel’s thyroiditis has been made in Nigeria, we report this case of a 61-year-old Nigerian man presenting with clinical feature initially suggestive of malignant goiter, which turned out to be Riedel’s thyroiditis after histological examination of the excised thyroid specimen. This is the first report of a case of Riedel’s thyroiditis in a living black African.

**Case Report**

A 61-year-old male carpenter of Yoruba tribe of Nigeria, was referred to our clinic with 2½ years history of progressive painless anterior neck swelling which was noticed to have rapidly increased in size 4 months prior to presentation. There was no toxic symptom. However, there was hoarseness of voice. There was no history of smoking cigarette, drinking alcohol or consumption of tobacco with the patient. Physical examination revealed a middle-aged well-nourished man with normal blood pressure of 130/90 mmHg, pulse rate was 88/min and a respiratory rate of 20/min. There was an enlarged thyroid gland with the left lobe greater than the right lobe. There were multiple hard non-mobile nodules on the left lobe and hard immobile left cervical lymph nodes enlargement [Figures 1 and 2]. The left carotid pulsation was not palpable (positive Berry’s sign).

Ultrasound scan of the neck revealed a normal right lobe of thyroid gland. The left lobe was enlarged measuring 8.8 cm by 5.8 cm by 8.5 cm (L × AP × Tr) with a predominantly echogenic solid heterogeneous mass. The left carotid and internal jugular vessels were displaced posteriorly while the trachea was displaced to the right. Soft tissue plain radiograph of the neck and thoracic inlet revealed an anterior soft tissue mass extending to the root of the neck with tracheal deviation to the right.

Thyroid function test revealed slightly elevated thyroid stimulating hormone (TSH) level of 5.2 IU/mL (reference: 0.4-4.0), a normal free triiodothyronine (T3) and free thyroxin (T4) level of 2.7 ng/mL (reference: 1.2-4.2) and 13.4pmol/L (reference: 9-22.2) respectively. Full blood count result showed white blood cell count of 7,800 cells/cmm (reference: 4,000-11,000) with neutrophils 43% (reference: 40-70), lymphocytes 54% (40-60) and eosinophils of 3% (reference: <2), platelets count was 109 × 10⁹/cmm (reference: 150,000-450,000) and packed cell volume of 41% (reference: 38-48).

Fine-needle aspiration cytology (FNAC) showed benign epithelial cells with central regular nuclei and a moderate cytoplasm. There was densely inflammatory background composed of both neutrophils and lymphocytes.

A clinical diagnosis of malignant thyroid neoplasia was made based on the clinical findings. He was scheduled for thyroidectomy. Intraoperatively, we found an enlarged multinodular left lobe of the thyroid with areas of hard nodules and cystic degeneration. The gland infiltrated and adhered to the sternocleidomastoid muscle, the strap muscles and the investing deep cervical fascia. It was also morbidly adherent to the tracheal as no tissue plane could be delineated. The midline structures were pushed to the right, and the left cervical vessels were displaced further to the left. There were multiple enlarged cervical lymph nodes. The right thyroid lobe was healthy looking.

He had isthmusectomy, right lobectomy and excision of small quantity of the left lobe that could be safely resected for histopathological examination. The bulk of the tumor mass could not be resected and was left behind.

He had an uneventful postoperative recovery and was placed on levothyroxine 0.2 mg daily, oral prednisolone 40 mg daily, oral tamoxifen 20 mg daily. He was thereafter discharged on 9th postoperative day. He was seen in the clinic with remarkable improvement noted 1-month after commencement of medications as adjudged by the marked reduction in the size of the thyroid gland [Figure 3] and improvement in the quality of the voice.

Histology of specimen was reported as Riedel’s thyroiditis with thyroid tissues composed of follicles of different shapes and sizes. Many of the follicles were filled with colloid that has flattened epithelial cells lining while others have scalloped margins. Adjacent to the follicles were areas of extensive fibrosis with focal areas of hemorrhage and some vascular channels. There were some inflammatory cells infiltrates around these vascular channels. No malignant cell was seen [Figures 4 and 5].
Riedel thyroiditis is an extremely rare form of thyroiditis characterized by extensive fibrosis involving the thyroid and contiguous neck structures.\[^6,11\] It may be associated with idiopathic fibrosis in other sites of the body, such as the retroperitoneum.\[^6,10,16\]

