SUBACUTE THYROIDITIS

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- DeQuervain's thyroiditis, commonly known as subacute thyroiditis (SAT) but also termed subacute nonsuppurative thyroiditis, granulomatous, pseudotuberculous, pseudo-giant cell or giant cell thyroiditis, migratory or creeping thyroiditis, and struma granulomatosa.

- This condition, most likely of viral origin, lasts for a week to a few months, with a tendency to recur.

Etiology

- A cause can rarely be established.
- A tendency for the disease to follow upper respiratory tract infections or sore throats has suggested a viral infection.
- The development during the illness of cell-mediated immunity against various thyroid cell particulate fractions or crude antigens appears to be related to the release of these materials during tissue destruction.

- Although the search for a viral cause has usually been unrewarding, a few cases seem to be due to the virus that causes mumps.

- The disease has been reported in association with other viral conditions including measles, influenza, H1N1 influenza, adenovirus infection, infectious mononucleosis, myocarditis, HIV, cat scratch fever, and coxsackie virus.

- Histo-compatibility studies show that 72% of patients with subacute thyroiditis manifest HLA-BW35.

- Familial occurrence of subacute thyroiditis associated with HLA-B35 has been reported.

- **Thus, the susceptibility to subacute thyroiditis is genetically influenced and it has also been suggested that subacute thyroiditis might occur by transmission of viral infection in genetically predisposed individuals**.

INCIDENCE and PREVALENCE

- Subacute thyroiditis is encountered in up to 5% of patients with thyroid illness.

- It had approximately one-eighth the incidence of Graves' disease.

- Although the disease has been described at all ages, it is rare in children.

- Female patients have outnumbered male patients in a ratio of 1.9-6:1, with a preponderance of cases in the third to fifth decades

- It has been noted as a rare cause of hyperthyroidism in pregnancy, reported to occur during the first trimester of pregnancy.

Clinical Manifestations

- Characteristically, the patient has severe pain and extreme tenderness in the thyroid region and difficulty in swallowing.

- A small number of patients has been noted to present with painless or minimally painful

- Transient vocal cord paresis may occur.

- At times, the pain begins in one pole and then spreads rapidly to involve the rest of the gland ("creeping thyroiditis").

- Pain may radiate to the jaw or the ears.

- Malaise, fatigue, myalgia and arthralgia are common.

- A mild to moderate fever is expected, and at times a high, swinging fever with temperatures above 40.0°C.

- The disease may reach its peak within 3 to 4 days and subside and disappear within a week.

- But more typically, a gradual onset extends over 1 to 2 weeks and continues with a fluctuating intensity for 3 to 6 weeks.

- Several recurrences of diminishing intensity extending over many months may be the unhappy fate of the patient.

- The thyroid gland is typically enlarged two or three times the normal size or larger and is tender to palpation, sometimes exquisitely so.

- It is smooth and firm.

- Occasionally the condition may be confined to one lobe.

- Approximately one-half of the patients present during the first weeks of the illness, with symptoms of thyrotoxicosis, including: **nervousness, heat intolerance, palpitations – including ventricular tachycardia, tremulousness, and increased sweating.**

- These symptoms are caused by excessive release of preformed thyroid hormone from the thyroid gland during the acute phase of the inflammatory process.

- Rarely thyroid storm due to subacute thyroiditis have been described and adverse cardiac outcomes have been reported even in individuals without preexisting cardiac history or lesions.

- As the disease process subsides, transient hypothyroidism occurs in about one-quarter of the patients.

- Ultimately thyroid function returns to normal and permanent hypothyroidism occurs in less than 10 percent of the cases.

- Occasionally the condition may be painless and present as fever of unknown origin or associated with other findings and mimicking conditions such as temporal arteritis.

- Liver function test abnormalities are found in half the patients and return to normal in a few months.

Diagnosis

- Laboratory examination may disclose a moderate leukocytosis.
- A curious and striking elevation of the erythrocyte sedimentation rate, at times above 100 mm/hr, or an elevated level of serum C-reactive protein is a useful diagnostic clue.
- Mild anemia and hyperglobulinemia may be present.

- Most helpful is the characteristic combination of elevated erythrocyte sedimentation rate, high serum T4, T3, and TG concentrations in the presence of low thyroidal RAIU, TSH, and an absent or low titer of circulating TPO and TG antibodies.

