SIENDO
Faculty of Medicine Siriraj Hospital

Interhospital Conference
Case 2

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F2 PORNRUMPA PENGKHUM

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Riedel Thyroiditis

History and incidence

- **Riedel thyroiditis (fibrous thyroiditis, RT)** was first described by Bernhard Riedel in 1896
- **Rare** inflammatory disorder, resulting in "eisenharte" (**iron-hard**), fixed, and usually painless enlargement of the thyroid
- Estimated incidence of 1:100,000, which affects more frequently **women between 30-50 years of age**
- Characterized by **fibrosis of the thyroid gland** and often the **adjacent structures**

Endocrine (2018) 60:185–192
J Clin Endocrinol Metab, October 2011, 96(10):3031–3041

Etiology

- Not completely understood
- Association with systemic fibrotic processes, autoimmune diseases and diseases from the spectrum of excessive IgG4
- Fibrosclerotic organ manifestations can either be a part of IgG4-related disease or solely be located in the thyroid and adjacent tissues
- Elevation of serum IgG4 can be found, IgG4- positive plasma cells with an IgG-4 ratio >40%
- But more often lymphoplasmocytic IgG4-positive plasma cells and storiform fibrosis are present in thyroid tissue

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Clinical presentation

- **Hard, palpable goiter,** clinically mistaken for malignancy, including anaplastic thyroid CA, thyroid angiosarcoma, or lymphoma
- **Obstructive/compressive symptoms** including dyspnea, dysphagia and hoarseness
- Affect adjacent structures: parathyroid glands, musculature in the neck, vocal cord paralysis
- Biochemical abnormalities: **hypothyroidism, hypocalcemia**

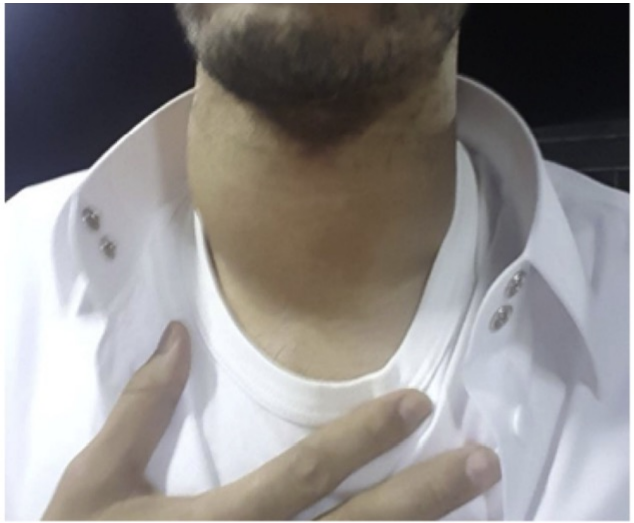

Fig. 1. Diffuse enlargement of thyroid at Presentation [more on right side]: Anterior view.

Annals of Medicine and Surgery 52 (2020) 5–9

Clinical presentation

TABLE 2. Clinical presentation of Riedel's thyroiditis and associated fibrotic conditions

Finding	Clinical symptoms	Pathology	Diagnostic evaluation
Goiter	Pressure	Encasement	Thyroid ultrasound
	Dysphagia	Esophageal	CT neck/UGI
	Vocal cord paralysis	Recurrent nerve	Laryngoscopy
	Dyspnea/stridor	Upper airway	CT neck
	CNS	Carotid encasement	Angiography
Hypothyroidism	Fatigue	Thyroid infiltration	TSH, FT4, ATAbs
Hypoparathyroidism	Tetany, cramping	Parathyroid infiltration	$CaPO_4$/Alb/PTH
Systemic fibrosis			
Retroperitoneal	Low back/flank pain	Hydroureteronephrosis	U/A, BUN/Cr, U/S, pyelogram
Mediastinal	SVC syndrome	SVC restriction	SVC venogram
	Pulmonary restriction	Pulmonary arteries or veins	Pulmonary angiogram
Cholangitis	Abdominal pain	Irregular hepatic ducts	Bili, AlkPhos, ALT, AST, ERCP
Pancreatitis	Abdominal pain	Irregular pancreatic ducts	Bili, AlkPhos, ALT, AST, ERCP
Orbital pseudotumor	Exophthalmos	Intraorbital mass	Orbital CT
Tumefactive fibroinflammatory	Head/neck mass	Soft tissue fibrosis	Head/neck CT, biopsy