Riedel thyroiditis is a very rare disease entity, and few cases have been reported in the medical literature. This reported case of Riedel thyroiditis is the first in the history of over 30 years existence of our hospital with over 50 thyroidectomies being performed per year. This translated to local hospital incidence rate of about 1 in 1,500 (0.067) cases of thyroidectomies. This figure is found to be similar to reports from other centers of the world.\[^11\] Riedel thyroiditis accounted for 20 cases in a review of 42,000 thyroidectomies in Mayo Clinic from 1920 to 1955 representing an incidence of 1 per 2,000 (0.05%) thyroidectomies.\[^11\] Another review of 57,000 thyroidectomies performed in the same hospital between 1920 and 1984 revealed an operative incidence of 0.06% with a population incidence of 1.06 per 100,000 population.\[^11\]
Women are mostly affected with a female to male ratio of 4:1 and peak age incidence is the fifth decade.[7,10,11,17] Although our patient a male, who is in seventh decade of life this does not coincide with the peak age incidence for Riedel thyroiditis. This also does not coincide with the peak age incidence for with the occurrence of thyroid carcinoma.[13] This couple with the fact that the patient presented with a multinodular goiter, enlarged cervical lymph node, hoarseness of voice and some degree of hypothyroidism made it so easy for this disease to mimic malignant thyroid enlargement. In fact, our initial clinical diagnosis was thyroid cancer. The differential diagnosis of anaplastic thyroid carcinoma was even reinforced by surgical findings a hard fibrous mass replacing the thyroid, firmly adherent to surrounding planes, and a microscopic pattern of interstitial fibrosis with a lymphoplasmacytic infiltrate and atrophic thyroid follicles in this patient. There have been reports of Riedel thyroiditis mimicking anaplastic carcinoma and sarcoma of the thyroid in the past.[18]

Another strong differential diagnosis of Riedel's thyroiditis is fibrosing variant of Hashimoto's thyroiditis which is characterized by extensive fibrous proliferation but without extension into the surrounding structures, thus distinguishing this lesion from Riedel's thyroiditis.[8,19] Which is characterized by the progressive fibrous replacement of the thyroid gland, with a spread of dense, inflamed fibrous tissue outside the thyroid capsule, involving the adipose tissue, muscle, and nerves that may encase vessels, parathyroid glands, trachea, and esophagus as is noted in this case.[19,20] It is also known that Riedel disease (RD) is not a real thyroiditis but rather a form of fibroinflammatory process of the thyroid involving also the soft peripheral tissues unlike the fibrosing variant of Hashimoto's thyroiditis, which is a real inflammatory process.[19,23]

There have been many postulations regarding the etiology and pathogenesis of Riedel's thyroiditis. The theory of “intrathyroidal hypothesis” claiming that Riedel's thyroiditis represent the late stage chronic inflammatory disorder of the thyroid characterized by progression of the fibrosis.[8,22,23] On the contrary, the “pharmacological hypothesis” suggests that some particular medications may trigger Riedel's thyroiditis development.[19,24] Although not proven, inherited susceptibility and development was hypothesized, as well.[9] Nowadays, the “systemic autoimmune hypothesis” seems to have the most support, and it basically views Riedel's thyroiditis as a manifestation of disordered fibroplastic proliferation because of hypersensitivity reaction and consequent release of stimulating growth factors.[23] This theory considers a fibroblast not only as a final cell responsible for fibrosis, but also as a main target for well-defined systemic autoimmune attack.[9,24]

More recently attention has been focused on the role of molecular expression in the etiology and pathogenesis of Riedel thyroiditis. A recent study did quantitative evaluation of thyroid tissue of a patient with Riedel thyroiditis for gene expression.[24] The following genes PIK3CA, PIK3CD, PIK3CG, Tg, transforming growth factor beta (TGFβ1), THRB, COL1, CDKN1C, CDH3, and CACNA2D were analyzed for gene expression level by real-time polymerase chain reaction method.[24] Out of 10 above genes It was found that (PIK3CA - responsible for coding alpha catalytic sub unit of class 1 PI3K phosphoinositide 3-kinase and CDH3 responsible for coding P-cadherin) gene expression level was higher than respective control of normal unchanged physiologic thyroid tissue.[24] Possible explanation for this may be that phosphoinositide 3-kinase/serine-threonine protein kinase (PI3K/Akt) pathway which participates in cellular signaling in response to various growth factors including fibroblast growth factor, when genetically activated and amplified lead to enhancement and stimulation PI3K/Akt kinase activity and Akt phosphorylation. Increased PI3K/Akt expression has been observed in both Hashimoto thyroiditis and well-differentiated thyroid cancer, advance liver fibrosis in chronic hepatitis.[24,26-28] The fibrosis I thyroiditis may be partly due to this molecular event.[24,27] It was also shown that CDH3 gene expression may increase in Riedel’s thyroiditis, as well. Cadherins, such as CDH3 are integral membrane glycoproteins responsible for calcium-dependent cell-cell adhesion. Our contemporary knowledge about the role of P-cadherin in fibrosis and autoimmune processes is well known but scanty.[24,29,30]

