

An Uncommon Endocrine Cause of Pyrexia of Unknown Origin

Varkey Alexander*, Thomas T Kurien**, Arijit Chattopadhyay***

Abstract

We report a previously healthy 43 yr old male who presented with prolonged fever, weight loss and neck pain for 3 weeks. Even after extensive work up for the possible causes of pyrexia, the cause remained elusive. In view of persistent tachycardia and neck pain, possibility of subacute thyroiditis was suspected. Thyroid function test (TFT) revealed thyrotoxicosis, which on further evaluation was found to be secondary to DeQuervains thyroiditis. He was treated with NSAIDs, beta-blockers and steroids. He improved rapidly but went on to develop hypothyroidism on follow-up and required levothyroxine replacement.

Introduction

Prolonged pyrexia may be due to infection, connective tissue diseases, tumors, drug-induced or due to miscellaneous causes. At times, even after thorough physical examination and detailed investigations, it may not be possible to reach a diagnosis. Subacute thyroiditis is the commonest cause of fever with a tender thyroid.¹ It is usually seen after an episode of upper respiratory tract infection. Patient presents with fever, anterior neck pain and or neck swelling. Tremor and tachycardia may be seen in the initial hyperthyroid phase. Physical examination reveals an enlarged, tender thyroid, which has to be differentiated from a thyroid abscess. We report a previously healthy male with history of prolonged fever and neck pain of one-month duration, whom on evaluation was found to have subacute thyroiditis. We describe the clinical findings and investigations of this patient with review of relevant literature.

Case Report

A 43-year-old previously healthy Pakistani male patient was admitted to the infectious disease hospital with persistent fever and neck pain of one-month duration. The patient empirically received multiple courses of antibiotics for suspected infective etiology. Fever reached a maximum of 39° Celsius. There was no history of upper or lower respiratory tract symptoms, bowel

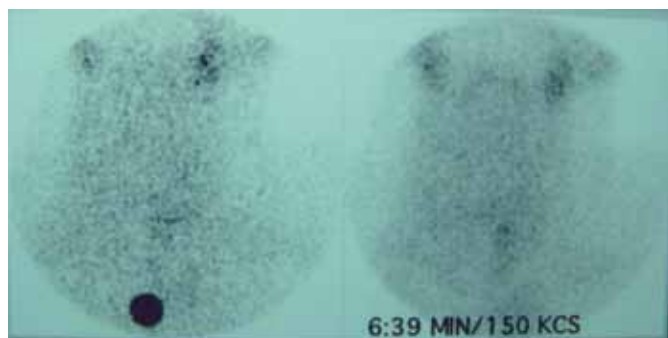


Fig. 1 : 99mTc uptake scan shows very low radio-tracer uptake in homogenous distribution of thyroid gland.

*Senior registrar, Medicine, **Registrar, Medicine, ***Senior registrar, Endocrinology, Department of Medicine, Al-Sabah Hospital, Ministry of Health, Kuwait.

Received: 15.4.2008; Accepted: 6.2.2009

or bladder disturbances or symptoms suggestive of connective tissue disease. There was no history of headache, vomiting, visual disturbance, seizures or weakness of limbs. There was no history of recent travel abroad or history of sexual promiscuity. On detailed enquiry, patient revealed history of palpitation on and off and significant weight loss of 14 kg over one month. Physical examination revealed fever, sinus tachycardia (HR 108/min.), tremor and excessive sweating. There was a large tender nodular goitre with predominant enlargement of right lobe of thyroid. There were no signs of thyroid associated ophthalmopathy. Examination of cardiovascular, respiratory, abdominal and central nervous system were within normal limits. Investigations showed increased WBC count ($16.4 \times 10^9 / \text{mm}^3$) with relative lymphocytosis, raised ESR 126 mm, mild increase in transaminases (AST 96 IU/L, ALT 104 IU/L), and normal CXR. An ECG revealed sinus tachycardia. Mantoux test was positive (11 mm) but three samples of sputum and early morning gastric lavage for AFB was negative. Extensive investigations for infectious aetiology like malarial parasite, brucella serology, Widal, Weil-Felix test, Monospot test, HBsAg, Anti-HCV, CMV, EBV were all negative. Thyroid function test (TFT) revealed elevated free thyroxine (FT4) 46.2 pmol/L and suppressed TSH (< 0.0001) level. Subsequently thyroid scan and radioiodine uptake (RAIU) showed reduced uptake (Fig. 1), negative thyroid autoantibodies (TPO antibody 16 IU/mL) and USG thyroid showed enlarged thyroid and large (5 cm) hypochoic nodule in the right side. With the evidence of a painful goiter in a febrile patient with high ESR, elevated FT4, negative thyroid auto-antibodies and low RAIU, a possibility of subacute thyroiditis was made. FNAC of thyroid confirmed granulomatous thyroiditis (Fig. 2). He was treated with non-steroidal anti-inflammatory agents (NSAIDs) and put on beta-blockers for symptomatic control of tremor and palpitation. However the patient continued to have pain in the thyroid. So he was given a course of prednisolone 60 mg for two weeks and gradually tapered over one month. Patient had dramatic relief of pain after the initiation of steroids. After 3 weeks of discharge, he presented with history of fatigue, somnolence and constipation. On evaluation, he was found to be hypothyroid (TSH 12.86 mIU/L) and was promptly started on levothyroxine 50 mcg per day. On the next review after one month, his symptoms subsided and he achieved a euthyroid status (TSH 1.42).

