

**Case Study #1**  
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51 year old Asian female with H/o hypothyroidism on levothyroxine 50 mcg daily presented with painful progressively enlarging goiter over the course of 3 months (R>L) associated with compressive symptoms like difficulty breathing and swallowing, no change in voice. Levothyroxine held for three weeks and CT soft tissue neck done which showed marked bilateral enlarged thyroid lobes and isthmus, R/L 9 cm/3.5-4.5cm displacing the trachea and mass effect of posteriorly displaced esophagus.

TSH 26 uIU/mL and FT4 0.7 ng/dl, TPO 21885 IU/mL and TSI 39 .

Thyroid ultrasound showed heterogeneous echogenicity suspicious for autoimmune thyroiditis with overall normal vascularity. Also two right sided solid and one left sided nodules, each > 1 cm found. FNA of the nodules- Both the right sided were negative for malignancy but the left one was indeterminate- cellular micro follicular proliferation indicating follicular neoplasm; probably adenoma but cannot exclude follicular carcinoma.

Differential at that time included- thyroid cancer/ lymphoma vrs thyroiditis. Patient was started on levothyroxine and prednisone taper with some improvement in symptoms. Surgery referral for thyroidectomy was done given the rapidity of the enlarging goiter, indeterminate finding on left thyroid FNA, and prior report of compressive symptoms (improved after prednisone taper)

After total thyroidectomy with parathyroid auto transplantation, initial pathology results consistent with Hashimoto's Thyroiditis with fibrous variant, but lots of plasma cells; immunohistochemistry showed presence of light chains. Free kappa, lambda light chains, Kappa to Lambda ratio, urine and serum electrophoresis within normal limits.

But the final pathology results were later added as follows- Immuno histochemical stains for CD10 and CD117 interpreted as negative within the plasma cell component, and kappa and lambda double stain interpreted as polytypic with variable kappa-to-lambda ratios of 4-5:1 to 2-3:1.

IgG4 was positive in > 20 plasma cells per high power field meeting a criterion outlined by Li, et al for IgG4 Hashimoto's Thyroiditis.

A form of Hashimoto's thyroiditis with lymphoplasmacytic sclerosing changes and increased numbers of IgG4-positive plasma cells has recently been reported in the literature. These histopathological features suggest that this subtype of Hashimoto's thyroiditis may be closely related to IgG4-related disease. Therefore, this unique form of IgG4-related Hashimoto's thyroiditis, which is referred to as IgG4 thyroiditis, has its own clinical, serological, and sonographic features that are distinct from those associated with non-IgG4 thyroiditis. It is associated with rapid progression,

subclinical hypothyroidism, higher level of circulating antibodies and diffuse low echogenicity and male predominance.

**Case Study #2**  
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Ms. A is a 42-year-old Nicaraguan woman with autoimmune hepatitis status-post liver transplant four months prior to admission presented with a three week history of fevers and severe anterior neck pain. Home medications included tacrolimus, trimethoprim/sulfamethoxazole, lamivudine for donor +hepatitis B, and ganciclovir for donor +CMV. Symptoms persisted despite one week of empiric broad-spectrum antibiotics; endocrinology was consulted for consideration of thyroiditis.

Physical exam revealed a normotensive female in moderate distress with fever, tachycardia and tachypnea. There was no exophthalmos. The thyroid was exquisitely tender to palpation, diffusely enlarged, smooth, and mobile without distinct nodule. The perithyroidal tissue demonstrated bogginess. There was left cervical lymphadenopathy.

Labs on admission showed leukopenia, normal liver enzymes, TSH 1.68  $\mu$ IU/ml (0.27-4.2  $\mu$ IU/ml), free t4 0.93 ng/dL (0.93-1.7 ng/dL) and T3 77.4 ng/dL (80-200 ng/dL). On US, the thyroid was enlarged and heterogeneous without definite nodules. Noncontrast CT showed normal thyroid, bilateral innumerable lung nodules and an ill-defined hepatic hypodensity.

Extensive infection workup including BAL, liver biopsy, and thyroid FNA was performed; the patient tolerated FNA poorly due to pain such that cytology sample was not obtained from the scant serosanguinous aspirate. Empiric voriconazole was initiated with resolution of fever and neck pain within 48 hours. Repeat CT showed improvement in the lung nodules.

All cultures were negative except for the thyroid specimen, which was positive for *Coccidioides immitis*. Antifungal therapy was changed to oral fluconazole; tacrolimus dose was decreased to achieve about half of the prior target while staying within the therapeutic range. Analysis of serum from the organ donor was consistent with coccidiomycosis infection; the other organ recipients were without infectious signs or symptoms.

One month later she remained clinically well but developed two enlarging, extremely firm, left thyroid masses. In the left upper pole there was a hypoechoic, avascular nodule measuring 1.1 x 1.2 x 1.0cm and in the left mid pole a 2.9 x 1.8 x 2.0cm, hyperechoic, avascular nodule. These yielded insufficient cytology sample from FNA; fungal culture was negative.

What is the etiology of these new masses? What should you do next?

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Due to overall improvement of her clinical status immune reconstitution syndrome was considered as an etiology for these new thyroid masses. After consultation with colleagues in surgery and infectious disease the decision was made to closely monitor these lesions.

Serial imaging of the thyroid revealed evolution into abscesses which paralleled a deterioration in her overall clinical status. She developed a diffuse eruption of subcutaneous skin nodules which

were culture positive for *C. immitis*, developed mastoid osteomyelitis, and the lung lesions progressed in both size and number. Primary hypothyroidism also developed and levothyroxine was initiated.

Parenteral amphotericin B was added to her regimen of oral fluconazole but the thyroid masses enlarged further and began spontaneously draining from a cutaneous fistula with continued development of subcutaneous nodules. Renal function deteriorated as a consequence of the antifungal therapies.

Given the dramatic progression of the thyroid masses in parallel with deterioration of her overall clinical status, the etiology of the thyroid masses was thought to be less consistent with immune reconstitution syndrome and more likely continued coccidiomycosis thyroiditis.

Decision was made to pursue total thyroidectomy to remove a presumed nidus of infection. Surgery was performed six months after initial presentation; the operation was complex as the left thyroid lobe was virtually indistinguishable from surrounding inflammatory tissue in the paratracheal and paraesophageal areas. A cuff of strap muscle was removed in the area of the cutaneous fistula. Recurrent laryngeal nerves and parathyroids were preserved on the right.

Pathology revealed necrotizing granulomatous thyroiditis extending to adjacent subcutis and skin; staining consistent with *Coccidioides*. She remains on antifungal therapies while her clinical status is being closely monitored.