Riedel's thyroiditis has long been linked to a generalized fibroinflammatory process termed “multifocal fibrosclerosis” (MFS).[31,32] One-third of patients with Riedel's thyroiditis develops fibrosing disorders in other organs over a 10-year period.[10,31] One-third of patients with Riedel's thyroiditis develop fibrosing disorders in other organs over a 10-year period.[13,34,36] IgG4-related systemic disease is known to affect the pancreas, biliary tree, salivary glands, the peri orbital tissues and ocular adnexa, kidneys, lungs, lymph nodes, meninges, aorta, breast, colon, mediastinum and prostate gland.[17] The histologic findings in IgG4-related systemic disease include a lymphoplasmacytic infiltrate, storiform fibrosis, an abundance of eosinophils, and obliterative phlebitis.[36] Up to 95% of patients have elevated serum IgG4 concentrations, which can be more than 25 times the upper limit of normal.[18,38,39] Recent reports suggest an association between MFS and IgG4-related systemic disease.[40,41] Riedel's thyroiditis and IgG4-related systemic disease share the histopathologic features of fibrosis, lymphoplasmacytic infiltration, tissue eosinophilia, and obliterative phlebitis.[4] Moreover, IgG4-related systemic disease and MFS have similar patterns of multiple organ involvement: Both have a tendency to involve the biliary system, retroperitoneum, salivary and lacrimal glands, and retrobulbar space.[4,36]
IgG4-related diseases have also been called various names like IgG4-related sclerosing disease, IgG4-related systemic sclerosing disease, IgG4-related autoimmune disease, hyper-IgG4 disease, and IgG4-related systemic disease.

The pathogenesis of IgG4-related sclerosing disease is still not clearly understood. The disease may represent a hypersensitive/allergic reaction as compared to being an autoimmune disease. An association of IgG4-related autoimmune pancreatitis with gastric ulcer and Helicobacter pylori infection has been proposed. Other proposed hypothesis regarding the pathogenesis include enhanced T-helper type 2 responses to intestinal microflora and an immune-mediated pathogenesis based on the ultrastructural finding of electron dense immune complex deposits along the basement membranes of pancreatic acini and renal tubules.

There are no clinical features pathognomonic of Riedel's thyroiditis. The patient usually present with a neck swelling which is usually painless with duration ranging from months to years. Pressure symptoms such as dyspnea, dysphagia and hoarseness may be present. Patient may also present with extrathyroidal features of fibroslerosing nature of the disease such as Renal failure. Other reported clinical features of Riedel thyroiditis resembling malignant neoplasm are recurrent laryngeal nerve injury, causing vocal cord paralysis and consequently, hoarseness.

The findings of hard, irregular and multiple nodulated mass in this patient initially suggested possible diagnosis of thyroid malignancy. This feature of multilobulated goiter is also similarly seen in Riedel thyroiditis where the thyroid mass is usually hard and fixed making it clinically impossible to differentiate it from thyroid cancer or lymphoma. The lesion can involve the cervical sympathetic trunk, which might produce Horner syndrome. Local invasion of the neck's structures by fibrous tissue also might cause fibrous mediastinitis, superior vena cava syndrome, cerebral venous sinus thrombosis, and occlusive vasculitis, causing an extensive sterile neck abscess. However, the initial symptoms of Riedel thyroiditis might resemble other thyroid diseases. The initial symptoms of Riedel thyroiditis might be represented by persistent slight temperature elevation, sore throat, and pain in the anterior portion of the neck, mimicking subacute (granulomatous; de Quervain) thyroiditis.

Cervical lymphadenopathy is usually not present in Riedel's thyroiditis but has been reported. The finding of inflammatory cells infiltrates in the FNAC and histology in our patient suggested that the cervical lymph nodes enlargement may be due to reactive inflammation.

There is no pattern of laboratory investigation result peculiar to Riedel's thyroiditis. About two-third are euthyroid and a third hypothyroid which is usually subclinical. Those with overt hypothyroidism usually have diffuse bilateral involvement of the thyroid. Our patient had feature of subclinical hypothyroidism evidenced by the marginally elevated TSH level though thyroxing (T4) and triiodothyronine (T3) were within normal limit, this is consistent with most cases reported in the literature. It is thought that the progressive fibroging and sclerosing nature of this disease eventually destroys the thyroid and parathyroid parenchyma cells thus leading to progressive hypothyroidism, in the long run.

Fine needle aspiration cytology cannot differentiate between Riedel's thyroiditis and carcinoma of the thyroid gland. In fact, the diagnosis of Riedel's thyroiditis is difficult to make on FNAC because of the dense fibrous tissues which precludes adequate aspiration of the gland. The role of FNA in thyroiditis especially Riedel's is to exclude the neoplasia primarily. FNA though may not differentiate it from conditions such as the fibromatosis or sclerosing malignancy of the thyroid, particularly spindle cell variant of anaplastic carcinoma. Where adequate specimen is obtained on FNA, it is often nondiagnostic because often only, follicular cells are obtained. It however may be suggestive. Some authors have opined that suggestive FNAC with physical examination findings, clinical laboratory data and radiological findings can be used as aid in the preoperative diagnosis that may exclude the need for surgical intervention in absence of indication other than obtaining specimen for histological diagnosis.

