Title

Subacute Thyroiditis: A Common Endocrine Cause of Fever of Unknown Origin

Journal

Proceedings of UCLA Health, 22(1)

Authors

Chhean, Forster

Oxman, Rachael

Publication Date

2018-08-28

CLINICAL VIGNETTE

Subacute Thyroiditis: A Common Endocrine Cause of Fever of Unknown Origin

Forster Chhean, MD and Rachael Oxman, MD, MPH

Case

A 48-year-old man with no significant past medical history presented to the emergency department with 5 weeks of persistent fever, sore throat, jaw pain, and headache. Prior to presentation, he had seen multiple other medical providers. After the first two weeks of symptoms, he was seen by dentistry without any abnormal dental findings. He was then seen by a primary care provider, tested positive for *Group A Streptococcus* on rapid antigen detection test, and completed five days of amoxicillin with no improvement. He was subsequently admitted to an outside hospital. Review of outside hospital records revealed the following: two negative blood cultures; transthoracic echocardiogram with no evidence of vegetation or valvular disease; and computed tomography (CT) of the chest, abdomen, and pelvis with no evidence of malignancy. He was ultimately discharged on doxycycline without a definitive diagnosis. He continued to experience the neck and jaw pain with daily fevers and night sweats and presented to the emergency department for further evaluation. On admission, he noted that his daughter had an upper respiratory infection a week prior to the start of his symptoms. Extensive travel history, exposure history, and social history were otherwise unrevealing.

On admission, vital signs were notable for temperature 39.3º C, heart rate 107 bpm, respiratory rate 25, blood pressure 143/77 mm Hg, oxygen saturation 97% on room air. He was well-appearing and had tender left cervical lymphadenopathy. Oropharynx was clear with moist mucous membranes. His heart rate was rapid without murmurs, rubs, or gallops. His lungs were clear. His abdomen was benign with no hepatosplenomegaly. He had no rash or skin breakdown. He had negative Kernig and Brudzinski signs and no nuchal rigidity.

Emergency department laboratory studies showed an elevated white blood cell count 12.5 $x10^3$/uL with 83% neutrophils, mildly low hemoglobin 11.9 g/dL, normal MCV 84 fL, normal basic metabolic panel, elevated erythrocyte sedimentation rate 87 mm/hr, elevated C-reactive protein 7.2 mg/dL, negative infectious mononucleosis antibody, and bland urinalysis. Blood and fungal cultures, HIV-1/2 Ag/Ab screen, MTB-Quantiferon ELISA, acute hepatitis panel were negative. Chest x-ray showed clear lungs and a normal cardiomediastinal silhouette. Peripheral smear was not suggestive of a hematologic malignancy.

Given his neck pain, a CT scan of the neck was ordered and showed a heterogenous, somewhat edematous thyroid suggestive of thyroiditis. Thyroid studies were then performed, revealing a suppressed thyroid-stimulating hormone (TSH) 0.05 mcIU/mL, elevated free T4 index 11.8, normal total T4 9.4 mcg/dL, and normal total T3 168 ng/dL. Further testing showed elevated thyroglobulin 161 ng/mL, mildly positive thyroglobulin antibody 4.4 IU/mL, normal thyroid peroxidase antibody level 11.5 IU/mL and normal thyroid stimulating immunoglobulin < 89. Thyroid ultrasound showed an enlarged thyroid with multiple isoechoic thyroid nodules and normal Doppler. Thyroid uptake scan was deferred given recent iodinated contrast exposure.

Patient denied any pre-existing history of thyroid disease, recent exposure to steroid medications, amiodarone or supplements with high iodine content and/or thyroid hormone content. He was diagnosed with subacute thyroiditis and treated with prednisone and ibuprofen. His fevers defervesced and his symptoms improved with the above treatment.

Discussion

Fever of unknown origin (FUO), as classically defined by Petersdorf and Beeson, has 3 criteria: (1) temperature greater than 38.3 degrees Celsius on multiple occasions; (2) fever lasting more than 3 weeks; and (3) diagnostic uncertainty after one week of inpatient investigation.[1] FUOs are most commonly caused by infectious, malignant, and rheumatologic diseases. While subacute thyroiditis is a less common etiology, it is the most common endocrinologic cause of FUO and should be considered in diagnostic evaluation.[2]