- While the estimation of thyrotropin receptor antibodies (TRAb) in a thyrotoxic patient may be clinically useful in identifying Graves' disease there have been reports of positive TRAb in patients with subacute thyroiditis although the frequency of this finding is low.

- **99m-Tc-pertechnetate** scintigraphy typically reveals little to no uptake and thus no visualization of the SAT process.

- Further imaging studies have shown diffuse increased uptake of **Tc-99m sestamibi and Tc-99m tetrofosmin** in the thyroid region of patients in the acute phase (thyrotoxic) of subacute thyroiditis suggesting an ability of both agents to detect the inflammatory process associated with the disease.

- Standard **ultrasonographic** images are characterized by hypoechoic appearance of the affected tissue the volume of which correlates with the severity of clinical discomfort.

- The application of newer technologies such as **sonoelastography** has the capacity to demonstrate markedly decreased elasticity (enhanced stiffness) in SAT lesions.

- Subacute thyroiditis with thyrotoxicosis may also be distinguished from Graves' hyperthyroidism by using **T1- and T2- diffusion weighted magnetic resonance imaging and as an intense area of uptake on (18) F-FDG PET/CT.**

- **Fine needle aspiration biopsy** is often diagnostic although patients are often alarmed at the prospect of this test due to the pain in the thyroid.

- However FNA may be helpful in ruling out malignancy and the infection associated with localized, painful lesions of AST.

- During the initial phase of the disease, the RAIU is depressed or entirely absent and the concentrations of serum T4 and T3 are often elevated.

- Due to the concomitant release of non-hydrolyzed iodoproteins from the inflamed tissue, the serum thyroglobulin level is also high.

- During this phase the serum TSH level is low.

- Analysis of the TSH suppression seen in thyrotoxic patients indicates that patients with SAT may demonstrate suppressed but detectable levels of TSH while those with Graves' disease or silent thyroiditis have undetectable TSH values.

- The TSH response to TRH is suppressed due to the high levels of circulating thyroid hormone.
- Administration of TSH will fail to produce a normal increase in RAIU.
- Evidently, thyroid cell damage reduces the ability of the gland to respond to TSH.
- As the process subsides, the serum T4, T3, and TG levels decline, but the serum TSH level remains suppressed.

- Later, during the recovery phase, the RAIU becomes elevated with the resumption of the ability of the thyroid gland to concentrate iodide.

- The serum T4 concentration may fall below normal; the TSH level may become elevated.