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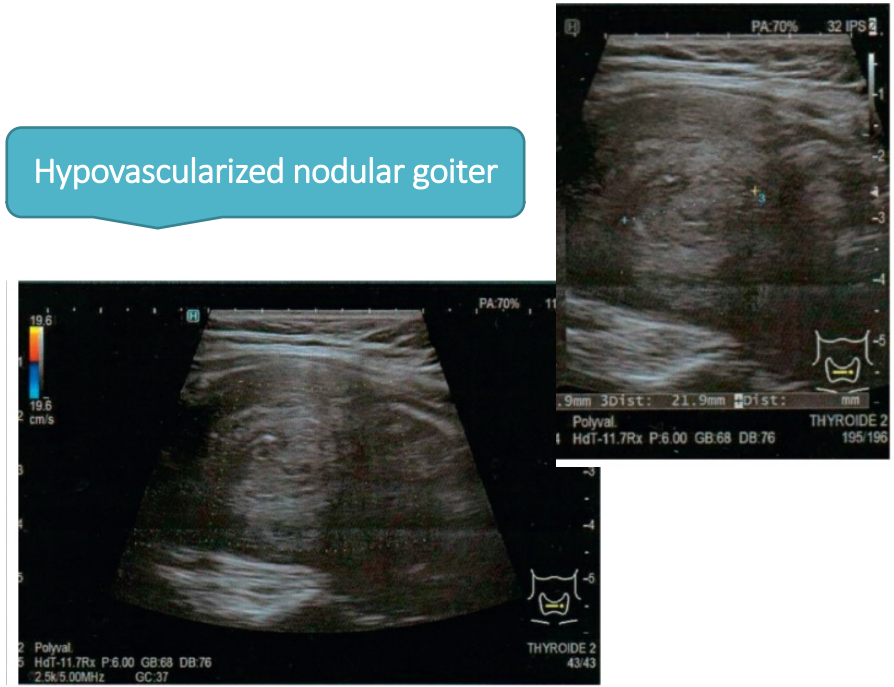
Thyroid ultrasound

- Diffuse, hypoechoic, hypovascular appearance due to extensive fibrosis
- Carotid artery encasement
- Application of thyroid US elastography demonstrates **significant stiffness**

