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## SUBACUTE THYROIDITIS

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### CLINICAL RECOGNITION

Subacute thyroiditis (SAT) is an inflammatory condition of the thyroid with characteristic presentations and clinical course. Patients with the classic, painful (DeQuervain's; Granulomatous) thyroiditis, (PFSAT) typically present with painful swelling of the thyroid. Transient vocal cord paresis may occur. At times, the pain begins and may be confined to the one lobe, but usually 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 fever of 104°F (40.0°C) may occur. The disease process may reach its peak within 3 to 4 days and subside and disappear within a week, but more typically, onset extends over 1 to 2 weeks and continues with fluctuating intensity for 3 to 6 weeks. The thyroid gland is typically enlarged, smooth, firm and tender to palpation, sometimes exquisitely so. Approximately one-half of the patients present during the first weeks of the illness, with symptoms of thyrotoxicosis. Subsequently patients often experience hypothyroidism before returning to normal (see figure 1). This painful condition lasts for a week to a few months, usually demonstrates a very high erythrocyte

sedimentation rate (ESR), elevated C- reactive protein (CRP) levels, and has a tendency to recur.

Painless (silent, autoimmune) subacute thyroiditis (PLSAT) occurs spontaneously or following pregnancy when it is referred to as postpartum thyroiditis [PPT]. Autoimmune thyroiditis is histologically similar to Hashimoto's thyroiditis and occurs following 3.9-10% of pregnancies. The combination of thyroid enlargement usually without discomfort and positive anti-thyroid antibodies, associated with typical thyroid function test abnormalities (see figure 1), over a 9-12 month course should alert the clinician to the presence of PLSAT.

### PATHOPHYSIOLOGY

A tendency for the painful form of the disease to follow upper respiratory tract infections or sore throats has suggested a viral infection. An autoimmune reaction is possible as patients with PFSAT often manifest HLA-Bw35 and those with PLSAT are frequently TPO or TG-ab positive. In both forms, clinical thyroid symptoms result from either the initial release of thyroid hormone from the inflamed tissue during the thyrotoxic phase or the lack of circulating thyroid hormones in the hypothyroid phase (See figure 1). Medications associated with SAT are summarized in table 4.

