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### Title

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## Subacute Thyroiditis

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#### Introduction

Subacute thyroiditis or subacute granulomatous thyroiditis, also known as de Quervain's thyroiditis, is a condition in which thyroid function progresses through all levels, starting with a period of hyperthyroidism, followed by a period of short-lived hypothyroidism, and finally returning to a state of normal thyroid function. The incidence of subacute thyroiditis is 12.1 cases per 100,000/year and occurs more often in women.<sup>1,2</sup> However in both men and women, the peak incidence was in the fifth decade of life.<sup>3</sup> Anterior neck pain is the most common presenting symptom, however other symptoms such as fever, severe thyroid gland tenderness and enlargement can also occur.<sup>1</sup> An upper respiratory infection often precedes the onset of symptoms. Hyperthyroidism is usually present at the onset of symptoms and subsequently TSH is often suppressed with a corresponding elevation in free thyroxine (FT4). We present a 48 year old woman who complained of symptoms suggestive of subacute thyroiditis.

#### **Case Presentation**

The patient is a 48-year-old female with past medical history of chronic variable immune deficiency, asthma, and chronic rhinosinusitis who presented to her Internal Medicine Primary Care Physician with a six day history of fever to 100.8 F, odynophagia, and sore throat. Rapid strep A returned positive and she was started on Amoxicillin. However 72 hours later she continued to have fevers and her antibiotic regimen was changed to Augmentin. 72 hours after starting Augmentin she reported worsening fevers with peak temperatures at 102 F, and was sent to ER and admitted given her persistent fevers and history of CVID. ID was consulted and antibiotics were changed to Ceftriaxone, however fevers had persisted. She underwent extensive evaluation including numerous repeat blood cultures, UA, respiratory viral panel, influenza, CMV, Cryptococcus, all which returned unremarkable. The only abnormal labs found were mild leukocytosis of 11, which resolved by time of discharge, and persistently elevated ESR which at its peak was 69. Imaging included CT neck, chest, abdomen, and pelvis, all also returned unremarkable. She was discharged 4 days after admission off all antibiotics, with ongoing fevers.

After discharge she continued to have daily fevers, and her symptoms progressed to diarrhea, malaise, poor appetite, and worsening neck pain. Her worsening symptoms prompted her to return to the ER now 4 weeks after her initial onset of

symptoms. She was re-admitted with fever of 103.1F. A Fever of unknown origin work up was initiated. Admission ESR returned elevated, at > 125, TSH was <0.02, FT4 was 6.2. Endocrinology obtained MRI of the thyroid which revealed diffuse thyroiditis. She was started on ibuprofen 800mg PO TID with aggressive IVF hydration with mild improvement in her symptoms. She was discharged to follow up with endocrinology and her PCP. The patient was seen by her Primary Care 3 days later with tachycardic to 110, febrile to 101 F, complaining of fatigue and ongoing neck pain. Ibuprofen was discontinued and she was started on Prednisone 40mg PO daily as well as Atenolol 25mg PO daily and instructed to follow up with endocrinology. At endocrine follow up, TPO and thyroglobulin antibodies were negative. She had improved on steroids and a steroid taper was established. The patient had complete resolution of symptoms with return to normal thyroid function within 3 months of onset of symptoms.

#### Discussion

Subacute thyroiditis is a transient, self-limited inflammatory disease of the thyroid and the most common cause of painful thyroiditis.<sup>3,4</sup> The etiology is unclear, viral infections are likely the cause, with seasonal clusters in the summer and early autumn months, with elevation in viral antibodies and onset of symptoms frequently preceded by an upper respiratory infection.<sup>4</sup> A genetic susceptibility has also been suggested, given that two thirds of all patients with subacute thyroiditis also have HLA Bw35.<sup>5</sup>

Subacute thyroiditis is most commonly characterized by the following clinical findings: unilateral neck pain, fever, and thyrotoxicosis symptoms including palpitations, sweating, and weight loss.<sup>4</sup> Other reported symptoms include development of a goiter, fatigue, anxiety and depression, heat intolerance, tremors, insomnia, hoarseness of voice, loss of hair, ear and face pain, and shortness of breath.<sup>3</sup> Laboratory findings include elevation of CRP and ESR, elevation of free thyroxine (FT4), and suppression of serum thyroid stimulating hormone (TSH). Other findings include decreased radioactive uptake to the thyroid gland in the acute phase and negative anti-thyroid autoantibodies. Liver function tests are also often abnormal during the hyperthyroid phase, with elevations in LFTs returning to normal within a few weeks.<sup>6</sup> Ultrasound imaging show hypoechoic lesion at the painful portion of the thyroid gland. The diagnosis of subacute thyroiditis can be made with

clinical observation in the majority of cases when patients present with a diffuse goiter, anterior neck pain that is ascending to jaw and ear, and a tender thyroid gland. If the diagnosis is unclear, laboratory findings will confirm the diagnosis in the acute phase when hyperthyroidism is detected with a suppressed TSH. The differential diagnosis of subacute thyroiditis, includes: acute exacerbation of chronic thyroiditis, bleeding into a thyroid cyst, acute suppurative thyroiditis, and thyroid anaplastic carcinoma.<sup>7</sup>

After the diagnosis has been made, treatment is focused on symptom management, namely relieving pain and controlling hyperthyroid symptoms. Given the self-limiting nature of this condition, most patients do not require long-term treatment. Short term treatment with beta-blockers, NSAIDS and finally steroids is considered. There is no consensus on initial therapy, but the mainstay of initial treatment is high dose NSAIDS such as Naproxen 500mg to 1000mg PO BID, Ibuprofen 600mg to 800mg PO TID or Aspirin 650mg PO Q6hrs.<sup>8</sup> If pain relief and systemic symptoms like fever, palpitations, and fatigue persist after 2-3 days of NSAIDs, steroids are prescribed. Prednisone 40mg is the typical starting dose, this dose is continued until pain relief is achieved, then Prednisone is tapered by 5mg per week over an eight week period.<sup>7</sup>

Hyperthyroid symptoms such as palpitations and anxiety, respond to beta blockers like propranolol ER 80mg daily or Atenolol 25 to 50mg PO daily. Methimazole and PTH have no role in the treatment of subacute thyroiditis as it is not a condition caused by the synthesis of excess thyroid hormone. Thyroid function should be tested every 2-4 weeks to monitor for transition from a hyperthyroid state to a hypothyroid state.

Hypothyroidism associated with subacute thyroiditis does not require treatment unless the TSH is greater than 10, or patients have significant symptoms related to hypothyroidism. Levothyroxine 50mcg to 100mcg is initially used, and may be continued for six to eight weeks and then discontinued to reassess for return to normal thyroid function.

In summary, subacute thyroiditis represents a self-limited, inflammation, of the thyroid which patients presenting with anterior neck pain, tender goiter, +/- symptoms associated with hyperthyroidism. Patients with subacute thyroiditis ultimately require little more than pain management with NSAIDs and close monitoring of thyroid function as it fluctuates through hyperthyroidism, to hypothyroidism, to euthyroidism. For cases where patients do not respond to NSAIDs, prednisone tapers are effective, and levothyroxine can be used for persistent, symptomatic or more severe hypothyroid states. Because it is usually preceded by an URI, subacute thyroiditis can be mistaken for progression of an upper respiratory infection. This condition should be considered in the differential for any patient that presents with anterior neck pain and tenderness.

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