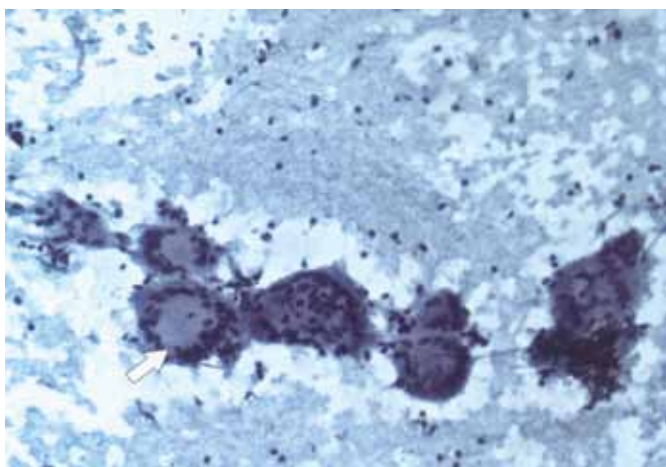


Fig. 2 : Fine needle aspiration cytology (FNAC) of thyroid demonstrates multi-nucleated giant cells (arrow) with granuloma formation in a background of abundant colloid distribution. Scattered distribution of neutrophils is also seen in the background.

Discussion

De quervain first described subacute thyroiditis in 1904. Subacute thyroiditis is also referred as granulomatous thyroiditis, subacute painful thyroiditis or giant cell thyroiditis. The peak incidence is seen in summer, which coincides with the highest incidence of Coxsackie, and Echo virus infection.² Genetic susceptibility with HLA Bw35 has also been reported.

Symptoms and signs of this disorder include sore throat, fatigue, fever, myalgia and tender thyroid enlargement. Upto 50% of the patients may present with features of thyrotoxicosis. Presence of tender goiter often suggest subacute thyroiditis but less common differential diagnoses include suppurative thyroiditis, acute hemorrhage into a cyst or nodule and radiation thyroiditis. Characteristically erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) concentration are markedly elevated.³ Radioiodine uptake (RAIU) of thyroid is typically suppressed in subacute thyroiditis.⁴ Thyroid autoantibodies are usually not detectable. FNAC of the thyroid is not routinely recommended in the diagnosis of suspected subacute thyroiditis but it may be employed in patients in whom the diagnosis of painful neck mass is not clear. Thyroid FNAC shows patchy distribution of non-caseating granuloma and multinucleated giant cells along with numerous plasmacytoid cells, monocytes

and neutrophils. USG of the thyroid reveal diffuse areas of hypoechogenicity and is used as an adjunct in the diagnosis of subacute thyroiditis. The course of subacute thyroiditis is generally benign with initial thyrotoxic phase for several weeks followed by a stage of euthyroidism and a third phase of hypothyroidism lasting for a period of few weeks to few months. Upto 10-15% of the patients become permanently hypothyroid requiring long-term thyroxine replacement.⁵ Recurrence rate of subacute thyroiditis is about 2%.¹ Treatment of subacute thyroiditis is directed towards relief of pain and inflammation and control of thyrotoxic symptoms. Salicylates or NSAIDs are used for pain relief but some patients may require a course of prednisolone 30-60 mg in divided doses for prompt relief of pain. It may be tapered after one week and stopped in 3-4 weeks time. If symptoms recur in the other lobe, prednisolone may be restarted at half of the initial dose and tapered gradually as described above. Thyrotoxic symptoms are usually controlled by beta-blockers like propranolol 10-40 mg three or four times daily. Antithyroid drugs have no role in the management of thyrotoxicosis because the thyrotoxic symptoms are related to dumping of stored hormones into the circulation. Levothyroxine supplementation is necessary if the patient remains in the hypothyroid phase for more than 6 weeks. Late recurrences are seen even after years but typically milder than the original episode.

We presented an interesting endocrine cause of pyrexia of unknown origin (PUO). Subacute thyroiditis is a form of self-limited inflammatory thyroid disorder. Characteristic features like painful goiter, raised ESR, low RAIU, evidence of giant cell thyroiditis on thyroid FNAC can help an early diagnosis and appropriate management.

References

1. Pearce EN, Farwell AP, Braverman LE. Thyroiditis. *N Engl J Med* 2003; 348: 2646-55.
2. Volpe R, Row VV, Ezrin C. Circulating viral and thyroid antibodies in subacute thyroiditis. *J Clin Endocrinol Metab* 1967;27:1275-84.
3. Pearce EN, Martino E, Bogazzi F, et al. The prevalence of elevated serum C-reactive protein levels in inflammatory and noninflammatory thyroid disease. *Thyroid* 2003; 13:643-8.
4. Ross DS. Syndromes of thyrotoxicosis with low radioactive iodine uptake. *Endo Metab Clin North Am* 1998; 27:169-86.
5. Sniezek JC, Francis TB. Inflammatory thyroid disorders. *Otolaryngol Clin North Am* 2003; 36: 55-71.

ANNOUNCEMENT

Recent Advances in Rheumatology

16th August, 2009 • Department of Immunology, SGPGI, Lucknow

Registration: Rs.300/-

CONTACT

Dr. Amita Aggarwal

SGPGI, Lucknow 226 014 • e-mail: amita@sgpgi.ac.in; aa.amita@gmail.com