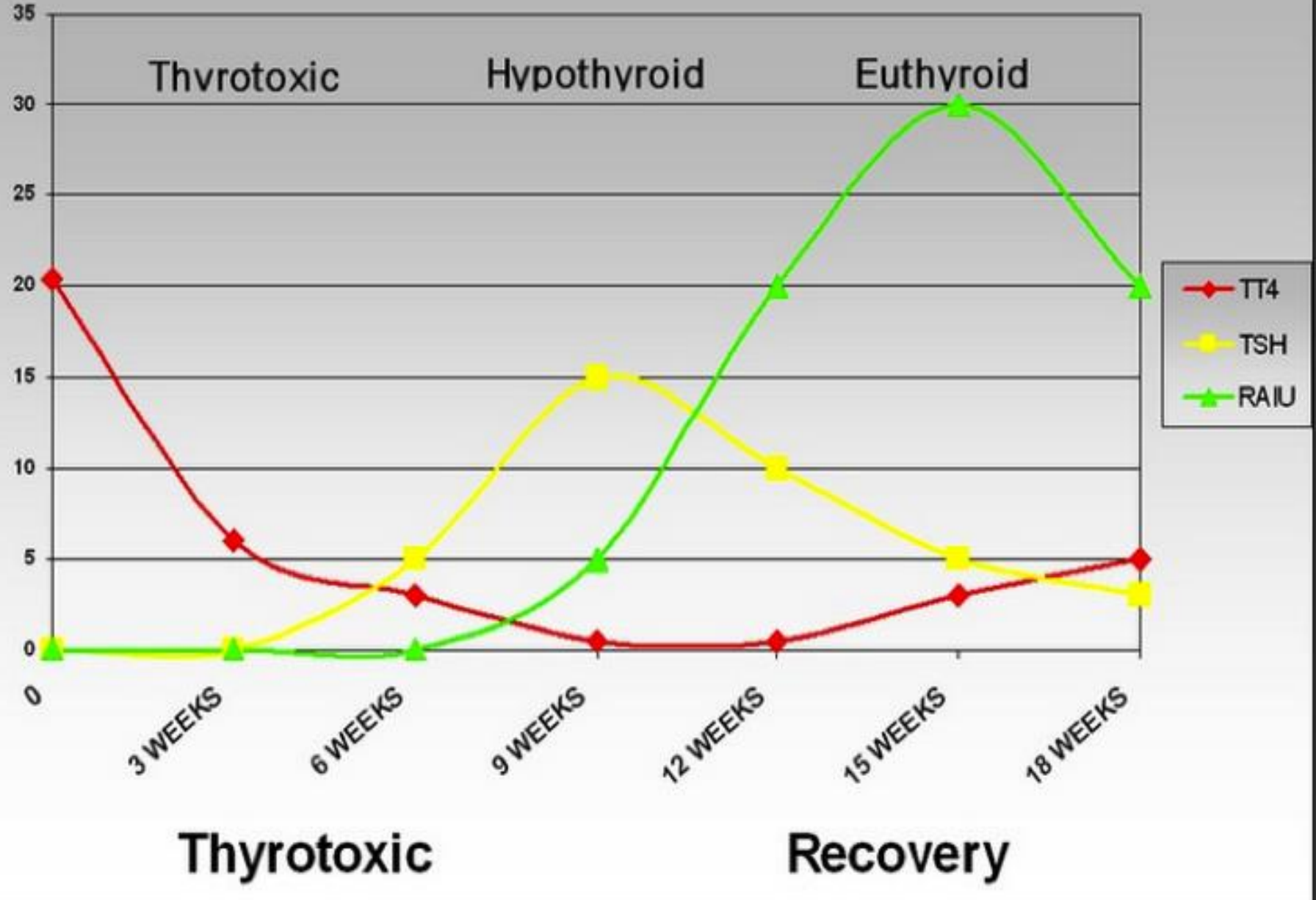
- Usually after several weeks or months, all the parameters of thyroid function return to normal.

- Restoration of iodine stores appears to be much slower and may take more than a year after the complete clinical remission.

- In about 2% of patients subacute thyroiditis may trigger auto-reactive B cells to produce TSH receptor antibodies, resulting in TSH antibody associated thyroid dysfunction in some patients.

- This finding may be a potential explanation of the apparent occurrence of Graves' disease following an episode of SAT.

Subacute Thyroiditis



Differential Diagnosis

- The patient presenting with painful neck symptoms is frequently empirically treated with antibiotics with minimal evaluation in general practice only later to be found to have thyroid related disease.
- With an acutely enlarged, tender thyroid, an RAIU near zero, and elevated serum T4, T3, thyroglobulin concentrations and ESR, the diagnosis is almost certain.
- Circulating thyroid autoantibodies are absent or the titer is low.

- Among the diagnostic alternatives, the uncommon presentation of thyrotoxicosis in infectious thyroiditis must be considered.

- Rarely a fever of unknown origin may suggest temporal arteritis but is actually due to subacute thyroiditis.

- Additionally, because of the radiation of painful thyroid into the jaw area the presence of dental pain may be confused with SAT.

- **The thyroid in Hashimoto's thyroiditis (HT)** may be slightly tender and painful, but this event is rare, and the typical disturbances in iodine metabolism and erythrocyte sedimentation rate are rarely found.

- **Markers of inflammation such as CRP as measured in the saliva are normal in HT when compared to controls but are grossly elevated in the patient with SAT.**

- Standard thyroid **ultrasonography** may appear similar with hypoechoic tissue in both HT and SAT but by sonoelastography the SAT gland is profoundly stiffer than HT tissue which is somewhat stiffer than normal controls.

- The **radio nuclide thyroid uptake** and scanning in HT is variable with elevated, depressed or normal results reported.

- **Hemorrhage into a cyst in a nodular thyroid gland** may be confused with subacute thyroiditis although the condition may be associated with an autonomously functioning nodule.