Subacute thyroiditis (also known as painful thyroiditis, de Quervain's thyroiditis, giant cell thyroiditis, and subacute granulomatous thyroiditis) is a self-limited inflammatory disorder that frequently follows an upper respiratory infection. The viral infection or post-viral inflammatory process disrupts thyroid follicles leading to the unregulated release of thyroxine (T4) and triiodothyronine (T3). Subacute thyroiditis is characterized by neck discomfort or pain; a tender, enlarged thyroid; and initial hyperthyroidism that can cause fatigue, fever, palpitations, weight loss, and/or increased diaphoresis. The pain of subacute thyroiditis may be localized to the thyroid region or radiate to the throat, jaw, or ears.[3] As thyroglobulin stores are depleted, the hyperthyroid phase transitions into a period of

euthyroidism and then hypothyroidism. The majority of people with subacute thyroiditis will regain normal thyroid function in 6-12 months once the thyroid follicles regenerate; 5-15% will have persistent hypothyroidism.[3-5] Subacute thyroiditis will recur in 1.6-10%. [5-7]

Laboratory studies typically show evidence of hyperthyroidism (low TSH; elevated free T4 and T3) in the early stages of the disease. Thyroglobulin levels are elevated in the majority (92%) of cases and thyroglobulin antibodies may also be positive.[8] ESR and CRP elevations are also commonly seen. Radioiodine uptake scan will show low uptake in the hyperthyroid phase (in contrast to other hypothyroid etiologies, e.g., Graves disease and toxic nodule, which have increased uptake). On ultrasound, the thyroid is hypoechogenic but may be either normal or enlarged in size. Doppler sonography will often show decreased flow while hyperthyroid. Fine-needle aspiration may be helpful when the diagnosis is uncertain. Pathology can show multinuclear giant cells, macrophages, neutrophils, and lymphocytes; epithelioid cell granulomas; and degenerated follicular epithelial cells.[9]

Treatment aims to alleviate pain and symptoms of hyperthyroidism. Pain is treated with nonsteroidal anti-inflammatory drugs, aspirin, or, if severe, steroids. Bothersome hyperthyroid symptoms may be treated with beta-blockers such as propranolol, which inhibits the peripheral conversion of T4 to T3. Treatment of hypothyroidism with levothyroxine is infrequently required but may be considered in people with TSH greater than 10 or those who are significantly symptomatic. Thyroid function tests should be monitored every 2 to 8 weeks.

REFERENCES

1. **Petersdorf RG, Beeson PB**. Fever of unexplained origin: report on 100 cases. *Medicine (Baltimore)*. 1961 Feb;40:1-30. PubMed PMID: 13734791.
2. **Cunha BA, Chak A, Strollo S**. Fever of unknown origin (FUO): de Quervain's subacute thyroiditis with highly elevated ferritin levels mimicking temporal arteritis (TA). *Heart Lung*. 2010 Jan-Feb;39(1):73-7. doi:10.1016/j.hrtlng.2009.06.006. Epub 2009 Sep 3. PubMed PMID: 20109988.
3. **Kitchener MI, Chapman IM**. Subacute thyroiditis: a review of 105 cases. *Clin Nucl Med*. 1989 Jun;14(6):439-42. PubMed PMID: 2743695.
4. **Farwell AP, Braverman LE**. Inflammatory thyroid disorders. *Otolaryngol Clin North Am*. 1996 Aug;29(4):541-56. Review. PubMed PMID: 8844729.
5. **Fatourechi V, Aniszewski JP, Fatourechi GZ, Atkinson EJ, Jacobsen SJ**. Clinical features and outcome of subacute thyroiditis in an incidence cohort: Olmsted County, Minnesota, study. *J Clin Endocrinol Metab*. 2003 May;88(5):2100-5. PubMed PMID: 12727961.
6. **Nishihara E, Ohye H, Amino N, Takata K, Arishima T, Kudo T, Ito M, Kubota S, Fukata S, Miyauchi A**. Clinical characteristics of 852 patients with subacute thyroiditis before treatment. *Intern Med*. 2008;47(8):725-9. Epub 2008 Apr 16. PubMed PMID: 18421188.
7. **Golden SH, Robinson KA, Saldanha I, Anton B, Ladenson PW**. Clinical review: Prevalence and incidence of endocrine and metabolic disorders in the United States: a comprehensive review. *J Clin Endocrinol Metab*. 2009 Jun;94(6):1853-78. doi: 10.1210/jc.2008-2291. Review. PubMed PMID: 19494161; PubMed Central PMCID: PMC5393375.
8. **Madeddu G, Casu AR, Costanza C, Marras G, Arras ML, Marrosu A, Langer M**. Serum thyroglobulin levels in the diagnosis and follow-up of subacute 'painful' Thyroiditis. A sequential study. *Arch Intern Med*. 1985 Feb;145(2):243-7. PubMed PMID: 3977482.
9. **Vural Ç, Paksoy N, Gök ND, Yazal K**. Subacute granulomatous (De Quervain's) thyroiditis: Fine-needle aspiration cytology and ultrasonographic characteristics of 21 cases. *Cytojournal*. 2015 May 21;12:9. doi: 10.4103/1742-6413.157479. eCollection 2015. PubMed PMID: 26085833; PubMed Central PMCID: PMC4453108.

Submitted August 2, 2018