There is no consensus of opinion when it comes to treatment of Riedel's thyroiditis. This is understandably so since it is a rare condition, and it would be difficult to conduct a clinical trial or accumulate enough subjects for the purpose of studying the ideal treatment of this condition. High-dose glucocorticoids particularly prednisolone has been found to produce a good response when given as a monodrug or in combination therapy with levothyroxine. Even though, there is no controlled trial on the use due to its rarity. It has been established that positive results can be obtained with other glucocorticoids and equivalent doses as low as 15-60 mg of prednisone per day. The best regimen and duration of therapy should be based on response and tolerability.

In patients who do not respond to steroid or experience recurrence on withdrawal of steroids, use of tamoxifen as sole agent or combined with steroid has been documented to improve therapy response. Report of tamoxifen toxicity like development of hot flushes and endometrial hyperplasia in female has prompted its substitution with raloxifene, which is preferred by most physician based on the excellent result produced by its use. Tamoxifen effect is unrelated to its anti-estrogen activity but is believed to act through modulation of TGF-B stimulation, a potent inhibitor of
fibroblast proliferation.\textsuperscript{14,56} Our patient responded to prednisolone 40 mg daily. However, response plateaued after 4 months of therapy. This necessitated the addition of tamoxifen 20 mg daily with further noticeable reduction in size within 2 months. No toxicity has so far been noted with any of these drugs in our patient.

Treatment for identified endocrine system deficiencies should include the initiation of Levothyroxine replacement therapy for those presenting with hypothyroidism and calcium as well as calcitriol therapy for control of concomitant hypoparathyroidism.\textsuperscript{[55]} In this report, levothyroxine therapy was commenced postoperatively owing to biochemical result which was suggestive of subclinical hypothyroidism as well as the fact that the resection of healthy looking right lobe and isthmus of the thyroid gland was carried out on the assumption of a malignant goiter before histological diagnosis was made. The use of Levothyroxine has no effect on goiter size or the fibro sclerosis.\textsuperscript{[14]}

Surgery plays a limited role in the management of Riedel’s thyroiditis and has been found ineffective and fraught with a plethora of complications when employed as a primary form of treatment.\textsuperscript{[58]} In most instances, the role of surgery has been confined to obtaining thyroid specimen in order to establish histological diagnosis, to relieve airway in case of obstructive airway symptoms and also to exclude malignancy.\textsuperscript{[24,31]} Surgery should be limited to isthmus ectomy and biopsy of the diseased tissue as resection is usually not possible because of infiltration and morbid adherence to adjacent structures as encountered in this patient. An attempt at resection in such situation would often result in unnecessary postoperative complications.\textsuperscript{[17]} Successful primary resection following Intraoperative diagnosis on frozen section has however been reported.\textsuperscript{[10]} The patient responded without requiring steroid. Careful follow-up to identify and treat recurrence is advocated in such case. Our patient had to undergo surgery because preoperatively, the diagnosis of Riedel’s thyroiditis was not made. An ultrasound guided core needle biopsy may obviate the need for surgery if the diagnosis is entertained preoperatively

The natural history of Riedel’s thyroiditis is often that of progression if untreated, although it may stabilize or even regress spontaneously.\textsuperscript{[14]} Relapse which may even be extra-thyroid is common following withdrawal of medications A third of patient will develop other fibrosing disorder over 10yrs. Disease-specific mortality is rare.\textsuperscript{[8,17]} The patient in this report responded to prednisolone with response sustained. However, the patient has only been followed-up for a year with almost complete resolution of the neck swelling. Closer and longer follow-up is necessary, especially on withdrawal of medications, to see if there will be relapse or symptoms of extra thyroidal fibrosis will develop.

Conclusion

This case illustrates the rarity of Riedel thyroiditis and how it can pose diagnostic challenges in confusing it easily with thyroid malignancy. FNAC may not particularly help in solving the diagnostic dilemma. Riedel thyroiditis can also present with extrathyroidal symptoms, which makes medical management the mainstay of treatment. Surgery has a limited role of obtaining tissue for histological diagnosis in case that is still uncertain before surgery. Riedel thyroiditis although rare should be considered in adult male with longstanding nodular goiter and other symptoms of malignancy, but in whom the patient is still well preserved and more healthy looking than the stage of the supposed malignancy would suggest.

References


Source of Support: Nil. Conflict of Interest: None declared.