- Hemorrhage is usually more sudden and transient, a fluctuant mass may be found in the involved region, and the erythrocyte sedimentation rate is normal.

- Occasionally, SAT mimics hyperthyroidism in a patient whose RAIU is suppressed by the administration of exogenous iodine.

- This event occurs particularly in **transient thyrotoxicosis induced by iodine.**

- The sudden onset of subacute thyroiditis, the presence of toxic symptoms without the typical signs of long-term hyperthyroidism, the tender gland, the constitutional symptoms, and the high erythrocyte sedimentation rate are helpful in making the differentiation.

- The single disease entity that is probably most difficult to differentiate from SAT is a variant of **lymphocytic thyroiditis**.
- This condition is unrelated to iodine ingestion and most likely is a variant of autoimmune thyroiditis.
- The patient presents with goiter, mild thyrotoxicosis, and a low RAIU. The course of the disease is indistinguishable from that of SAT and proceeds from a thyrotoxic phase through a hypothyroid phase to spontaneous remission with normalization of thyroid function.

- The goiter is however, typically painless and there are no associated systemic symptoms.
- This condition has been formerly confused with subacute (de Quervain's) thyroiditis, which likely has led to the descriptive terms of silent, painless, or atypical subacute thyroiditis to refer to this entity.
- The most helpful distinguishing features, short of histologic examination of biopsy material, are the absence of pain and a normal erythrocyte sedimentation rate.

Therapy

- In some patients with SAT, no treatment is required.

- However, for many, some form of analgesic therapy is required to treat the symptoms of the disease until it resolves.

- At times, this relief of symptoms can be achieved with **non-steroidal anti-inflammatory agents or aspirin**.

- However, if this fails, as it often does when the symptoms are severe, and after acute suppurative thyroiditis had been definitively ruled out, **prednisone** administration should be employed.

- Large doses promptly relieve the symptoms through non-specific anti-inflammatory effects.

- Treatment is generally begun with a single daily dose of 40 mg prednisone.

- However, a dose as low as 15 mg of Prednisolone has been shown to be as effective.

- After one week of this treatment, the dosage is tapered over a period of 6 weeks or so.

- The relief of the tenderness in the neck is so dramatic as to be virtually diagnostic of subacute thyroiditis.

- A newer therapeutic approach with local injection of lidocaine and dexamethasone through an insulin syringe has been reported to alleviate symptoms earlier than standard treatment with prednisone.

- Alternatively oral cholecystographic agents (such as sodium ipodate or sodium iopanoate) may be used safely and effectively for the management of the thyrotoxicosis in these patients even when they have relapsed after corticosteroid therapy.

- The recurrence rate of SAT after cessation of prednisolone therapy is about 20% but no difference has been found in routine laboratory data between recurrent and non-recurrent groups of patients.

- Levothyroxine administration has been touted as useful in situations where the patient is not already hyperthyroid due to the release of thyroidal contents into the circulation.

- It is also of course necessary to administer thyroid hormones, at least transiently, if the patient enters a phase of symptomatic hypothyroidism subsequent to the acute inflammation.

- Levothyroxine should only be administered for up to a year, otherwise, the return of thyroid function to normal, which presumably is facilitated by TSH, may be prevented or delayed.

- Surgical intervention is not the primary treatment for SAT.

- Because of the possibility of associated papillary cancer further cytological examination should be performed in patients presenting with a persistent hypoechoic area larger than 1 cm by ultrasonography.

Prognosis

- In 90% or more of patients, there is a complete and spontaneous recovery and a return to normal thyroid function.
- SAT may recur in up to 2.8 to 4 % of population with subacute thyroiditis.
- Up to 10% of the patients may become hypothyroid and require permanent replacement with levothyroxine.

- However, permanent hypothyroidism is significantly less common in SAT compared to the outcome noted in amiodarone induced thyrotoxicosis type 2 (destructive thyroiditis).

- It is of interest that elevated levels of serum thyroglobulin may persist well over a year after the initial diagnosis, indicating that disordered follicular architecture and/or low grade inflammation can persist for a relatively long period.

ACUTE AND SUBACUTE, AND RIEDEL'S THYROIDITIS

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Thank You