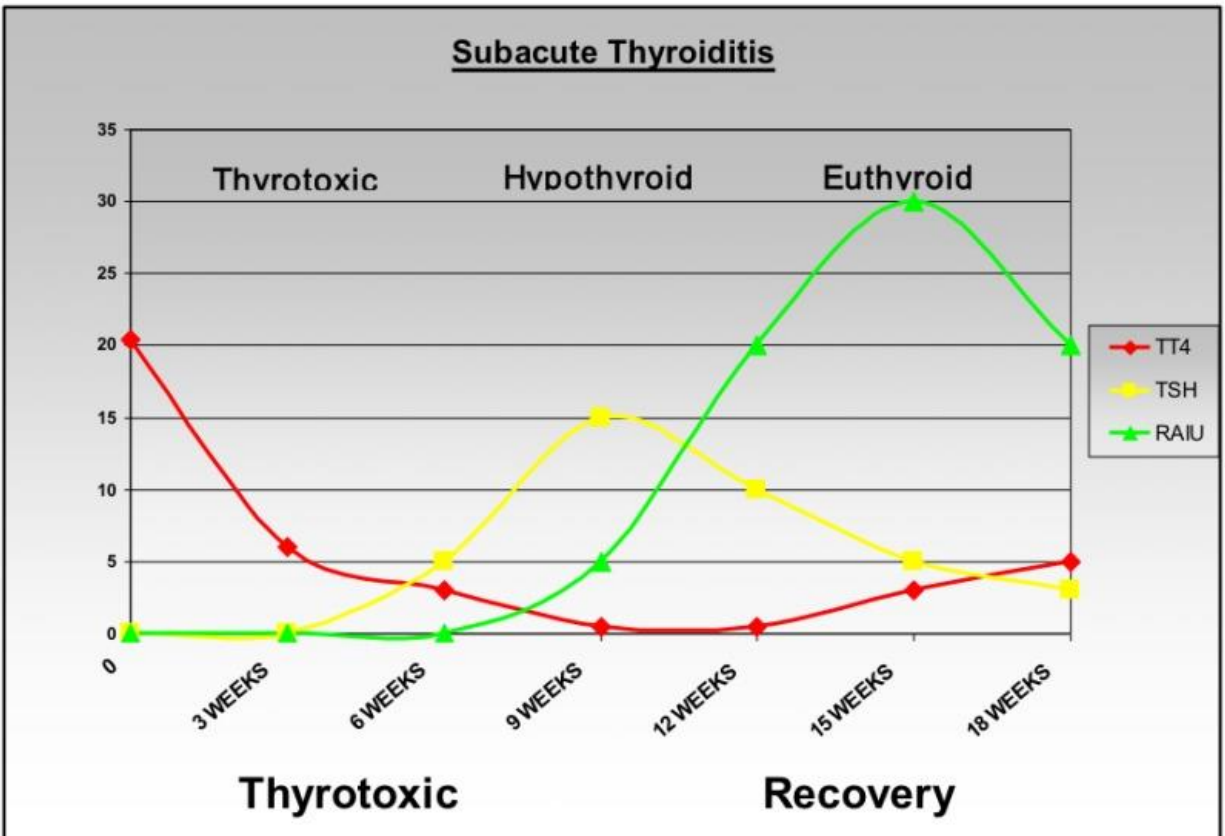


Figure 1. Time Course of Subacute Thyroiditis

### DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Subacute thyroiditis is a diagnosis made clinically. Anterior neck pain, preceded by an upper respiratory inflammation, alerts the clinician to the classic PFSAT. Differential diagnostic considerations include acute (suppurative, thyroid abscess) thyroiditis (see table 1), which is usually a painful nodular enlargement of the thyroid or unusual presentations of Graves' or nodular thyroid disease (see table 2 below) with pain generated by capsular stretching.

Thyroid function tests (see table 3) during the painful (initial) phase of SAT often reveal a suppressed TSH and elevation of total T4 and T3 levels consistent with the thyrotoxic state. T3 (ng/dl) to T4 (ug/dl) ratio is less than 20 in all forms of SAT. ESR is almost always greater than 50 and WBC counts and CRP levels are

usually elevated in PFSAT. PLSAT (including PPT) is typically associated with the presence of anti-thyroid peroxidase (TPO-ab) and thyroglobulin (Tg-ab) antibodies, both of which are usually absent or present only in low titers in PFSAT. Thyrotropin receptor antibodies (TRAb) are usually positive in Graves' disease and absent or low level in patients with PFSAT as well as PPT.

Radioactive iodine uptake and scan typically reveals a low RAIU and poor visualization of the thyroid in PFSAT and PLSAT whereas significant uptake is expected in Graves' disease (GD) or toxic nodular goiters (TNG). PLSAT must be differentiated from other forms of low uptake thyrotoxicosis (see Table 2). Iatrogenic thyrotoxicosis (factitious [I-thyroxine (LT4), I-triiodothyronine (LT3) or T4/T3 combination] results in a suppressed thyroglobulin (TG) level. Ectopic

thyroid hormone production in a Struma Ovarii or functional metastatic thyroid cancer can be detected with total body scanning. Iodine contamination after a contrast enhanced CT, obliterates the RAIU and obscures the presence of the more frequently encountered Graves' disease or a toxic multinodular goiter. A recent CT scan will frequently alert the clinician to this artifact. Urine iodine measurement can quantify the degree of iodine contamination present.

Thyroid ultrasound typically shows a heterogeneously hypoechoic pattern and has a suppressed vascular pattern in SAT while patients with Graves' disease demonstrate hyper-vascularity. The presence of thyroid nodules supports the presence of a toxic nodular goiter. Localized PFSAT, can be suggestive of thyroid cancer. Usually the pain, elevated erythrocyte sedimentation rate and leukocytosis, and clinical remission or spread to other parts of the gland make clinical differentiation possible but may require a fine needle aspiration for definitive diagnosis.

**Table 1. Features Useful in Differentiating Acute Suppurative Thyroiditis (AST) and Subacute Thyroiditis (SAT)**

Characteristic	AST	SAT
Prior URI	88%	17%
Fever	100%	54%
Symptoms of Hyperthyroidism	Uncommon	47%
Sore throat	90%	36%
Painful thyroid swelling	100%	77%
Left side affected	85%	not specific
Migrating tenderness	Possible	27%
Erythema of skin	83%	not usually
Elevated WBC count	57%	25-50%
Elevated ESR	100%	85%
Abnormal TFTs	5-10%	60%
Enzymes- Alk-phos.↑, AST/ALT ↑	Rare	common
FNA Purulent, bacteria or fungi present	~100%	0
Lymphocytes, macrophages, PNMs, giant cells	0	~100%
<sup>123</sup> I uptake low	Rarely	~100%
Abnormal thyroid scan	92%	—
Scan / US helpful in D/D	75%	Non-specific
Gallium scan positive	~100%	~100%
Barium swallow = fistula	Common	0
CT scan useful	Rarely	not useful
Clinical response to glucocorticoid treatment	Transient	100%
Incision/drainage required	85%	No
Recurrence following operative drainage	16%	No
Pyriform sinus fistula discovered	96%	No

URI= Upper Respiratory Infection, WBC= white blood cell count, ESR= Erythrocyte Sedimentation Rate, TFT's= Thyroid function tests, Alk-Phos= Alkaline Phosphatase, AST= Aspartate Aminotransferase, ALT= Alanine Aminotransferase, FNA= Fine needle aspiration, US= Ultrasound examination, ↑= elevated