Hypovascularized nodular goiter



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CT scan

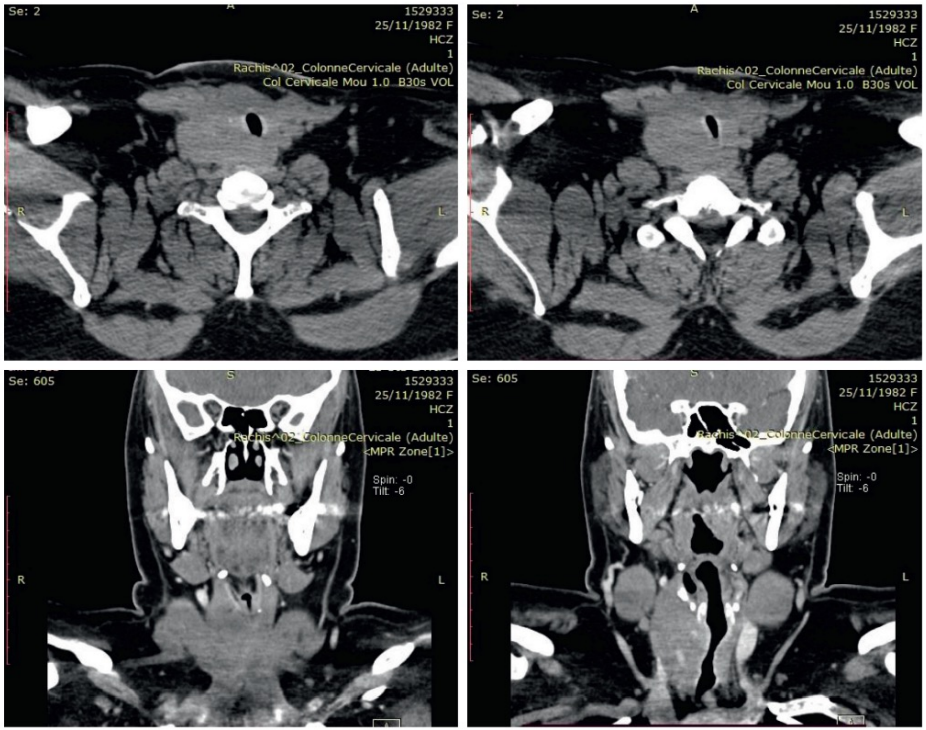

FIGURE 2: CT image in transverse and coronal sections showing a large goiter with tracheal deviation and stenosis.

- If clinically indicated by obstructive symptomatology, CT images of the neck reveal enlargement of affected area and hypodense tissue, which does **not enhance with contrast**
- **Evidence of the extrathyroidal invasion** and may demonstrate vascular encasement with >50% of carotid arteries and 1/3 of internal jugular veins

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Clinical evaluation

- **18F-FDG PET:** intense uptake in the fibrotic inflammation area
- PET may also be useful in identifying **other areas of fibrosis** and especially in the follow-up
- Radionuclide imaging of the thyroid with Tc-99 or 123/131-I demonstrates heterogeneous and **typically low RAIU** as is commonly seen in **other forms of chronic thyroiditis**

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Inflammatory markers

- Inflammatory markers were tested in only a minority but were commonly abnormal
- Elevated C-reactive protein (CRP) was found in 72%
- Erythrocyte sedimentation rate (ESR) was elevated in 97%
- Owing to various laboratory reference ranges and often incomplete data provision, median or mean levels could not be calculated

J Clin Endocrinol Metab, September 2020, 105(9):e3469–e3481

Pathology

- **Firm to hard (woody) palpable mass** that similar in appearance to a malignant lesion
- Typically no tissue planes discernable macroscopically, making precise surgical resection impossible
- **Normal tissues are replaced by inflammatory cells**, predominantly a mixed of lymphocytes, plasma cells, eosinophils, and small amounts of colloid in a dense matrix of hyalinized connective tissue