**Table 2. Differential Diagnosis of Thyrotoxic Patients Based on Radioactive Iodine Uptake (RAIU)**

Normal to ↑ 123-I RAIU	Near absent 123-I RAIU
Graves' disease	Painless (silent) thyroiditis
Toxic multinodular goiter	Amiodarone-induced thyroiditis
Toxic solitary nodule	Subacute (painful) thyroiditis
Trophoblastic (hCG mediated) disease	Iatrogenic or factitious thyrotoxicosis
TSH-producing pituitary tumor	Ectopic tissue (Struma Ovarii, functional cancer)
Thyroid hormone resistance	Acute thyroiditis

**Table 3. Differential Diagnostic Considerations in the Thyrotoxic Patient (Typical findings in each disease)**

	PFSAT	PLSAT	PPT	Graves'
Neck Pain	Yes	No	No	No
Recent URI	Yes	No	No	No
Systemic symptoms	Yes	No	No	No
Recent Pregnancy	No	No	Yes	No
Thyroid symptoms	Yes	Yes	Yes	Yes
ESR	Elevated	Normal	Normal	Normal
CRP	Elevated	Normal	Normal	Normal
TSH	↑/ ↓/ NI	↑/ ↓/ NI	↑/ ↓/ NI	Suppressed
FT4	↑/ ↓/ NI	↑/ ↓/ NI	↑/ ↓/ NI	NI/↑
TT3	↑/ ↓/ NI	↑/ ↓/ NI	↑/ ↓/ NI	NI/ ↑
T3/T4	< 20	< 20	< 20	> 20
Thyroglobulin	Elevated	Elevated	Elevated	Elevated
TPO-ab	Negative	+/-, Pos	+/-, Pos	+/-, Pos
Tg-ab	Negative	+/-, Pos	+/-, Pos	+/-, Pos
TSHR-ab	Negative	Neg	Neg	Pos
RAIU/Scan	Low/ Not visible	Low/ Not visible	Low/ Not visible	High/ diffuse
US Echogenicity	Hypo-echoic	Hypo-echoic	Hypo-echoic	Hypo-echoic
Vascularity	Decreased	Decreased	Decreased	Increased

PFSAT= painful subacute thyroiditis; PLSAT= painless subacute thyroiditis; PPT= postpartum thyroiditis

**Table 4. Causes of Drug Associated Thyrotoxicosis**

<b>Drug</b>	<b>Mechanism</b>	<b>Timing</b>	<b>Therapy</b>
Amiodarone	Iodine (AIT 1)	months to years	Supportive, ATDs, Perchlorate, Surgery
Amiodarone	Thyroiditis (AIT 2)	Often > 1 year	Supportive care, Surgery, Prednisone
Lithium	Thyroiditis	Often > 1 year	ATDs, Supportive
Interferon- $\alpha$	Thyroiditis or Graves'	Months	Supportive, ATDs, and /or 131-I (Graves' only)
Interleukin-2	Thyroiditis or Graves'	Months	Supportive, ATDs, and /or 131-I (Graves' only)
Contrast (I)	Thyroid autonomy	Weeks to months	ATDs
131-I Ablation	Destructive thyroiditis	1-4 weeks	Supportive, prednisone
131-I Rx of TMNG	Graves' disease	3-6 months	131-I, surgery, ATDs
Check Point Inhibitors	Thyroiditis or autoimmune	Weeks to months	Supportive, 131-I, surgery, ATDs
Tyrosine Kinase Inhibitors	Thyroiditis	Weeks to months	Supportive

ATD= Anti thyroid drugs, TMNG= Toxic Multinodular Goiter

## **THERAPY**

In some patients, no treatment is required. For many, analgesic therapy for relief of pain can be achieved with non-steroidal anti-inflammatory agents. If this fails, prednisone administration should be employed with daily doses of 20-40 mg prednisone. After one to 2 weeks of this treatment, the dosage is tapered over a period of 6 weeks. Most patients have no recrudescence of symptoms, but occasionally this does occur and the dose must be increased again. The recurrence rate of painful subacute thyroiditis after cessation of prednisone therapy is about 20%. Beta blocking agents are usually administered for relief of thyrotoxic symptoms in the initial stage of SAT. Antithyroid drugs have no role in the management of established SAT as the excess thyroid hormone levels result from release of preformed thyroxine and triiodothyronine from inflamed tissue. Levothyroxine administration may be useful, at least transiently, if the patient enters a phase of hypothyroidism. Surgical intervention is not the primary treatment for subacute

thyroiditis but is safe and with low morbidity, if necessary, because of the possibility of associated papillary cancer based on cytological examination.

## **FOLLOW-UP**

In 90% or more of patients with classic painful subacute thyroiditis, there is a complete and spontaneous recovery and a return to normal thyroid function. However, the thyroid glands of patients with subacute thyroiditis may exhibit irregular scarring between islands of residual functioning parenchyma. Up to 10% of the patients may become hypothyroid and require permanent replacement with levothyroxine. Rates of permanent hypothyroidism after antibody positive PLSAT and especially PPT are significantly higher.

## **GUIDELINES**

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