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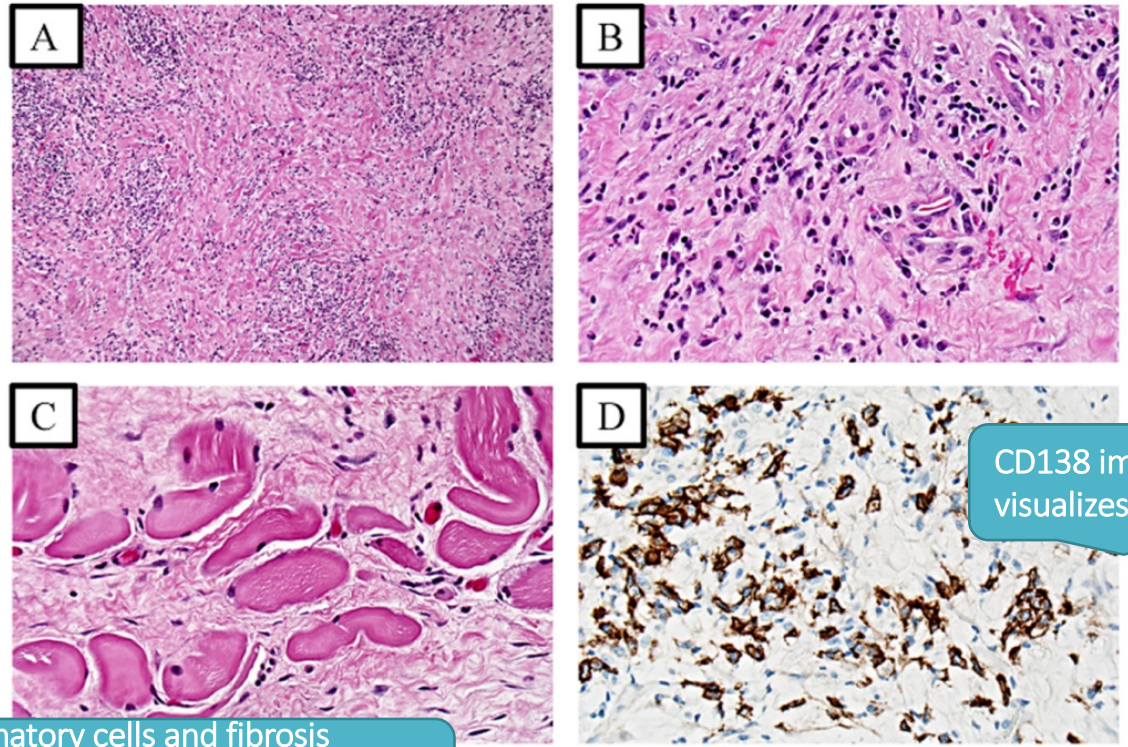
A,B Storiform, keloid-like fibrosis, and inflammatory cells have replaced the thyroid parenchyma



CD138 immunohistochemistry visualizes infiltrative plasma cells

Inflammatory cells and fibrosis engage the perithyroidal skeletal musculature

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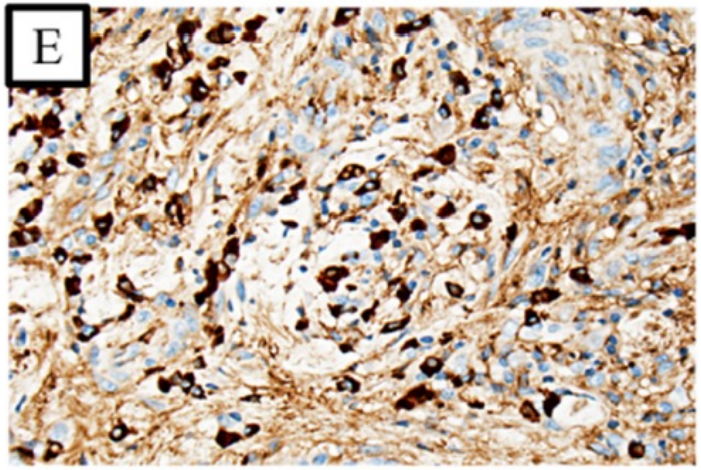
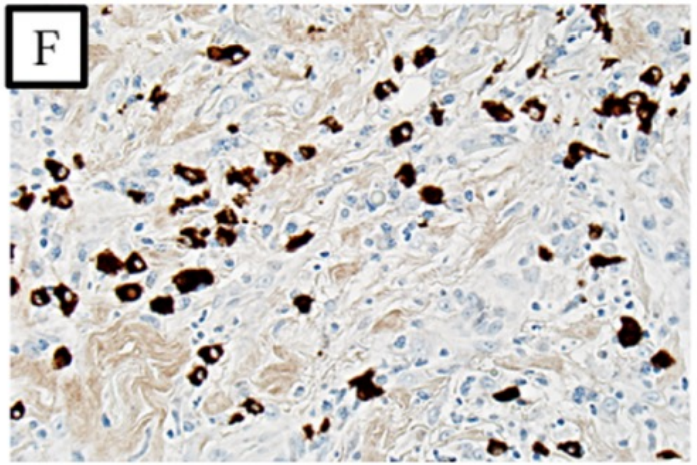
Pathology



IgG-positive and IgG4-positive cells respectively in the same area

The number of IgG4-positive cells >10/HPF, IgG4/IgG ratio >0.5, suggestive of IgG4-related disease



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Diagnostic criteria

Definitive diagnosis is made only with histopathology, the following are required to establish the diagnosis of Riedel thyroiditis

1. Inflammatory process in the thyroid with extension into surrounding tissue
2. The inflammatory infiltrate should contain no giant cells, lymphoid follicles, oncocytes, or granulomas
3. There should be evidence of occlusive phlebitis
4. There should be no evidence of thyroid malignancy

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Diagnostic criteria

- **FNA are usually nondiagnostic**, but some may yield findings of inflammation, fragments of fibrous tissue with bland spindle-shaped cells and myofibroblasts, or even cytopathology consistent with follicular neoplasm
- Immunohistochemical plasma cell assessment and circulating IgG4 levels into the diagnostic criteria remains to be defined

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- RT must be differentiated from malignancies, esp. anaplastic thyroid cancer, thyroid lymphoma, and sarcoma of the thyroid
- Additional differentiation must be made with the fibrosing variant of Hashimoto's thyroiditis, which accounts for approximately 10% of Hashimoto's cases

TABLE 1. Differentiation of fibrosing Hashimoto's and Riedel's thyroiditis

Finding	Riedel's thyroiditis	Fibrosing Hashimoto's
Thyroid antibodies	Yes, moderate titer	Yes, high titer
Normal thyroid tissue	Yes, sharp demarcation	No, diffuse involvement
Venulitis	Yes	No
Extrathyroidal invasion	Yes	No
Hürthle cells	No	Yes
Lymphocyte light chains	λ dominant (71%)	κ dominant
Plasma cell production	IgA increased (47%)	IgG dominant, IgA (<15%)
Associated autoimmune disease	Yes	Yes
Associated de Quervain's	Yes	No
Ultrasound appearance	Hypoechoic	Hypoechoic
Doppler flow	Diminished	Enhanced

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Clinical course and prognosis

- The course of RT is **quite variable**
- **Slowly progressive course of most cases**, the diagnosis is delayed for variable range from >10 months to 2 years after the onset of observable signs such as goiter
- **30-40% of cases having developed hypothyroidism**, >80% are hypothyroid during the course of follow-up

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Clinical course and prognosis

- Mortality in older reports has resulted from tracheal compression, upper airway compromise and respiratory failure
- Rates of disease-specific death have ranged in frequency from 6 –10%
- A recent series from the Mayo Clinic reported **no mortality over a mean follow-up of 9.5 yr** and **86% of the subjects followed were stable** or improved symptomatically

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Surgical treatment

Surgical management is considered, the indications are essentially two:

1. Histopathological diagnostic confirmation
2. Relieving compression or obstruction

The complete resection of the gland is not recommended due to the high risk of damaging nearby structures because of the lack of resection margins

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Medical therapy: Glucocorticoids

- Currently no standardized treatment
- Glucocorticoids (GC) are usually the first step to decrease the inflammation
- Prednisone was the most commonly used GC, usually at 40 mg orally OD (0.5-100 mg) and duration of treatment was 3 months
- Dramatic improvement in symptoms associated with the inflammatory mass
- Reduction in the size and consistency of the mass and upper airway symptoms

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Medical therapy

- Tamoxifen: unknown mechanism, **inhibit fibroblast proliferation**
  - ✓ 10-20 mg, with GC or monotherapy, significantly reducing mass size and clinical symptoms with persistent effectiveness in most cases
- Other nonglucocorticoid agents: **Mycophenolate mofetil, rituximab and azathioprine**
- Few reports of the use of low-dose radiation, no systematic evaluation

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Thank you